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Neural binocular summation and the effect of defocus on the pattern electroretinogram and visual evoked potentials for different pupil sizes

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Abstract

Purpose: To evaluate the influence of defocus and pupil size on subjective (visual acuity [VA]) and objective (electrophysiology) descriptors of human vision and their effect on binocular visual performance by means of neural binocular summation (BS).

Methods: Fifteen healthy young subjects were recruited in this crossover study. Pattern electroretinogram (PERG) and visual evoked potentials (VEP) were measured under two levels of positive (+1.5 and +3.0 D) spherical and astigmatic defocus (axis 90°). Pupil size was controlled to reduce the inter-individual variability factor.

Results: Low- and high-contrast VA showed poorer visual performance in the monocular versus the binocular condition. Positive BS (for VA) was higher with greater pupil size and higher levels of defocus. In the visual electrophysiology tests (i.e., VEP and PERG), peak time and amplitude were affected by pupil size and defocus. The increase in peak time was larger and the reduction in amplitude was more significant with greater levels of defocus and smaller pupil sizes. For the VEP, positive BS was found in all conditions, being stronger with larger amounts of defocus and pupil size (for the P100 amplitude). Significant negative correlations were observed between the P100 amplitude and VA BSs.

Conclusion: Smaller pupil size and levels of defocus produced greater changes in cortical activity as evidenced by both the PERG and VEP. Considering these changes and the obtained positive BS, the mechanism could be initiated as early as the retinal processing stage, then being modulated and enhanced along the visual pathway and within the visual cortex.

KEYWORDS
binocular summation, defocus, electroretinogram, pupil size, visual evoked potential

INTRODUCTION

Binocular vision plays an important role in visual information processing along the visual pathway. In studies of visual performance, binocular summation (BS) can be used to evaluate the effectiveness of the binocular visual system. The BS ratio quantifies binocular visual performance with respect to monocular viewing in visual function.[1–5] Several studies have previously mentioned the importance of this BS ratio for the improvement of many visual parameters, including visual acuity (VA), contrast sensitivity[2,6–10] and tolerance of light disturbance.[5,8,11] Plainis et al.[7] found that BS reduced

the impact of retinal blur (induced by defocus) on spatial visual performance. They suggested that a large decrease in the contrast of the visual stimulus (induced by blur) could allow the activation of more neurons in the binocular condition, thereby facilitating the cortical response.[7] Similarly, Escandon-Garcia et al.[12] determined a 30% improvement in light disturbance under binocular versus monocular conditions after the implantation of a multifocal intraocular lens.

In a previous study,[13] we examined different defocus levels in healthy young subjects (while pupil size was maintained at 3 and 5 mm) to evaluate BS using a number of visual functions such as high- and low-contrast VA and light disturbance. Positive BS was observed with increasing levels of defocus (both spherical and astigmatic). The increase in BS could therefore involve a neural factor, rather than just an optical input, as the change in BS may not only result from the expected reduction in pupil size under binocular conditions and the resulting improvement in the optics forming the retinal image (optical effects), but also involve the ability of the visual cortex to resolve details of this image (neural effect).[13] Visual electrophysiology allows us to investigate the electrical activity of the visual system objectively in a non-invasive or minimally invasive manner. Using such techniques, Fernandes et al.[14] recently found a reduction in the amplitude and delay in peak time of retinal activity (using the multifocal electroretinogram) during adaptation to multifocal contact lenses. They suggested that this delay may partially occur at the retinal level.[14] On the other hand, binocular improvements in visual evoked potentials (VEPs) may occur with an increase in positive defocus,[7] and VA improves with a decrease in pupil size, thus limiting high-order ocular aberrations such as spherical aberration.[15] To the best of our knowledge, there is a lack of published work on the interrelationship between visual electrophysiology testing (PERGs and VEPs) and binocular visual summation in conditions designed to limit inter-individual variability (such as pupil size).[5,7,16]

Taking these considerations into account, the purpose of the present study was to evaluate the influence of defocus and controlled pupil size on subjective (VA) and, particularly, objective descriptors of human vision (i.e., PERGs and VEPs) in order to understand their effect on binocular visual performance by examining neural BS in healthy subjects. An additional aim was to evaluate whether such changes in cortical activity (using VEPs) could be identified in the early stages of the visual pathway by investigating inner macular activity using PERGs. The novelty and contribution of this investigation is a comprehensive examination of monocular and binocular visual performance in the presence of induced blur (spherical and astigmatic defocus) under controlled pupil size. By assessing both subjective (VA) and objective measures (PERG and VEP), the study addresses a crucial aspect of visual perception while minimising potential variations arising from changes in pupil size. This approach enables a more precise evaluation of the influence of blur on binocular visual performance and provides valuable insights into the neural mechanisms involved in visual processing, particularly neural BS.

Key points

- Smaller pupil size and higher levels of defocus produced greater impairments (in peak time and amplitude) in cortical activity (P100 component) compared to the retinal activity (pattern electroretinogram).
- Partial neural binocular summation was observed for the amplitude, particularly in the P100 component where the highest binocular summation was achieved with greater spherical defocus and a larger pupil.
- Beyond the optical improvement due to the greater binocular pupil constriction, neural factors are also involved in improving binocular visual performance under image quality degradation.

METHODS

Subjects and procedure

A total of 15 young subjects (11 female and 4 male) were recruited in this crossover study. Their mean age was 28.5 (7.7) years. Healthy young subjects were chosen to rule out age as a factor influencing the BS results.[17,18] The inclusion criteria included no ocular pathologies, no previous ocular surgery and no current pharmacological treatment that could affect vision or pupil response, and a logMAR (logarithm of the Minimum Angle of Resolution) VA of 0.00 or less. The refractive examination included a monocular subjective refraction for best-corrected monocular VA followed by a binocular balance test. Only myopic patients with spherical refraction less than −3.0 D and astigmatism lower than 1.0 D (negative cylinder notation) were enrolled in the study. Table 1 expresses the mean refractive formula in the form of three independent components (power vector coordinates).[19] **M** represents the spherical equivalent, while $\mathbf{J}_0$ and $\mathbf{J}_{45}$, two pure cylindrical components, correspond to the horizontal and oblique astigmatic component, respectively. The three-dimensional

TABLE 1 Mean (standard deviation [SD]) photopic pupil diameter and power vector coordinates **M**, $\mathbf{J}_0$, $\mathbf{J}_{45}$ for the subjects enrolled in the study.

n = 15	Mean values (SD)
Natural pupil diameter (mm)	6.1 (0.6)
Power vector coordinates	
M (D)	−0.54 (0.94)
$\mathbf{J}_0$ (D)	0.001 (0.22)
$\mathbf{J}_{45}$ (D)	−0.004 (0.16)

Abbreviation: D, dioptres.

representation of the dioptric space allowed the characteristics of any refractive error to be visualised easily by a single vector; the principal coordinate of the power vector is given by the spherical equivalent (Table 1: mean $\mathbf{M} = -0.54$ (0.94)).

