Alterations in Heart rate Variability in Blind Patients

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Abstract

Blindness affect the daily life activities and the causes and prevalence are different worldwide. This study aimed to investigate the pattern of the autonomic nervous system modulation on the heart in blind and normal vision subjects submitted acutely to low vision. Normal vision (NV) subjects (N = 32) and blind patients (N = 24) were submitted to HRV analysis during resting, intervention and recovery periods. Intervention consisted of handling objects, short walking, and cognitive activities performed with pedagogic games while using sleeping masks. No difference was observed in indexes in the time and frequency domain, and in the geometric indexes comparing blind and NV subjected to acute low vision during resting and recovery. Nevertheless, during intervention, RMSSD, pNN50, and SD1 were found lower in blind than in NV subjects. Therefore, blind patients showed similar HRV at resting or upon possible stressful challenges compared to NV subjects acutely subjected to low vision, indicating absence of differences in the cardiovascular risk between groups. In addition, blind patients show a smaller reduction in parasympathetic modulation on the heart during possible stressful challenges than NV individuals submitted to low vision, which is likely an important physiological adaptation for an adequate function of the cardiovascular system in blindness.

Introduction

People with visual impairment (VI) have vision loss at different levels, which can affect their activities of daily living. Blindness, low vision, subnormal vision, visual incapacity are synonymous of visual impairment, nevertheless there are peculiarities among them [1]. Thus, according to international organizations, people with 20/20 visual acuity will see at 20 feet (6 m) what is normally expected. Low vision people would be the ones with visual acuity less than 20/70 to 20/400 in the best eye, and with blindness, those with visual acuity worse than 20/400 in both eyes, which means that blind people cannot see at 20 feet or 6 meters what normally get at 400 feet or 120 meters [2].

The causes of blindness and prevalence in the population show differences along the time. The number of people with VI worldwide in 2002 was greater than 161 million, of whom about 37 million were blind. Those numbers were not distributed uniformly throughout the world and the least developed regions presented the largest rates [3]. Globally, the number of people of all ages visually impaired was estimated to be 285 million in 2010, of whom 39 million were blind, with uncertainties of 10–20% [4]. As the global population has increased and aged between 1990 and 2010, the number of blind people has increased by 0.6 million people [5]. This is of concern because the global gross prevalence of preventable VI and blindness in adults aged 50 and over did not change between 2010 and 2019 [6].

The autonomic nervous system (ANS), through the sympathetic and parasympathetic branches, helps to provide the physiological integrity of cells, tissues, and organs throughout the body upon perturbations elicited by both the external and internal environments [7]. The cardiac function is regulated by the interaction of the sympathetic and parasympathetic nervous system. Thereby, the evaluation of heart rate variability (HRV) can be an useful tool to investigate the influences of the ANS on the sinus node (SN), the
natural heart pacemaker. Visual impairment is an adverse condition that can elicit changes in the ANS activity, such as on heart rate, blood pressure, changes in body temperature and electrical conductivity of the skin, among others [8].

The HRV measures the variations between consecutive R-R intervals. Linear methods at time and frequency domains or nonlinear methods can be used to perform HRV analysis [9]. Time domain analysis consider the R-R intervals in a specific time period and calculates through mathematic methods the fluctuations during the cardiac cycle [10, 11]. Frequency domain analysis decomposes the heart rate variation in a time interval into its fundamental oscillatory components using spectral analysis, i.e., the time series is decomposed into different frequency components [12, 13]. Nonlinear analysis evaluates the fluctuations of heartbeats during normal sinus rhythm, which are partially attributed to deterministic chaos [14]. The chaos theory approach considers systems, dynamic, and is governed by nonlinear equations and sensitive to initial conditions [15]. It has been suggested that the nonlinear analysis adequately reflect changes in the autonomic modulation of biological systems as the mechanisms involved in cardiovascular regulation probably interact non-linearly with each other [16].

Acute low vision or chronic visual impairment can affect the cognition and attitudes of the patients, and it would be expected a possible interference in the cardiac autonomic modulation. Different pathological conditions, not involving the visual apparatus, have shown that alterations in autonomic modulation can be observed by reduction in HRV, suggestion a worse prognosis in cardiovascular diseases [15, 17] or appearance of arrhythmias and sudden death [18, 19].

