The effect of diabetic retinopathy on standing posture during optic flow stimulation

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Abstract:	Background Diabetic retinopathy is a principal cause of visual damage and blindness, in which laser treatment offers proven therapy. The progressive degeneration of the retina, secondary to diabetes, is believed to cause postural instability although this is not well documented. The aim of this research was to assess how optic flow stimuli contribute to the control of stance in people with impaired retinal functions. Research question Does the different retinal functionality correspond to different specific patterns of movements and muscles recruitment? Methods Postural mechanisms and motor strategies were measured by testing subjects in quiet stance on a force platform with surface electromyography under different optic flow stimulations. Root mean square values of the center of pressure time-varying signals and normalized EMG values were used to evaluate the postural sway. Results People with diabetic retinopathy, and to a greater extent laser group, were more unstable than healthy subjects. The greater amplitude of the body sway observed in the retinopathy group, and especially in the laser group, could be an expression of the difficulty for this population in processing this kind of visual information. Significance The increase in muscle activity indicates that there are musculoskeletal and postural changes in the lower limb musculature with increasing severity of diabetic retinopathy. An impaired retinal function might negatively affect postural control in a way that is dependent on the severity of retinal damage.
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Conflict of interest statement

All authors disclose any financial and personal relationships with other people or organisations that could inappropriately influence their work.

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Abstract

Background: Diabetic retinopathy is a principal cause of visual damage and blindness, in which laser treatment offers proven therapy. The progressive degeneration of the retina, secondary to diabetes, is believed to cause postural instability although this is not well documented. The aim of this research was to assess how optic flow stimuli contribute to the control of stance in people with impaired retinal functions.

Research question: Does the different retinal functionality correspond to different specific patterns of movements and muscles recruitment?

Methods: Postural mechanisms and motor strategies were measured by testing subjects in quiet stance on a force platform with surface electromyography under different optic flow stimulations. Root mean square values of the center of pressure time-varying signals and normalized EMG values were used to evaluate the postural sway.

Results: People with diabetic retinopathy, and to a greater extent laser group, were more unstable than healthy subjects. The greater amplitude of the body sway observed in the retinopathy group, and especially in the laser group, could be an expression of the difficulty for this population in processing this kind of visual information.

Significance: The increase in muscle activity indicates that there are musculoskeletal and postural changes in the lower limb musculature with increasing severity of diabetic retinopathy. An impaired retinal function might negatively affect postural control in a way that is dependent on the severity of retinal damage.

Keywords: neuropathy; laser photocoagulation; body sway; centre of pressure; diabetes; electromyography

Introduction

Diabetes is a chronic illness produced by elevated levels of blood glucose, accompanied by disturbed metabolism of fats and proteins. Uncontrolled diabetes leads to complications in many organs, including impaired vision (diabetic retinopathy) and nerve damages (diabetic neuropathy) [1].

Diabetic retinopathy (DR) is a microvascular complication that increases with duration of pathology. The DR is characterized by a progressive degeneration of the retina, which at first may cause no symptoms or only mild vision problems. Eventually, it can cause loss of the visual function [2]. Primary interventions, such as intensive glycemic and blood pressure control, can reduce the incidence of DR, while secondary interventions, such as laser photocoagulation, may prevent further progression of DR and vision loss [3].

Vision plays an essential role in the multisensory control of postural balance [4–6]; it is the system primarily involved in planning locomotion and in avoiding obstacles along the way [7]. Postural instability is increased when visual, proprioceptive or vestibular cues are absent or degraded [8]. In elderly persons, standing balance deteriorates due to age-related physiologic diminution of visual and vestibular function and lower extremity muscle strength; thus, this deterioration increases the risk of falling [9]. DR reduces the autonomy and quality of life [10]. Postural instability, which causes limitations in the daily activity, is among the complications associated with diabetes mellitus [11]. In diabetic patients with a long history of severe retinopathy, the degree of instability is expected to be greater than in non-diabetic subjects [12].

Therefore, it is thought that the concurrent effects of neuropathic symptoms and retinopathic damage are associated with increased postural instability among patients with one or both factors [13]. Additionally, the effects of neuropathy upon gait and posture appear strong when retinopathy is considered [12]. Moreover, peripheral neuropathy has an effect on muscle function, causing higher effort from the lower limb musculature to produce a sample action during gait, with an earlier fatigue that can be demonstrated by the increase in EMG muscle amplitude. This is probably due to the lack of blood being provided to the muscles and the effect of glycosylation, with more muscle exertion and longer time in fibers contraction to produce the action [14].