All subjects had a pupil diameter ≥5 mm under photopic lighting conditions (the luminance was 86.23 (1.75) cd/m^2) and the illuminance was 170.27 (3.86) lux (see Table 1). The pupil diameter was measured using a NeurOptics infrared pupilometer (NeurOptics VIP TM-200, neuroptics.com), which has been shown to have very good repeatability.[20] Pupil size was measured while subjects viewed the fixation cross in the centre of a reversing black-and-white checkerboard pattern stimulus (luminance of the white square was 220.32 (1.23) cd/m^2 and illuminance of the screen was 152.64 (0.94) lux).

Two positive spherical defocus lenses (+1.5 and +3.0 D) to create myopic defocus and two positive astigmatic defocus lenses (+1.5 and +3.0 D axis 90°) were used to induce the controlled degradation of the retinal image. Defocus was achieved with trial lenses. Two artificial diaphragms (5.0 and 3.0 mm diameters) were used to control pupil size. These diaphragms were placed in a trial frame and positioned 12 mm from the cornea. To ensure correct alignment of the pupil with the diaphragm, the interpupillary distance was measured and the height of the trial frame adjusted. Similarly, the tests were performed starting randomly from either monocular or binocular measurements. In addition, the order of the different conditions (pupil size and defocus) and the measured parameters was randomised.

The protocol followed the Declaration of Helsinki. All patients were informed about the purpose of the study and all the methods to be implemented. They had the opportunity to ask questions and all signed an informed consent form before being enrolled in the investigation. The study protocol was reviewed and approved by the Ethics Subcommittee for Life and Health Sciences at the University of Minho.

High- and low-contrast distance VA

Best-corrected distance VA was measured using an Early Treatment of Diabetic Retinopathy Study logMAR chart at a distance of 4 m under low-contrast (LCDVA, 10%) and high-contrast (HCDVA, 100%) conditions. Measurements were obtained under photopic illumination conditions (corresponding to the same illumination conditions as when the natural pupil diameter was measured). The different defocus levels and pupil diameters were presented in random order to avoid any learning effect that may influence the results.

PERG and VEP

The effect of spherical and astigmatic defocus and pupil diameter on the cortical (VEP) and retinal (PERG) electrophysiological responses was assessed using a RETI-port/scan21 (Roland Consult, roland-consult.de), following the standard guidelines of the International Society for Clinical Electrophysiology of Vision (ISCEV).[21,22]

As recommended by the ISCEV guidelines,[21,22] both pupils were dilated with two drops of 1% phenylephrine (Davinefrina; DAVI, davi.pt), and the subjects were optically corrected for the distance of the display (1.0 m). Before placing the electrodes (Figure 1), the skin was cleansed with an abrasive gel (Nuprep Skin Prep Gel, weaverandcompany.com). Then, gold cup ground and reference electrodes were filled with conductive gel (Ten20 Conductive Neurodiagnostic Electrode Paste, weaverandcompany.com) and placed in the respective positions as recommended by the ISCEV guidelines.

To minimise PERG electrode instability, the active electrode (recording electrode) was a DTL-plus electrode (Dawson-Trick-Litzkow, roland-consult.de) placed into the lower conjunctival fornix in contact with the anterior corneal surface. The reference electrode was positioned on the skin near the ipsilateral outer canthus of each eye (zygomatic bone). The ground electrode (for PERG and VEP)

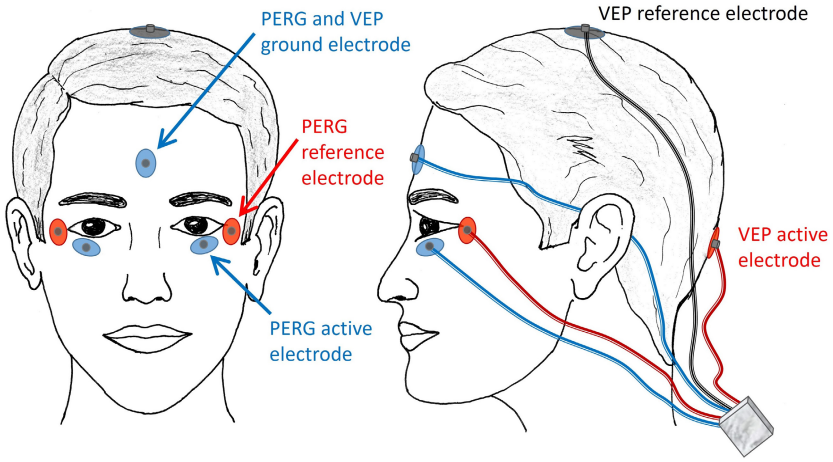

FIGURE 1 Electrode placement for pattern electroretinogram (PERG) and visual evoked potential (VEP) measurements.

was placed on the forehead, approximately 10% above the nasion. For VEP, the scalp electrodes were positioned relative to bony landmarks, in proportion to the size of the head. The anterior/posterior midline measurements were based on the distance between the nasion and the inion over the vertex. The active electrode was placed on the occipital scalp over the visual cortex.

Subjects were light adapted for 10 min prior to the examination and asked to fix their gaze on the red cross in the centre of the stimulus screen while using the optical correction for that distance. The impedance was checked before each measurement (monocular and binocular) and recordings were only performed when it was <10 KΩ. Monocular recordings were performed with the contralateral eye covered with an opaque black patch. During the recording, 200 sweeps were averaged for VEPs and PERGs (with a stimulus frequency of 4.29 Hz) using bandpass filters of 1–50 and 5–50 Hz, respectively. All blinking artefacts were removed.