However, limited literature has been published highlighting the correlation between VI and HR, which strengthens and justifies the accomplishment of this research. In this study, we focused on the investigation of the autonomic nervous system modulation on the heart in blind and normal vision subjects submitted acutely to low vision condition.

Results

1. Anthropometric profile, age, fasting glycemia and gender of study participants

Table 1 shows that blind patients (N = 24) and normal vision (N = 32) subjects were age-matched, with no significant difference in body weight, height, body index mass (BMI), and fasting glycemia. The number of male and female subjects in blind and normal vision groups was similar.
Table 1
Sample characterization by evaluation of age, body weight, height, body index mass (BMI), fasting glycemia and sex.

| Visual Acuity (N) | Age (Years) | Body weight (kg) | Height (m) | BMI (kg/m²) | Glycemia (mg/dl) |
|-------------------|-------------|------------------|------------|-------------|-----------------|
| Blind patients (24) | 48.33 ± 3.46 | 68.24 ± 3.47 | 1.62 ± 0.02 | 26.36 ± 1.02 | 96.00 ± 4.24 |
| Normal vision (32) | 42.28 ± 2.93 | 78.79 ± 3.74 | 1.64 ± 0.02 | 28.44 ± 0.99 | 92.19 ± 2.76 |

Sex, n (%)

|                    | Male     | Female   |
|--------------------|----------|----------|
| Blind patients (24) | 10 (41.67) | 14 (58.33) |
| Normal vision (32)  | 14 (43.75) | 18 (56.25) |

Data are as mean ± SEM. Unpaired Student t-test.

2. Arterial pressure measurement and heart rate variability during the resting period in blind patients and normal vision subjects submitted acutely to low vision

At the resting condition, systolic, diastolic and mean arterial pressure as well as heart rate were not different comparing blind and normal vision groups (Table 2). Linear analysis of HRV demonstrated that blind patients (N = 24) showed similar values of mean RR, SDNN, STD HR, RMSSD, and pNN50 compared to normal vision group (N = 32) (Table 3). Likewise, LF, HF and LF/HF ratio were not different comparing blind patients and normal vision subjects during the resting period (Table 4). Geometric analysis of HRV also indicated that SD1, SD2, sample entropy, a1 and a2 indexes were similar in blind compared to normal vision patients at resting condition (Table 5).
Table 2
Systolic arterial pressure (SAP, mmHg), diastolic arterial pressure (DAP, mmHg), mean arterial pressure (MAP, mmHg), and heart rate (HR, bpm) at resting, intervention and recovery periods.

| Clinical Data | Resting  | Intervention | Recovery |
|---------------|----------|--------------|----------|
| SAP (mmHg)    |          |              |          |
| Blind patient | 127 ± 2  | 126 ± 3      | 127 ± 3  |
| Normal vision | 121 ± 3  | 117 ± 3      | 119 ± 3  |
| DAP (mmHg)    |          |              |          |
| Blind patient | 83 ± 2   | 82 ± 2       | 82 ± 2   |
| Normal vision | 79 ± 2   | 75 ± 2       | 77 ± 2   |
| MAP (mmHg)    |          |              |          |
| Blind patient | 98 ± 2   | 97 ± 2       | 97 ± 2   |
| Normal vision | 93 ± 2   | 89 ± 2       | 91 ± 2   |
| HR (bpm)      |          |              |          |
| Blind patient | 73 ± 3   | 74 ± 2       | 72 ± 3   |
| Normal vision | 75 ± 2   | 77 ± 2       | 75 ± 2   |