Retinopathy affects the retina with microaneurysms and haemorrhages, resulting in visual acuity problems, loss of binocular vision, and increment in postural instability. Diabetes alters endothelial function and permeability of the blood brain barrier, thus affecting microcirculation and regional metabolism, with alteration (hypoperfusion) in cerebral blood flow of the frontal, temporal, parietal, occipital, and cerebellar areas [15]. This altered vasoreactivity, accompanied with white matter atrophy, was most prominent in the temporal region, with consequences even in the postural control [16]. Moreover, white matter hyperintensities (WMHs), a diffuse hyperintense areas, secondary to vascular complications, are strongly associated with age, hypertension and diabetes [17]. In older adults, Novak et al., [17] have found a correspondence between the WHMs of the fronto-temporal and parieto-occipital regions with the increased postural instability in both mediolateral and anteroposterior direction. The main function of the occipital area is to process visual information and visual perceptions. Patients with DR show a greater postural instability because visual perception is closely linked to postural control providing afferent feedback regarding postural sway to the cerebellum. Therefore, diabetic retinopathy results in impairments of visual perception, visual processing, and transfer of the somatosensory information to the parietal and frontal areas with subsequent impairments of attention, behavioural response and executive functions [18]. Common laser treatments applied to patients with sight-threatening forms of diabetic retinopathy are effective in preventing but not reversing visual loss. It is therefore imperative that patients with sight-threatening disease are referred before visual loss occurs, and the most affected retinal area was the peripheral visual field, with the extent of the loss depended from the size, density and intensity of the coagulation [19].

Postural control is a complex task which make considerable demands on the peripheral nervous system and might therefore be affected by peripheral neuropathy. Since orientation information from the various senses are not always accurate (diabetic retinopathy), the postural control system must be regulated to maintain balance in a different environmental condition [8]. This is the sensorimotor integration problem that we investigated by evoking body sway using optic flow stimulation in both healthy and disease subjects. In the present study, we induced a self-motion perception in a quiet standing using optic flow stimuli while simultaneously recording the center of pressure (COP) displacement and the pattern of lower-limb muscular activity. We performed the experiments in patients with retinopathy, patients with laser treatment and healthy age-matched controls. Based on the literature cited above, and to the best of our knowledge, no study has investigated the different postural sway and lower-limb muscle activity between patients with retinopathy and retinopathic patients after laser treatment. We hypothesised that specific patterns of movements and different muscles recruitment correspond to different retinal functionality that is the functional part of the retina, which could be damaged due to diabetic consequences.

Methods

Participants

Thirty-six subjects gave their written informed consent to take part in this study and were subdivided into 3 groups: thirteen people with type II diabetes mellitus and in the early stage of retinopathy, eight people with type II diabetes mellitus submitted to laser treatment on the peripheral retina, and fifteen healthy subjects (Table 1). The experimental protocol was approved by the Bioethics Committee of our University. The experiments were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Exclusion criteria were the assumption of any drug that could have an effect on the central nervous system, the presence of any musculoskeletal problem and/or major complications of diabetes that could affect the standing posture. The hand and foot laterality of each subject was assessed by a laterality questionnaire [20] using the following formula:

$$[(\text{right preference} - \text{left preference}) / (\text{right preference} + \text{left preference})] \times 100$$

A positive laterality index was indicative of a right dominance, while a negative index was indicative of a left dominance.

****Table1****

Procedure and apparatus

Participants were divided into three groups based on the ophthalmoscopic measurement operated by one of the authors (S.Z.S). People with non-proliferative retinopathy and presenting only a few micro-aneurysms were assigned to the “retinopathy group”. People with proliferative retinopathy who had already undergone laser photocoagulation treatment in the peripheral retina were included in the laser treated group “laser group”. All participants included in the laser group had an intact central area of about 30° of radius corresponding to

the entire macula and a portion of peripheral retina. “Control group” were healthy people with normal retinal functionality.

All experiments were performed in a dark room. Participants were placed, in a standing posture, in front of a translucent screen in which the optic flow visual stimuli were back projected. Feet were placed at the same position for all subject. We have identified a line in which they had to place the upper extremity of their halluces. They were instructed to fixate the center of the screen for the entire duration of the stimulation meanwhile COP and electromyographic (EMG) activity were simultaneously recorded.

Optic flow stimuli

Optic flow stimuli comprised white dots (1.3 cd/m2, size 0.4°), in a black background, presented with a retro video projector (Sony VPL EX3) positioned 415 cm away from a translucent screen. The screen covered 135×107° of visual field and was placed 115 cm from the subjects’ eyes. The dots speed was set at 5°/s [4].