Subjects were asked to focus their attention on the fixation cross in the centre of a reversing black-and-white checkerboard pattern stimulus (Figure 2a), with a check size of 0.8°, presented on a 19-inch RGB display (60 Hz frame rate) positioned 1.0 m in front of the eye (field size of 15°), at a reversal rate of 1.54 Hz (3.08 rev/s). The reversal rate is the frequency of pattern inversion (white/black). The luminance for the white and black squares was 220.32 (1.23) and 1.47 (0.06) cd/m^2, respectively, with 98% contrast. The mean illuminance of the screen was maintained at 152.64 (0.94) lux during the recordings.

Pattern electroretinograms were analysed for valley and peak responses N35, P50 and N95 and the amplitude of P50 to N95 (Figure 2b). VEPs were analysed for peak times of valleys and peaks of N75, P100 and N135 (in ms), as well as the amplitudes of P100 to N135 (in μV), as shown in Figure 2c.

Peak (or implicit) time refers to the time from stimulus to the maximum positive or negative deflection of the VEP and/or PERG.[21,22] Amplitude corresponds to the size of the electrical response.

Binocular summation

For low- and high-contrast VA, the BS ratio (BS_{VA}), which characterises the binocular visual performance,[8,17,23] was calculated by dividing the binocular VA value by the best monocular finding following Equation 1[24]: The conversion from logMAR to decimal VA values was as follows:

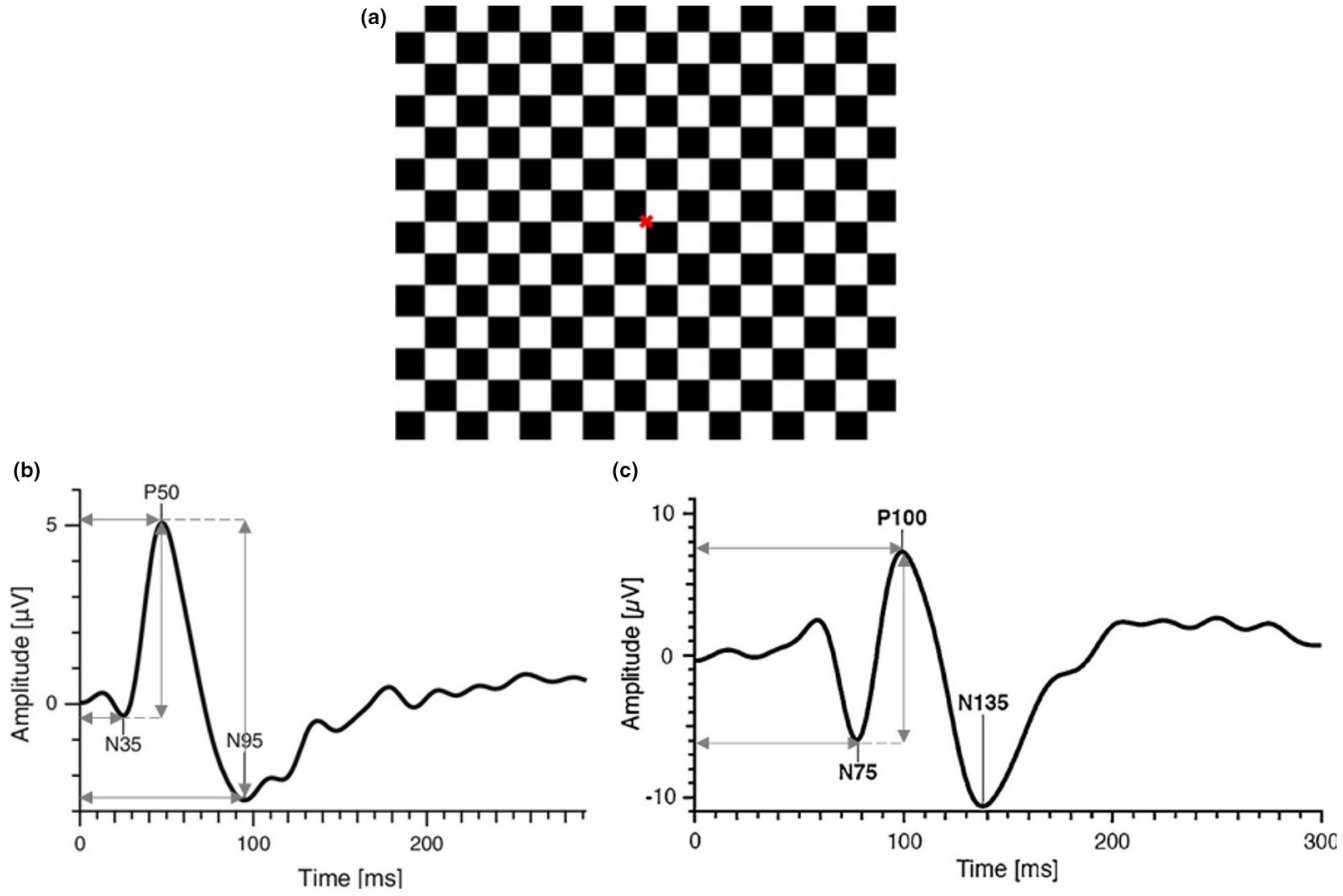

FIGURE 2 (a) Checkerboard pattern for pattern electroretinogram (PERG) and visual evoked potential (VEP) stimulation with the red cross as the fixation point. (b) Typical PERG waveform; the horizontal arrows indicate the implicit time of N35, P50 and N95 (ms) and the vertical arrows indicate the amplitude values of P50 and N95 (μV). (c) Typical VEP waveform; the horizontal arrows indicate the implicit time of N75 and P100 (ms) and the vertical arrows indicate the amplitude of P100 (μV).

$$BS_{VA} = \frac{VA_{bin}}{VA_{best\_mon}} \quad (1)$$

where VA_{bin} corresponds to the value of binocular VA and VA_{best_mon} to the best monocular finding (the highest of the two monocular values).

For the VEP peak time parameters, the BS ratio, $BS_{VEP\ Peak\ time}$, was calculated dividing the two monocular values by the two peak times of the binocular value following Equation 2:

$$BS_{VEP\ Peak\ time} = \frac{VEP\ Peak\ time_{RE} + VEP\ Peak\ time_{LE}}{2 \times VEP\ Peak\ time_{bin}} \quad (2)$$

where $VEP\ Peak\ time_{RE}$ refers to the peak time value of the right eye, $VEP\ Peak\ time_{LE}$ is the peak time of the left eye and $VEP\ Peak\ time_{bin}$ is the binocular peak time.[25–28]

Following other studies which calculated the BS for the VEP amplitudes,[25–28] the BS ratio, $BS_{VEP\ Amp}$, was calculated by dividing the two amplitudes of the binocular value by the two monocular amplitude values using Equation 3:

$$BS_{VEP\ Amp} = \frac{2 \times VEP\ Amp_{bin}}{VEP\ Amp_{RE} + VEP\ Amp_{LE}} \quad (3)$$

where $VEP\ Amp_{bin}$ refers to the binocular VEP amplitude, $VEP\ Amp_{RE}$ is the VEP amplitude of the right eye and $VEP\ Amp_{LE}$ is the VEP amplitude of the left eye.