Data are as mean ± SEM. Two-way ANOVA.
| INDEX- TIME DOMAIN | RESTING         | INTERVENTION     | RECOVERY        |
|--------------------|-----------------|------------------|-----------------|
| **Mean RR (ms)**   |                 |                  |                 |
| Blind patients (n = 24) | 838.08 ± 35.43 | 800.46 ± 31.62# | 864.75 ± 34.27& |
| Normal vision (n = 32) | 801.95 ± 17.65 | 749.78 ± 15.60# | 805.21 ± 16.24& |
| **SDNN (ms)**      |                 |                  |                 |
| Blind patients (n = 24) | 57.12 ± 7.29   | 52.59 ± 2.85     | 53.60 ± 3.59    |
| Normal vision (n = 32) | 51.37 ± 3.59   | 50.12 ± 2.41     | 54.24 ± 2.82    |
| **Mean HR (bpm)**  |                 |                  |                 |
| Blind patients (n = 24) | 75 ± 3.17      | 78 ± 2.82        | 72 ± 2.56&      |
| Normal vision (n = 32) | 75 ± 2.50      | 82 ± 1.79#       | 76 ± 1.61&      |
| **STD HR**         |                 |                  |                 |
| Blind patients (n = 24) | 7.73 ± 2.05    | 5.47 ± 0.43      | 4.68 ± 0.38     |
| Normal vision (n = 32) | 5.39 ± 0.52    | 5.51 ± 0.24      | 5.21 ± 0.28     |
| **RMSSD (ms)**     |                 |                  |                 |
| Blind patients (n = 24) | 30.88 ± 2.77   | 26.98 ± 2.10*#  | 32.05 ± 3.08    |
| Normal vision (n = 32) | 29.27 ± 2.49   | 21.98 ± 1.19#   | 29.30 ± 2.53    |
| **NN50**           |                 |                  |                 |
| Blind patients (n = 24) | 108.50 ± 25.09 | 86.79 ± 18.06*  | 123.92 ± 27.26*& |
| Normal vision (n = 32) | 69.31 ± 12.32  | 33.47 ± 5.44#   | 70.97 ± 12.12&  |
| **pNN50**          |                 |                  |                 |
| Blind patients (n = 24) | 10.67 ± 2.59   | 8.11 ± 1.83*    | 12.44 ± 2.96&   |
| Normal vision (n = 32) | 8.35 ± 1.86    | 3.74 ± 0.72#    | 8.46 ± 1.60&    |

Data are as mean ± SEM. Two way ANOVA followed by Student Newman-Keuls posttest. *P < 0.05 vs. Normal vision, #P < 0.05 vs. Resting intragroup, &P < 0.05 vs. Intervention intragroup.
Table 4
Index of heart rate variability in the frequency domain.

| Index-Frequency Domain | Resting     | Intervention | Recovery       |
|------------------------|-------------|--------------|----------------|
| **LF**                 |             |              |                |
| Blind patients (n = 24)| 63.98 ± 4.33| 67.24 ± 3.75 | 67.90 ± 3.32   |
| Normal vision (n = 32)| 69.37 ± 2.84| 70.87 ± 2.21 | 71.84 ± 2.47   |
| **HF**                 |             |              |                |
| Blind patients (n = 24)| 35.87 ± 4.29| 32.65 ± 3.73 | 32.03 ± 3.31   |
| Normal vision (n = 32)| 30.53 ± 2.84| 28.97 ± 2.21 | 27.90 ± 2.42   |
| **LF/HF ratio**        |             |              |                |
| Blind patients (n = 24)| 2.85 ± 0.45 | 3.06 ± 0.44  | 2.94 ± 0.40    |
| Normal vision (n = 32)| 3.25 ± 0.44 | 3.14 ± 0.32  | 3.36 ± 0.33    |

Data are as mean ± SEM. Two-way ANOVA.
### Table 5
Index of heart rate variability – geometric indexes.