We randomly presented seven optic flow stimuli (Fig.1). Fixation on a dark screen (baseline, BASE) and random dots motion (RAN) were used as control stimuli. Two types of optic flow motion: in the first condition the dots speed accelerated to the left to simulate left-heading direction (direction left – fixation central; LEFT), while in the second condition the speed accelerated to the right to simulate right-heading direction (direction right – fixation central; RIGHT). Finally, three expanding optic flow stimuli were presented full field (FULL), in the foveal region (FOV; the stimulated area had a radius of 7°) and in the peripheral region (PERIP; the blank area in the centre had a radius of 20°) [4]. All stimuli had a fixation point placed to the center of the screen, and participants had to maintain fixation there for the entire duration of the stimulation. For each stimulus we recorded five trials lasting 30 s each. Optic flow stimuli were made using Matlab psychophysical toolbox (The Mathworks Inc.).

****Fig.1****

Stabilometric and surface electromyography

Stabilometric data were recorded using two Kistler® force platforms (Kistler Instrument Corp. NY, USA) placed side by side. Participants were instructed to place a foot on each platform with both arms along the trunk. EMG data were acquired with PocketEMG (BTS Bioengineering Inc.) using Ag/AgCl disposable electrodes 32x32 mm (RAM Apparecchi Medicali s.r.l.). Electrodes had an active area of 0.8 cm^2 with an inter-electrode distance of about 2 cm. At the beginning of the experiment, subjects were prepared for the electromyographic recordings. Electrodes were positioned on the muscular belly of the following muscles: left tibialis anterior (LTA), right tibialis anterior (RTA), left soleus (LSOL), right soleus (RSOL). The reference electrode was placed on the malleolus bone (electrically neutral tissue). After placing the electrodes, we acquired the maximum voluntary contraction (MVC) of each muscle using isometric machines, with subjects seated in a chair, with knees at 90° and toes lies on a platform. They had to produce the maximum EMG levels via plantar

flexion (soleus) and dorsiflexion (tibialis anterior) movements against a heavy load. The peak of the MVC was used for the normalization of EMG values [5,21].

Data Analysis

Both EMG and stabilometric signals were recorded at 1000 Hz. EMG signals were positively rectified and band pass filtered (Butterworth, 20–450 Hz) using SMART Analyzer (BTS Bioengineering Inc.), then data were resampled at 250 Hz and normalized to the maximum voluntary contraction. The normalized root mean square (RMS) values were calculated in 100 ms bins.

Stabilometric data were low-pass filtered at 15 Hz and resampled at 250 Hz. Antero-posterior (AP) and medio-lateral (ML) directions of COPs of each foot were analysed using either SMART Analyzer and Matlab. Then, we obtained the global COP, computed from a weighted average of the left and right COP, according to the following formula [13]:

$$COP_{global} = COP_L * R_{VL}/(R_{VL} + R_{VR}) + COP_R * R_{VR}/(R_{VL} + R_{VR}),$$

where RVL and RVR are the vertical reaction forces from left and right feet, respectively.

The COP velocity reflects the total distance travelled by the COP over time on each axis, while the COP area represents the enclosed area covered by the COP as it oscillates within the base of support [5].

Statistical analysis

Repeated-measures ANOVA was done on each COP parameters (COP_{AP}; COP_{ML}; COP_{Area} and $COP_{Velocity}$) in which stimuli (BASE; RAN; LEFT; RIGHT; FULL; PERIP; FOV) was the within-subjects factor, while group (control; retinopathy; laser) was the between-subjects factor.

Repeated-measures ANOVA was also used for muscle activity, in which muscles (RTA; LTA; RSOL; LSOL) and stimuli (BASE; RAN; LEFT; RIGHT; FULL; PERIP; FOV) were the within-subjects factors, group (control, retinopathy, laser) the between-subjects factor.

Multiple comparisons were done with Bonferroni post-hoc test. Mauchly's test was used to assess any violations of sphericity. Effect size of the repeated measure ANOVAs were expressed using partial eta-squared (η_p^2), with values of 0.01, 0.06, and 0.14 representing small, medium, and large effects respectively (Cohen, 1988). Statistical significance was set at $p < 0.05$.

Results

All subjects were right-handed. Responses from the laterality questionnaire resulted in values ranging from 80 to 100. Twenty-four subjects showed a laterality index of 100, meaning that they were completely right-handed. The rest of the participants showed values in the range between "80-100" indicating a strong right laterality in all three body segments. No subject turned out to be left-oriented.