A BS ratio >1 indicates a positive BS showing that the visual system performance (higher acuity, shorter peak time and larger amplitude) was better under binocular rather than under monocular conditions.[25–28]

Statistical analysis

Statistical analysis was performed using SPSS 23.0 software (SPSS Inc., ibm.com) for Windows. Normality was checked using the Shapiro–Wilk test. For normal data, a *t*-test for two paired samples was performed to compare the results of the two experimental conditions. In addition, a repeated measures ANOVA with Bonferroni correction was used for multiple comparisons between the baseline, defocus and pupil size for: LCDVA, HCDVA, VEP and PERG peak times, as well as VEP and PERG amplitudes. For non-normal data, the Wilcoxon test was used. The differences were considered statistically significant when $p < 0.05$.

RESULTS

High- and low-contrast distance VA

Table 2 shows the mean distance VA in logMAR and the BS for low-contrast (LCDVA) and high-contrast (HCDVA) conditions. The monocular LCDVA and HCDVA values were found to be significantly worse than the binocular findings under all conditions (for LCDVA, $p = 0.03$; for HCDVA, $p = 0.01$). Additionally, for all of the different defocus levels, mean values of LCDVA and HCDVA showed greater impairment under the 5 mm pupil size condition (for LCDVA, $p = 0.01$; for HCDVA, $p = 0.02$), except for binocularly under the baseline condition ($p = 0.12$).

It was observed that the BS increased significantly with the larger pupil size under all conditions ($F_{1,14} = 6.444$, $p = 0.02$ for baseline; $F_{1,14} = 31.818$, $p < 0.001$ for spherical defocus and $F_{1,14} = 11.477$, $p = 0.004$ for astigmatic defocus), and the highest level was achieved with +3.00 D spherical defocus (1.99 [0.59]). For the HCDVA, the BS increased significantly with pupil size for the +1.5 D spherical defocus ($F_{1,14} = 6.115$, $p = 0.03$) and +3.0 D astigmatic defocus ($F_{1,14} = 5.210$, $p = 0.04$).

Electrophysiology

VEP peak time

Figure 3 shows the mean values of monocular and binocular VEP peak times under different levels of astigmatic and spherical defocus and with varying pupil size (5 and 3 mm).

In general, for the two pupil sizes (5 and 3 mm), both monocularly and binocularly, the N75 peak times revealed significant effects with defocus (monocularly, $F_{2,14} = 11.199$, $p = 0.01$; binocularly, $F_{2,14} = 10.927$, $p = 0.01$). The monocular N75 peak times increased with respect to the binocular findings for all measured conditions (5 mm, $F_{2,14} = 6.560$, $p = 0.02$; 3 mm, $F_{2,14} = 7.550$, $p = 0.02$). For both monocularly and binocularly, the mean P100 peak times showed significant main interactions with defocus and pupil size ($p = 0.01$).

For N135, the mean peak time values increased proportionally with greater defocus levels for the monocular and binocular conditions and for the two pupil sizes (monocularly, $F_{2,14} = 10.182$, $p = 0.01$; binocularly, $F_{2,14} = 8.259$, $p = 0.01$).

VEP amplitudes

Figure 4 shows the monocular (better eye) and binocular mean VEP amplitudes under different astigmatic and spherical defocus levels, and different pupil sizes (5 and 3 mm). The 'better eye' condition corresponds to the best value for a specific parameter when comparing the two eyes. For the P100 amplitude, the highest peak amplitude was observed for the binocular baseline condition with a 5 mm pupil: 16.4 (6.5) μV. Repeated measures ANOVA for P100 amplitudes revealed some significant main effects and interactions with defocus for both monocular and binocular conditions and for both pupil sizes tested ($p < 0.001$).

For the N135 amplitude, only defocus had a significant main effect under monocular and binocular conditions ($p < 0.001$).

Table 3 shows the mean BS values for the peak times and VEP amplitudes for the different levels of defocus

TABLE 2 Mean and standard deviation values of distance visual acuity (VA) and binocular summation (BS) for low-contrast (LCDVA) and high-contrast (HCDVA) conditions under spherical (Sph) and astigmatic defocus (Cyl) for 3 and 5 mm pupils.

Condition	Pupil size	Defocus	Monocular logMAR VA	Binocular logMAR VA	*p*-Value	BS
LCDVA	5 mm	Baseline	0.08 (0.10)	0.02 (0.08)	<0.001	1.16 (0.12)
		Sph +1.5 D	0.61 (0.16)	0.43 (0.14)	<0.001	1.52 (0.24)
		Sph +3.0 D	1.16 (0.24)	0.90 (0.20)	<0.001	1.99 (0.59)
		Cyl +1.5 D	0.43 (0.13)	0.33 (0.13)	<0.001	1.26 (0.22)
		Cyl +3.0 D	0.75 (0.12)	0.61 (0.11)	<0.001	1.39 (0.19)
	3 mm	Baseline	0.02 (0.09)	0.00 (0.08)	0.04	1.07 (0.12)
		Sph +1.5 D	0.44 (0.14)	0.38 (0.15)	0.04	1.18 (0.30)
		Sph +3.0 D	0.99 (0.23)	0.79 (0.13)	<0.001	1.69 (0.63)
		Cyl +1.5 D	0.34 (0.12)	0.29 (0.13)	0.04	1.12 (0.18)
		Cyl +3.0 D	0.62 (0.12)	0.54 (0.09)	<0.001	1.22 (0.18)
HCDVA	5 mm	Baseline	−0.16 (0.07)	−0.20 (0.07)	<0.001	1.10 (0.10)
		Sph +1.5 D	0.26 (0.14)	0.15 (0.14)	<0.001	1.31 (0.16)
		Sph +3.0 D	0.68 (0.20)	0.54 (0.16)	<0.001	1.47 (0.39)
		Cyl +1.5 D	0.18 (0.11)	0.10 (0.12)	<0.001	1.23 (0.18)
		Cyl +3.0 D	0.51 (0.10)	0.37 (0.14)	<0.001	1.44 (0.36)
	3 mm	Baseline	−0.19 (0.07)	−0.21 (0.07)	<0.001	1.06 (0.06)
		Sph +1.5 D	0.16 (0.16)	0.10 (0.14)	0.002	1.16 (0.17)
		Sph +3.0 D	0.55 (0.19)	0.45 (0.14)	0.02	1.39 (0.47)
		Cyl +1.5 D	0.12 (0.12)	0.05 (0.12)	0.01	1.17 (0.20)
		Cyl +3.0 D	0.40 (0.11)	0.30 (0.10)	<0.001	1.26 (0.24)

Note: The baseline data (no defocus) is also included. Repeated measures ANOVA included Bonferroni correction.