| Geometric indexes | Resting       | Intervention   | Recovery     |
|-------------------|---------------|----------------|--------------|
| **SD1 (ms)**      |               |                |              |
| Blind patients (n = 24) | 21.85 ± 1.96  | 19.06 ± 1.48*# | 22.66 ± 2.18& |
| Normal vision (n = 32) | 20.71 ± 1.76  | 15.56 ± 0.84#  | 20.73 ± 1.79& |
| **SD2 (ms)**      |               |                |              |
| Blind patients (n = 24) | 76.90 ± 10.40 | 71.56 ± 3.99   | 72.00 ± 4.76 |
| Normal vision (n = 32) | 69.18 ± 4.96  | 68.98 ± 3.39   | 73.60 ± 3.74 |
| **Sample entropy**|               |                |              |
| Blind patients (n = 24) | 1.30 ± 0.09   | 1.22 ± 0.07    | 1.33 ± 0.05  |
| Normal vision (n = 32) | 1.25 ± 0.05   | 1.09 ± 0.48#   | 1.24 ± 0.05& |
| **α1**            |               |                |              |
| Blind patients (n = 24) | 1.19 ± 0.06   | 1.26 ± 0.06    | 1.24 ± 0.05  |
| Normal vision (n = 32) | 1.24 ± 0.04   | 1.27 ± 0.04    | 1.30 ± 0.04  |
| **α2**            |               |                |              |
| Blind patients (n = 24) | 0.89 ± 0.05   | 0.95 ± 0.04*   | 0.95 ± 0.03  |
| Normal vision (n = 32) | 0.98 ± 0.03   | 1.04 ± 0.02#   | 0.97 ± 0.02& |

Data are as mean ± SEM. Two-way ANOVA followed by Student Newman-Keuls posttest. *P < 0.05 vs. Normal vision, #P < 0.05 vs. Resting intragroup, &P < 0.05 vs. Intervention intragroup.

3. Arterial pressure analysis and heart rate variability during the intervention period in blind patients and normal vision subjects submitted acutely to low vision

During the intervention period, systolic, diastolic and mean arterial pressure showed no differences comparing blind and normal vision groups (Table 2). Heart rate significantly increased in normal vision patients during intervention compared to the respective resting value, nevertheless, showed no significant difference compared to blind patients (Table 2). Despite that, linear analysis of HRV showed that either blind (N = 24) or normal vision patients (N = 32) presented a significant decrease in mean RR, RMSSD, and pNN50 compared to resting values. Nevertheless, RMSSD, and pNN50 values were significantly higher in blind than in normal vision subjects during the intervention (Table 3 and Fig. 3). No difference was observed in LF, HF, and LF/HF ratio during intervention comparing blind and normal vision patients.
and compared to the respective intragroup resting value (Table 4). Geometric analysis of HRV demonstrated that SD1 was found significantly reduced in both blind and normal vision individuals during intervention compared to resting values, however, remained higher in blind than in NV patients. SD2, sample entropy and $\alpha_1$ were similar during intervention period comparing blind and NV patients. An increase in $\alpha_2$ was observed on normal vision subjects during intervention, and the $\alpha_2$ value was significantly higher in the NV group compared to blind patients during intervention (Table 5 and Fig. 4).

### 4. Arterial pressure measurement and heart rate variability during the recovery period in blind patients and normal vision subjects submitted acutely to low vision

At the recovery period, systolic, diastolic and mean arterial pressure as well as heart rate were similar comparing blind and normal vision groups (Table 2). However, HR was in a significant lower value compared to the intervention period in blind and NV patients and showed no difference in comparison to the respective intragroup resting value (Table 2). Linear analysis of HRV demonstrated that no significant differences were observed in mean RR, SDNN, STD HR, RMSSD, and pNN50 comparing blind patients (N = 24) and normal vision subjects during recovery (N = 32). Those parameters, which have decreased during intervention, returned to resting levels in both blind and normal vision groups during the recovery period (Table 3). No difference was also observed in LF, HF, and LF/HF ratio during recovery comparing blind and normal vision patients and compared to intervention and resting period intragroup values (Table 4). Geometric analysis of HRV showed that SD1, SD2, sample entropy, $\alpha_1$, and $\alpha_2$ have no difference during recovery comparing blind and normal vision subjects, and compared to the respective intragroup value at resting (Table 5).

### Discussion

Our data demonstrated that blind and normal vision subjects showed similar age, anthropometric profile, normal fasting glycemia and the number of male and female participants was equivalent between groups. Nevertheless, the BMI was a little higher than the normal weight range, and the participants of this study were in an overweight range [20]. In addition, cardiovascular parameters measured at resting indicated that systolic, diastolic and mean arterial pressure as well as heart rate was normal in both blind and normal vision subjects submitted acutely to low vision. The HRV analysis in the time domain showed that the indexes (SDNN, RMSSD, pNN50) evaluated in this study were similar during the resting period comparing blind patients and normal vision subjects. The SDNN is considered a marker of the total power (variance) of the HRV, expressing the long-term component responsible for the variability in the period of registration of the HR [21]. The SDNN index were not different in blind and normal vision subjects during resting, intervention and recovery, and regardless the period appraised in this study, the SDNN values were above 50 ms and below 100 ms. The SDNN is the "gold standard" for medical stratification of cardiac risk when recorded over a 24 h period [22, 23]. Subjects with SDNN value in a
range between 50–100 ms have compromised health [22, 23], however SDNN was equivalent in both blind and normal participants of this study. It is noteworthy that the SDNN was not evaluated for 24 h in the subjects of this study, indeed we cannot classify the participants as compromised health subjects. Geometric analysis of HRV also demonstrated similarity in the indexes (SD1, SD2, DFA-α1 and DFA-α2) evaluated comparing blind and normal vision subjects during the resting period. SD1 and SD2 indicates the standard deviation of the instantaneous variability of the beat-to-beat heart rate, whereas SD2 indicates the standard deviation of long-term continuous R-R interval variability [22, 24], demonstrating that the heart rate variability at resting is similar in blind and normal vision patients. DFA-α1 requires short recording times (~ 200 beats or 2 min of recording, depending on beats per minute) for a valid calculation and a steady-state is not mandatory [25, 26, 27]. DFA-α1 has been applied for cardiovascular risk assessment as well as prognosis and prediction of mortality in clinical settings during resting conditions [28, 29, 30, 31]. Values of DFA-α1 that differ from the normal value of ~ 1.0 are associated with higher morbidity or worse prognosis regardless of the disease or age group [29, 31]. In present study, DFA-α1 has normal values in both blind and normal vision subjects during resting, intervention or recovery periods and show no difference among periods or comparing the groups, which is suggestive that both groups do not show difference in the risk of morbidity or cardiovascular risk. The RMSSD reflects the beat-to-beat variance in HR and estimates the parasympathetic modulation on the heart [32] and is identical to the geometric index SD1, which reflects short-term HRV [33]. The pNN50 is related to parasympathetic system [34] and correlates with RMSSD. HRV analysis in the frequency domain showed no difference in the LF, HF and LF/HF ratio comparing blind and normal vision patients during resting, intervention or recovery periods. LF power may be produced by both the parasympathetic and sympathetic nervous system, whereas HF power reflects vagal modulation of HR [23]. Sample entropy showed no difference at any period evaluated (resting, intervention and recovery), which indicates similar signal regularity and complexity in the recordings of blind and normal vision subjects. Thereby, during the resting period, the parasympathetic modulation of the HR is similar in blind and normal vision patients.

During the intervention, systolic, diastolic and mean arterial pressure were not increased at the time point of measurement of these parameters in both blind and normal vision subjects submitted acutely to low vision. Heart rate increased during intervention compared to resting value in normal vision individuals, which is underpinned by the reduced RMSSD and pNN50 indexes in this group during intervention compared to resting period. Interestingly, RMSSD and pNN50 showed a smaller reduction in blind patients than in normal vision subjects. As RMSSD and pNN50 indexes reflect the parasympathetic modulation on the heart [23, 35], this finding suggests that the vagal modulation on the heart is higher in blind patients than in normal vision individuals. In addition, as RMSSD and pNN50 are more diminished during intervention in normal vision group, it is likely that these subjects have a greater sympathetic modulation on the heart than blind patients in this period of recording. Geometric indexes analyzed during intervention showed that SD1 is decreased in both blind and normal vision groups compared to the respective resting values, nevertheless, the reduction was smaller in blind than in normal vision patients. SD1 measures show the standard deviation of the instantaneous variability of the beat-to-beat HR and correlate with baroreflex sensitivity [23]. Our data suggest that blind patients likely show an
improved baroreceptor sensitivity upon stressful stimuli compared to normal vision subjects, which can avoid sustained increases in heart rate, and consequently in cardiac output and arterial pressure. Despite DFA indexes have been demystified [36], the fact that DFA-$\alpha_2$ slightly increases only in normal vision subjects during intervention compared to resting period, but not in blind patients, suggest a different fractal influence on HRV series in normal vision subjects.