(spherical and astigmatic) and pupil sizes (5.0 and 3.0 mm). For the BS of P100 amplitude, a positive interaction was obtained with the highest defocus and pupil size. Nevertheless, no significant differences were observed for the BS in any of the VEP parameters ($p = 0.27$), based on a repeated measures ANOVA with Bonferroni correction.

PERG peak time

Figure 5 shows the monocular mean values (right and left eye) for the PERG peak time parameters under different levels of astigmatic and spherical defocus and pupil size (5.0 and 3.0 mm). For the N35 peak time, no significant differences were observed under any conditions when comparing the pupil sizes and each eye. However, N35 peak times increased significantly with defocus for the 5 mm pupil size: for spherical defocus of +1.5 D, $F_{2,14} = 7.137$, $p = 0.02$ and for an astigmatic defocus of +3.0 D: $F_{2,14} = 5.940$, $p = 0.03$. Both defocus and pupil size had a significant effect on the P50 peak time (for +1.5 D, $F_{2,14} = 5.548$, $p = 0.04$ and for +3.0 D, $F_{2,14} = 9.325$, $p = 0.01$) and the N95 peak time (for spherical and astigmatic defocus of +1.5 D, $F_{2,14} = 7.711$, $p = 0.02$).

PERG amplitudes

Figure 6 shows the monocular mean values (right and left eyes) for the PERG amplitude parameters under different levels of astigmatic and spherical defocus and pupil size (5 and 3 mm). For the P50 amplitudes, no significant differences were observed between the two eyes in any of the conditions examined (baseline: $p = 0.79$; spherical: $p = 0.23$; astigmatic: $p = 0.08$). For the right eye (pupil size of 5 mm), P50 amplitudes decreased significantly for all defocus conditions ($F_{2,14} = 8.168$, $p = 0.02$) with respect to the baseline except for an astigmatic defocus of +1.5 D ($F_{2,14} = 4.491$, $p = 0.06$). Similarly, for the left eye (pupil size of 5 mm), P50 amplitudes changed significantly between the baseline and a defocus of +3.0 D (spherical: 3.0 (0.7) vs. 1.6 (0.8) μV, $F_{2,14} = 107.933$, $p < 0.001$; astigmatic: 3.0 (0.7) vs. 2.2 (1.3) μV, $F_{2,14} = 6.501$, $p = 0.03$). For the left eye (pupil size of 3 mm), P50 amplitudes decreased significantly with defocus ($F_{2,14} = 9.328$, $p = 0.01$). For pupil sizes of 3 and 5 mm, defocus had a significant effect on the N95 amplitude ($F_{2,14} = 5.48$, $p = 0.04$).

Table 4 shows the Spearman coefficient correlations (Spearman's rho) between the BSs of LCDVA, HCDVA and the binocular amplitude of P100 for different levels of defocus and pupil size (5 and 3 mm). In all defocus conditions measured (spherical, astigmatic and combined), significant negative correlations were found with the 3 mm pupil between the BS of HCDVA and the P100 amplitude, that is, the higher the BS for VA, the lower the BS of the P100 amplitude and vice versa. Similarly, under the 5 mm pupil and astigmatic defocus condition, a significant negative correlation was observed between the BS of LCDVA and the P100 amplitude.

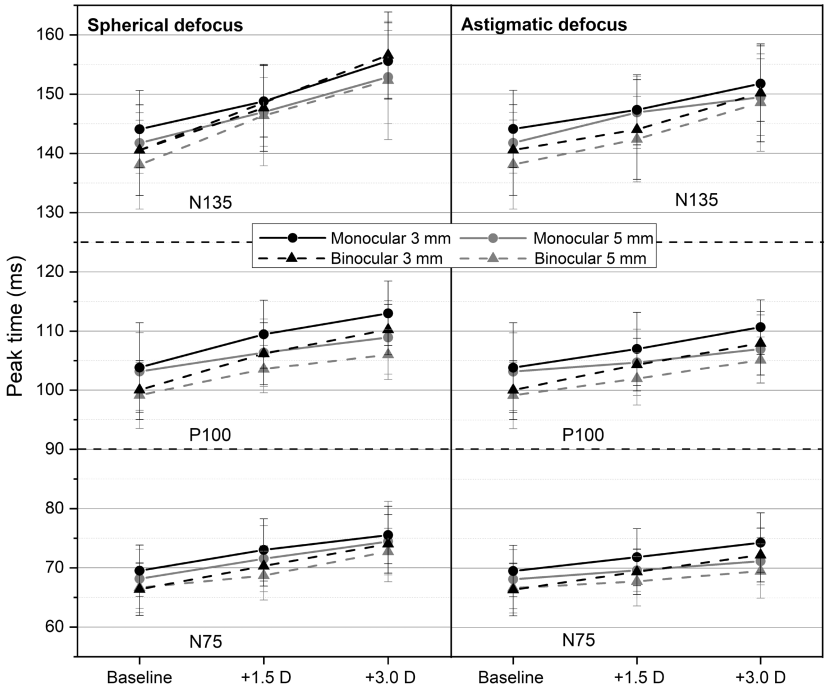

FIGURE 3 Mean values of monocular (best eye) and binocular visual evoked potentials for the three measured peak time parameters (N75, P100 and N135) under different levels of astigmatic and spherical defocus and pupil size (5 and 3 mm).