At the recovery period, all the indexes evaluated in time and frequency domain HRV analysis as well as the geometric indexes have returned to values similar to those observed at resting period in both blind and normal vision patients submitted acutely to low vision, demonstrating a fully ability to re-establish the baseline indexes in both groups.

Although the current study has shown that blind patients have a smaller reduction in parasympathetic modulation on the heart during intervention than normal vision subjects submitted to low vision, a sympathetic modulation on heart in blind patients likely enhances. Massot et al. (2010) [8] investigated the impact of environmental conditions on 27 blind pedestrians in an urban environment at Lyon (France) and demonstrated the effect of mental stress on visually impaired subjects by measurement the heart rate for HRV analysis, temperature and electrical resistance (conductivity) of the skin. A differentiated activation of sympathetic nervous system was observed in different scenarios depending on they were considered stress “hotspots” due to the requirement of decision on the part of the blind person that can increase the stress levels [8].

The neural consequences of sensory loss as blindness leads to functional and organizational principles of the brain. Although the blind visual cortex has been involved in the cross-modal processing of nonvisual inputs for some time, evidence has shown that certain cortical organizational principles are preserved even in the case of complete sensory loss [37]. The understanding of the mechanisms underlying cross-modal plasticity driven by sensory deprivation is not fully understood and the specific pathways underlying the redirection of non-visual information still need elucidation. An important cross-modal recruitment occurs after transient deprivation in sighted individuals and suggests that significant new wiring may not be necessary after blindness [37].

Interestingly, earlier studies have demonstrated that melatonin, a major pineal hormone, modulates the autonomic nervous system, increasing the cardiac vagal tone in healthy men [38]. Aubin et al. (2017) [39] demonstrated that blind subjects, reporting no conscious light perception, show a greater overall melatonin concentration throughout the 24-h period [39]. Thereby, the smaller reduction in the parasympathetic modulation on the heart, even upon the different challenges during the intervention period in blind patients in the current study can be underpinned, at least in part, by those previous studies.

**Conclusions**

The findings of this study suggest that blind patients show similar heart rate variability at resting or upon possible stressful challenges compared to normal vision subjects acutely submitted to low vision, which indicates absence of differences in the cardiovascular risk between groups. In addition, blind patients
show a smaller reduction in parasympathetic modulation on the heart during possible stressful challenges than normal vision individuals submitted to low vision, which is likely an important physiological adaptation for an adequate function of the cardiovascular system in blindness.

Methods

This study was carried out following the experimental procedures previously described elsewhere [40] and it is in accordance with the guidelines that regulate human research in Resolution No. 466/12 of the National Health Council. The study was approved by the Research Ethics Committee of the Faculdade de Medicina do ABC (CAAE: 73945017.0.0000.0082). This study is registered in the Brazilian Registry of Clinical Trials (RBR-9sm-9dp, first registration at 23/01/2019). All subjects who agreed to participate in the study signed the Informed Consent Form (ICF). The ICF is also available in audio and Braille versions. For blind patients, the ICF was signed by the parent/ legal guardian, or by the blind patient fingerprint, or signed with the patient initials. This study is also reported in the Brazilian Registry of Clinical Trials under the number RBR-9sm9dp.

Participants of the study

This study followed the items of the Standard Protocol for Randomized Trials. HRV was evaluated in this study in a randomized clinical trial. Blind patients (N = 24, Group 1) have attended the Pedagogical Service of Support Center for People with VI (Fig. 1) and normal vision (N = 32, Group 2) subjects were invited from the Eye Health Center (CSO), both institutions located at Rio Branco, AC, Amazonia Brasileira, BR, where the participants lived.

Eligibility criteria

The Group 1 was constituted by people with more than 18 years of age, both genders, with blindness, with good general health, and without other physical and mental disabilities. Present visual acuity less than 20/400, finger counts at 1 m, and with lack of light perception in the best eye, according to the criteria of the World Health Organization [41]. People older than 18 years-old, of both sexes, with good visual acuity, healthy were eligible to form Group 2. Individuals who presented visual acuity better than 20/30 in at least one eye, i.e., without VI, were assigned to Group 2 (control), without VI. Individuals who do not comply the clinical criteria described or refused to participate or continue in the survey were excluded. Volunteers were instructed for not drinking alcohol and/or caffeine within 24 h before the intervention.

Intervention
The intervention phase was performed as previously reported by Moreno et al. (2019) [40] and consisted of sensorial activities by handling objects, of motor activities in which the individuals were submitted to walking blind folded for 5 min through the corridors and clinic rooms, and at the end, of cognitive activities performed with pedagogic games. The individuals from both groups were monitored for 45 min, divided into 3 periods of 15 min each. On each of the phases, the HRV was evaluated and the phases were named as resting-intervention-recovery. The phase with greater intensity was the intervention, because the period of this phase was divided into 3 phases of 5 min each. On each sub-phase of 5 min, the individuals performed 3 different activities. The 1st task was to serve glasses with water and food. After that, the next task was locomotion through the clinic areas and the last stage activities consisted of pedagogical toys assembly (Figs. 2 and 3).

Data collection

All data was collected as earlier described by Moreno et al. (2019) [40].

First step: personal and sociodemographic data of the study participants was obtained from the Pedagogical Support Center CAP-AC database, a public institution which exclusively provides socioeducational support services to low vision patients and from the Centro de Saude Ocular (CSO that is a private clinic of ophthalmologic care in Rio Branco City. The information about the participants was complemented with clinical data according to the execution of medical examinations and interventions. This was necessary for search people to be included in the Groups (Fig. 1). Individuals for Group 2, which had good visual acuity, were invited from the CSO, seeking to match them as closely as possible with Group 1, regarding gender, age, occupation, etc. All the data was collected individually on the working days from 8:00 to 12:00 AM in order to avoid potential sources of bias. The venues of data collection were discrete and isolated, which could be in the outpatient or recreation/training environment of CAP-AC and the CSO in Rio Branco.

After initial selection, volunteers were subjected to routine clinical-ophthalmological examination for general health evaluation and investigation about the use of medication that may interfere with autonomic nervous system, among others. Other aspects of eye health as visual acuity, corrective lenses, and history of ophthalmic surgery were also evaluated. Clinical and ophthalmological examinations to provide the study independent variables were carried out at the CSO, which has qualified human resources and medical equipment for anamnesis, visual acuity measurement, ocular pressure measurement, among others, with no costs for participants.

Second step: as shown in Fig. 2, data of HRV in groups 1 and 2 was collected, continuously, beat-to heart beat, with brief breaks for clarification. Both groups randomly were submitted to a protocol divided in 3 phases of 15 min each: resting - intervention - recovery. After taking anthropometric measures and blood samples were collected for glycemia determination, the participants were given a brief rest in seated position, in a quiet environment, and then the systolic, diastolic, and mean arterial pressure (AP) were measured to determine the baseline condition (resting phase). Then, in the second phase or intervention,
both eyes of the participants were blindfolded with a sleeping mask that provides maximum occlusion, remaining with vigilance and companionship. Certain confidentiality regarding this phase was maintained to the participant so that the anxiety did not affect the autonomic modulation on the heart.

Intervention phase consisted of different possible stressful challenges and was subdivided into 3 periods of 5 minutes each, in which were performed three different tasks as previously reported by Moreno et al. (2019) [40]:

1. First task: the blindfolded participant was requested to perform manual activities, serving water and/or cookies on a tray, sitting with objects placed on the table in front of him.
2. Second task: motor locomotion was carried out by walking through clinic areas between corridors and rooms.
3. Third task: ludic-pedagogical activities were performed as fitting of different objects according to their mold like a puzzle.

At each period of 5-min intervention activities, the patients were monitored for their systolic and diastolic AP and HR and level of blood glucose. In the third phase named recovery with a duration of 15 min, the participants sat relaxing and resting for continuing to monitor the collection of autonomic cardiac activity through the HRV [40].