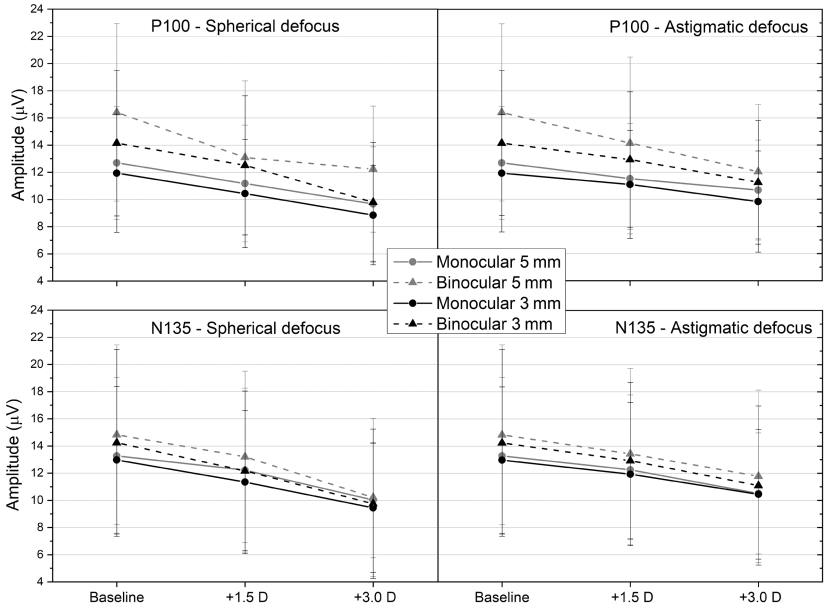

FIGURE 4 Mean values of monocular (better eye) and binocular visual evoked potential for the two amplitude parameters measured (P100 and N135) under different levels of astigmatic and spherical defocus and pupil size (5 and 3 mm).

DISCUSSION

First, the binocular performance was higher than the monocular performance for LCDVA and HCDVA under all levels of defocus. Additionally, the results were significantly improved at all levels of defocus for the 3 mm pupil compared with the 5 mm pupil, apart from the binocular baseline condition. This latter result could be explained by the high threshold achieved in baseline binocular viewing. Banton and Levy[29] found binocular superiority for low-contrast stimuli when measuring vernier acuity. They suggested that under higher contrast conditions, the binocular advantage diminishes due to saturation. Under all conditions in the present investigation of LCDVA and HCDVA, mean BSs were >1, highlighting the superior performance under binocular conditions. The present results

TABLE 3 Mean binocular summation (BS) values for the different peak times and visual evoked potential (VEP) amplitudes for the different levels of astigmatic (Cyl) and spherical (Sph) defocus and different pupil sizes (5 and 3 mm).

			VEP BS mean values			
Pupil size	**Defocus**	**N75 peak time**	**P100 peak time**	**N135 peak time**	**P100 amplitude**	**N135 amplitude**
5 mm	Baseline	1.05 (0.08)	1.06 (0.06)	1.05 (0.04)	1.36 (0.27)	1.22 (0.32)
	Sph +1.5 D	1.07 (0.08)	1.04 (0.06)	1.03 (0.05)	1.26 (0.25)	1.20 (0.38)
	Sph +3.0 D	1.04 (0.07)	1.04 (0.04)	1.03 (0.07)	1.40 (0.23)	1.14 (0.36)
	Cyl +1.5 D	1.06 (0.07)	1.04 (0.03)	1.05 (0.04)	1.31 (0.30)	1.23 (0.33)
	Cyl +3.0 D	1.06 (0.08)	1.04 (0.04)	1.03 (0.06)	1.23 (0.26)	1.22 (0.39)
3 mm	Baseline	1.08 (0.11)	1.06 (0.07)	1.04 (0.03)	1.28 (0.33)	1.17 (0.39)
	Sph +1.5 D	1.07 (0.09)	1.05 (0.04)	1.02 (0.03)	1.30 (0.34)	1.20 (0.34)
	Sph +3.0 D	1.05 (0.07)	1.04 (0.05)	1.02 (0.04)	1.33 (0.46)	1.27 (0.46)
	Cyl +1.5 D	1.06 (0.10)	1.04 (0.04)	1.04 (0.03)	1.25 (0.28)	1.21 (0.37)
	Cyl +3.0 D	1.06 (0.06)	1.04 (0.04)	1.03 (0.04)	1.25 (0.36)	1.24 (0.49)

Note: Standard deviation is shown in parentheses.

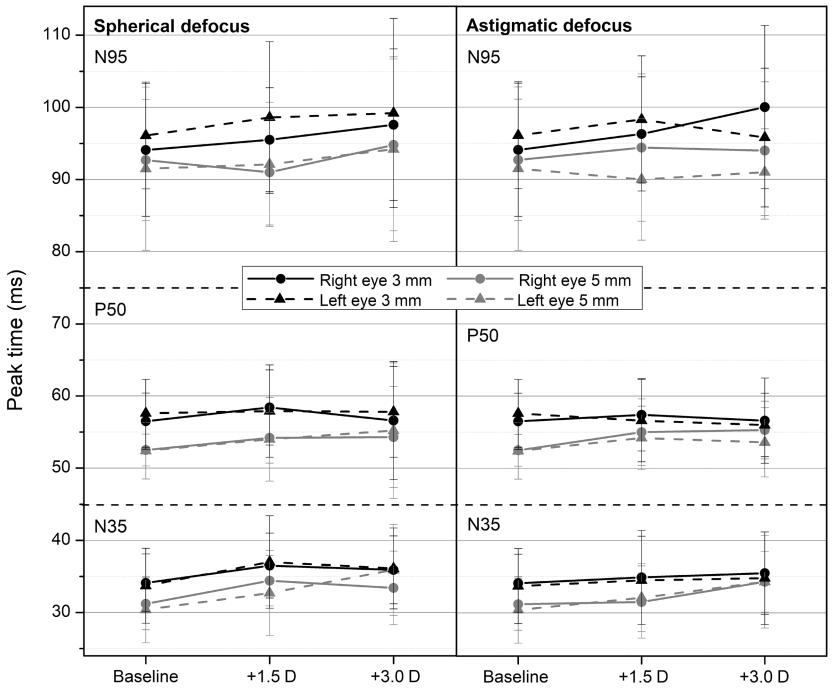

FIGURE 5 Mean values of monocular (right and left eye) pattern electroretinogram for the three peak time parameters measured under different levels of astigmatic and spherical defocus and pupil size (5 and 3 mm).