The HR monitoring for further analysis of HRV was obtained during the estimated 45 min of evaluation [40]. During collection, a capture strap was placed on the participant's chest with an electrical activity sensor in the precordial region, distal third of the sternum and the Polar® S810i heart rate receiver (Polar Electro, Finland) on the wrist, device previously validated for beat-to-beat heart rate capture and for use of your data for HRV analysis [42, 43]. The receiver temporarily stores the data collected for later processing in the computers. The recorded pulses were directed to a computer through an infrared signal emitting interface for analysis of the HRV by Polar® Precision Performance software (v. 3.0, Polar Electro, Finland). After storage in the software, the data was filtered at a moderate intensity for the elimination of ectopic beats and/or noises. The HRV analysis was performed in time and frequency domain (linear analysis) and also by geometric analysis based on directives from the Task Force guidelines [22]. Specific details of HRV analysis have been previously documented [44, 45].

HRV was analyzed in the time (RMSSD: root-mean square of differences between adjacent normal RR intervals, SDNN: standard deviation of all normal RR intervals, pNN50: percentage of adjacent NN intervals that differ from each other by more than 50 ms) and frequency domain (LF: low frequency band ranging from 0.04 to 0.15, HF: high frequency band ranging from 0.15 to 0.4) in absolute units. HRV analysis also included sample entropy, Poincaré plot [(SD1: standard deviation of the instantaneous variability of the beat-to-beat heart rate, SD2: standard deviation of long-term continuous RR interval variability [22, 24], and Detrended Fluctuations Analysis (DFA): α1 (short-term fractal exponent, which corresponds to a period of 4–11 beats) and α2 (long-term fractal exponent, which represents periods longer than 11 beats) [46]. The α1 and α2 indexes are frequency-weighted versions of the spectral ratios
LF/(HF + LF) and VLF/(LF + VLF), respectively, multiplied by two (giving a range of 0–2) [36]. We employed the Kubios® HRV v. 2.0 software to compute these indexes [47].

**Statistical Analysis**

Data was analyzed using the Statistical Package for Social Science, version 22.0. Descriptive analysis was performed for all variables. Sample distribution was evaluated with the Shapiro–Wilk test. Data are as mean ± standard error. For comparison of initial and final values between groups, the unpaired Student t-test for parametric distributions was used. Statistical level was set at P < 0.05.

**Declarations**

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**Author contributions**

R.D. Moreno and N. Moreno-Mantilla have collected the data. R.D. Moreno, M.V. M. de Lima, M. J. D. Morais, V.E. Valenti, R.D. Raimundo and M.A. Sato performed the data analysis and statistics. R.D. Moreno, V.E. Valenti, L.C. de Abreu, R.D. Raimundo, and M.A. Sato helped in design of the study and discussions. R.D. Moreno and M.A. Sato have written the manuscript.

**Competing interests**

The authors declare no competing interests.

**Data availability**

The datasets generated and/or analyzed during the present study are available from the corresponding author on reasonable request.

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**Figures**

**Figure 1**

Schematic depicting of the experimental groups and their profiles.
Evaluation of heart rate variability with duration of 45 minutes for group 1 and group 2

First moment – 15 min of rest: relaxed sitting with heart rate monitoring.

Second moment – 15 min of intervention com ambos os olhos vendados. Divided into three stages of 5 min each, as follows:

- **First stage:** handling objects; help yourself to water and / or cookies.
- **Second stage:** locomotor activity, walking between corridors and clinic rooms.
- **Third stage:** ludic pedagogic activities. Assembly of toy cubes. Puzzle.

Third moment: 15 min recovery, where the individual was relaxed, resting in the room.

Note: at the end of each moment, an evaluation of systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR).

**Figure 2**

Schematic representation of the experimental protocol.
Figure 3

Heart rate variability in the frequency domain (RMSSD and pNN50 indexes) in blind and normal vision subjects submitted acutely to low vision during resting, intervention and recovery periods. * P<0.05 vs. Normal Vision.
Figure 4

Geometric indexes (SD1 and α2) in blind and normal vision subjects submitted acutely to low vision during resting, intervention and recovery periods. * P<0.05 vs. Normal Vision.