corroborated that BS is increased for both low- and high-contrast VA.[30,31] Therefore, the results show that BS for VA is particularly relevant when the visual conditions were more challenging: that is, greater degrees of defocus and larger pupil size. The findings indicated strong enhancement of BS with increased defocus. Plainis et al.[7] also found that BS for VA was higher in a group of young subjects with greater amounts of spherical defocus, even though they did not control for pupil size unlike the present study. They hypothesised that the observed increase in BS with retinal blur could be attributed to the activation of a larger population of neurons during close-to-threshold detection, resulting in less contrast being required for binocular stimulation compared with monocular stimulation, in order to engage the same proportion of cells involved in contrast detection.[7,32]

Second, our results showed significant increases in peak times (N75, P100 and N135) and decreases in amplitudes (P100 and N135) for all VEP components with higher amounts of defocus and a smaller pupil. In particular, the P100 component (in terms of peak time and amplitude) was most deteriorated by defocus and pupil size. This is

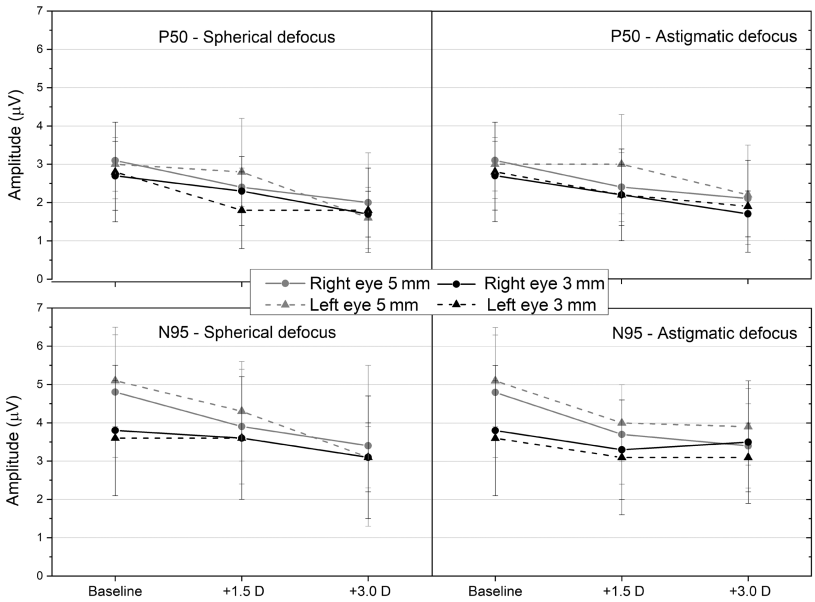

FIGURE 6 Mean values of monocular (right and left eye) pattern electroretinograms for the two amplitude parameters measured (P50 and N95) under different levels of astigmatic and spherical defocus and pupil size (5 and 3 mm).

TABLE 4 Spearman correlation coefficients (Spearman's rho) for binocular summation (BS) of low-contrast distance visual acuity (LCDVA), high-contrast distance visual acuity (HCDVA) and a visual evoked potential (VEP) amplitude of P100 for different levels of defocus and pupil sizes (5 and 3 mm).

BS	Pupil size	Spearman's ρ (VA BS-VEP amplitude BS)	
		Defocus	P100 Amplitude BS
HCDVA	3 mm	Spherical	−0.304 ($p = 0.04$)
		Astigmatic	−0.324 ($p = 0.03$)
		Total	−0.321 ($p = 0.01$)
LCDVA	5 mm	Astigmatic	−0.423 ($p = 0.004$)

Abbreviation: VA, visual acuity.

in accordance with Sokol et al.[33] who found that the P100 peak increased and P100 amplitude reduced with spherical defocus of +3.0 D. In addition, Pieh et al.[34] confirmed that spherical defocus of +2.0 D or more led to a sizeable deterioration in the central VEP responses. We also observed similar effects for astigmatic defocus. This could be due to the vertical axis selected (90°), which is known to be the direction that most degrades the quality of vision.[35] The present results are consistent with the detrimental effects of refractive error (which reduce VA) and smaller pupil size on VEP responses.[22] Furthermore, the mean binocular values were significantly better compared with the monocular findings for all VEP peak times and peak amplitudes (particularly for the P100 component). These results are in line with other studies that reported lower binocular P100 peak time values and higher P100 amplitudes compared with the monocular results.[7,36–38] A defocused image leads to a decrease in VA,[39] contrast sensitivity[40] and sharpness.[41] Consequently, the resulting defocused image on the retina appears smaller. Under this condition, only retinal cells with small receptive fields and higher resolution are activated. These cells are primarily located in the central retina and have slower conduction velocities. As a result, the P100 component generated under reduced VA (induced by the different levels of defocus) with stimulation from small check patterns is prolonged, and the amplitudes are reduced due to fewer selectively stimulated receptors, particularly in the central visual field, compared to normal VA.[42] Other studies[7,43] have suggested that a large decrease in the contrast of the visual stimulus (induced by blur) at the neural level could allow the activation of more neurons under binocular conditions, thereby facilitating the cortical response. It is well established that the VEP response (peak time and amplitude) is influenced by several non-pathophysiological parameters, including background luminance, check size, reversal rate, pattern contrast, noise, patient age, refractive error, fixation and extremely large or small pupil sizes.[22,44] As previously noted, in the present study the pupil size was controlled and limited to a diameter of either 3.0 or 5.0 mm, thereby limiting one source of inter-individual variability. Martins et al.[45] investigated the effect of pupil size on multifocal pattern visual evoked potentials (mfVEP) with pupil sizes of 2, 4, 6 and 8 mm. They found that artificially varying pupil size affected the mfVEP, producing a slight reduction in amplitude only at extreme miosis (2 mm), and a decline in peak times with increasing pupil area.[45] We confirmed that latencies and amplitudes for the 3-mm pupil deteriorated with respect to the 5-mm diameter for all VEP components. In contrast to our experiment, Martins et al. did not investigate the effect of pupil size on the PERG and the combined effect of controlling the pupil size and image quality deterioration (induced by different levels of defocus).

On the other hand, we observed positive partial BSs ($1 < BS < 2$) for all peak times and amplitudes of the VEP components, showing the superiority of the binocular system over monocular viewing; this being most significant for the P100 and N135 amplitudes. In the present study, the highest BS was obtained for the greatest defocus and pupil size for the P100 amplitude component (1.40 [0.23]). This is in line with Mizota et al.,[46] who also found a mean BS for the P100 peak time in normal patients of 1.05, and 1.30 for the P100 amplitude, thus showing a greater and partial BS for the VEP amplitudes. Similarly, Heravian-Shandiz et al.[47] found an increase of 27% in the mean binocular amplitude compared with the mean monocular finding, indicating partial positive BS under normal conditions. They suggested that binocularity depends largely upon a cortical modulatory mechanism. Recently, Amini-Vishteh et al.[48] investigated the effect of BS before and after corneal surgery, finding partial positive BS in both situations (i.e., pre- and post-surgery) for peak times and amplitudes, even though a decrease in BS occurred after surgery. In contrast to our work, the pupil size was not controlled in these studies. Skrandies[49] mapped brain electrical activity and observed that binocular stimuli activated more neurons, resulting in the superiority of binocular over monocular processing for many visual tasks. Therefore, their topographic data illustrated that physically identical stimuli activated different neural elements within the human visual cortex depending on whether they were presented to only one eye or to both eyes simultaneously.[49] We found a trend towards improvement in the P100 amplitude BS (1.40 [0.23]) with a larger pupil size (5 mm) and greater defocus (+3.0 D). As suggested above under binocular conditions, pattern-reversal VEPs could activate a higher number of cortical neurones to low-contrast detection in comparison with the monocular condition.[7,32,50]

Third, similar to VEP, PERG activity was influenced by defocus and pupil size. Indeed, our results showed significant delays in peak times and decreases in amplitudes (P50 and N95) for a higher amount of defocus and smaller pupil diameter. We also observed similar effects for the astigmatic defocus compared to the spherical condition. This could be due to the selected vertical axis (90°), which is known to be the direction that most degrades the quality of vision.[35] Leipert and Gottlob[51] found decreased PERG amplitudes due to the defocused retinal image. Furthermore, they indicated a maximum PERG amplitude for a 5.5-mm pupil (P100 amplitude) and 4.5 mm pupil (N135 amplitude), as well as a significant decrease in PERG amplitudes for pupil sizes ≤2.5 mm. This is consistent with our findings where the amplitudes were higher for a pupil size of 5 mm compared with 3 mm. Previous studies[52,53] also confirmed significant deteriorations in PERG amplitudes and peak times produced by spherical defocus. Bach and Mathieu[52] suggested that these impairments were significant when VA was <0.8 (in decimal notation). In addition, Vizzeri et al.[53] showed that PERG amplitudes and peak times were significantly impaired for defocus ≥ +3.0 D. Contrary to the present investigation, they did not control important factors of inter-individual variability such as pupil size. We also confirmed the findings of previous studies[43,54] that blur caused by defocus had a lower effect on PERG peak times and amplitudes than VEP parameters.

Finally, significant correlations were observed between HCDVA and P100 amplitude BSs with spherical and astigmatic defocus and for a 3-mm pupil size. This is in line with Jeon et al.,[55] who also found a correlation between VA and the N135 amplitude; in the present study, we found a correlation between VA (HCDVA and LCDVA) and the P100 amplitude BS. As noted, the VEP P100 component is considered stable and repeatable in electrophysiology.[22]

Plainis et al.[7] showed that binocular vision ameliorates the effect of defocus in both subjective (VA) and electrophysiological (P100 component) findings. Indeed, they found that even if the VEP and VA BSs might differ, they would be linearly related to defocus. Unlike this earlier work, we controlled pupil size and examined the effect of astigmatic defocus. Under these conditions, we did not find a linear relationship between the binocular gain in VEP BS and VA.

Limitations of the present study include the fact that the subjects' pupil size was not measured during the VA and electrophysiology measurements (VEP and PERG). However, after measuring the pupil with an infrared pupilometer under photopic conditions without a trial frame, it is expected that the natural pupil behind the artificial pupil diaphragm would always be larger than the reference measurement. It is therefore assumed that the aperture limiting the entrance of light to the eye was the artificial diaphragm (i.e., the 3.0- and 5.0-mm pupil).

The novelty and contribution of this research lies in its comprehensive assessment of monocular and binocular visual performance under the effects of induced blur through spherical and astigmatic defocus and controlled pupil size. By measuring both subjective (VA) and objective (PERG and VEP) visual parameters, this work addresses an important aspect of visual perception and minimises the potential variability introduced by individual differences in pupil size. This approach allows for a more accurate evaluation of the impact of blur on binocular visual performance and provides valuable insights into the underlying neural mechanisms of visual processing (neural BS).

In summary, a complete framework of VA and electrophysiology was evaluated, measuring all peak times and amplitudes of the VEP and PERG parameters, highlighting significant deteriorations under different defocus conditions (including spherical and astigmatic positive defocus) and controlling pupil size. By limiting pupil size, an important source of inter-individual variability, significant changes (in peak time and amplitudes) were observed, firstly in retinal activity (PERG), although the strongest change was seen in cortical activity (VEP), with this being worse for the smaller pupil size measured. Similarly, the greater the defocus, the stronger the impairment affecting PERG and VEP in terms of peak time and amplitude. Specifically, higher levels of defocus affected the quality of the retinal image and cortical activity, mainly

in the P100 component. However, partial neural BS was observed for the amplitude, particularly in the P100 component where the highest level of BS was achieved with greater spherical defocus (+3.0 D) and a larger pupil (5 mm). Thus, beyond the optical improvement due to the greater binocular pupil constriction, neural factors are also involved in improving binocular visual performance under image quality degradation (from defocus and the larger pupil size).

Finally, correlations between the P100 amplitude and VA BSs confirm that the P100 component is a stable parameter that can be useful for evaluating binocular visual performance.

AUTHOR CONTRIBUTIONS

Francesco Martino: Data curation (lead); formal analysis (equal); investigation (equal); methodology (equal); validation (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). **Ana Amorim-de-Sousa:** Formal analysis (equal); investigation (equal); methodology (equal); validation (equal); writing – original draft (equal); writing – review and editing (equal). **Paulo Fernandes:** Formal analysis (equal); investigation (equal); methodology (equal); supervision (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). **Jose Juan Castro-Torres:** Formal analysis (equal); funding acquisition (equal); validation (equal); visualization (equal); writing – review and editing (equal). **José Manuel González-Méijome:** Conceptualization (equal); funding acquisition (equal); investigation (equal); resources (equal); supervision (equal); validation (equal); visualization (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets generated during the current study are available from the corresponding author upon reasonable request.

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