Stabilometric parameters

All COP parameters showed significant main effects for group ($F_{2, 30} = 7.34$; $p < 0.05$; Fig.2). Concerning ML direction, significant differences were observed for retinopathy and laser in comparison to control group (mean diff = 5.18; $F_{2, 30} = 4.14$; $p = 0.046$; 95% CI: 0.25-16.62 and mean diff = 6.27; $F_{2, 30} = 4.34$; $p = 0.043$; 95% CI: 0.16-12.38, respectively). Same result was obtained for the AP direction (mean diff = 7.74; $F_{2, 30} = 6.64$; $p = 0.026$; 95% CI: 0.74-14.75 and mean diff = 12.05; $F_{2, 30} = 8.34$; $p = 0.004$; 95% CI: 3.33-20.76 for retinopathy and laser group respectively). The COP area showed significant difference between laser and control group (mean diff = 62.50; $F_{2, 30} = 5.14$; $p = 0.031$; 95% CI: 4.63-120.37), meanwhile COP velocity between retinopathy and control group (mean diff = 8.18; $F_{2, 30} = 4.22$; $p = 0.046$; 95% CI: 0.25-16.62).

****Fig.2****

Stimuli x group ($F_{12, 180} = 2.03$; $p = 0.024$; $n_p^2 = 0.12$) interaction effects was found for the ML direction. This analysis demonstrated that retinopathic and laser groups were more unstable than control subjects on all visual stimuli, included baseline and random motion conditions (Fig.3).

****Fig.3****

Electromyographic activity

Repeated measures ANOVA was applied to the normalized RMS values. Results revealed a significant main effect for groups ($F_{2, 29} = 4.76$; $p = 0.016$; $n_p^2 = 0.25$), muscle ($F_{3, 87} = 3.60$; $p = 0.017$; $n_p^2 = 0.11$), stimuli ($F_{6, 174} = 2.40$; $p = 0.030$; $n_p^2 = 0.08$), and an interaction effect for muscle x stimuli x group ($F_{36, 522} = 1.80$; $p = 0.003$; $n_p^2 = 0.11$) (Fig.4).

****Fig.4****

Bonferroni post hoc analysis showed a significant difference between retinopathy and control group (mean diff = 2.60; $F_{2, 30} = 7.38$; $p = 0.014$; 95% CI: 0.44-4.75). All participants activated mostly both left and right soleus muscles, with the greatest values shown by retinopathy group, meanwhile, left and right tibialis anterior were mainly activated by laser in comparison to control group (mean diff = 1.42; $F_{2, 30} = 7.08$; $p = 0.018$; 95% CI: 0.44-3.65).

Discussion

The aim of this research was to assess how optic flow stimuli contribute to the control of stance in people with different retinal functionality. Our results showed that people with diabetic retinopathy, and to a greater extent people who have received laser treatment, were more unstable than healthy control subjects. The velocity, range and distribution of postural sway during stance have been shown to be greater in patients with diabetic peripheral neuropathy than in age-matched control subjects [22]. The postural unbalance, as a consequences of neuropathy, is related to electrophysiological measures of nerve conduction, but it does not occur in diabetic patients without neuropathy [23]. Laser treatment leads to a loss of retinal

receptors, mainly in the peripheral visual field [24]. The literature has widely demonstrated the functional importance of the peripheral retina in postural stabilization [4,25], and its preference for processing forward motion [26]. To better understanding, we have tried to investigate the relative contribution of visual receptors in the control of posture during eccentric optic flow stimulation.

The slightly but not significantly higher values of the COP parameters (ML; AP; Area) found in the laser with respect to retinopathy group, as well as the significantly differences in comparison to the control subjects, make us consider the functional importance of the peripheral retina in the postural stabilization. We can speculate that the damage of the peripheral visual field of the laser group may have played the most important role during standing posture [for a review see 27], leading us to understand the functional significance of different retinal damage in modulating the self-motion perception, and consequently the associated muscular responses and COP dynamics. The lack of the peripheral retina seems to induce a significant wider COP sway in the medio-lateral and antero-posterior direction, and mainly in the COP area when compared to the control group (Fig.2). Indeed, the COP area defines the overall postural instability, and the literature demonstrates how unsteadiness tends to be related to the availability of the sensorimotor information [28]. Complications associated with diabetes lead to a lack of one or more sensory information in entrance to the postural system, a condition that predisposes this population to a risk of fall 15 times greater than age-matched healthy subjects [1]. In the same way, data of the present study suggest that postural instability is proportionate to the retinal damage and to the visual information available. Regarding the COP velocity, it is proportional to the postural unsteadiness, and people with high risk of falling present high values of COP velocity [29]. COP velocity was the only parameter in which we found the highest value on the retinopathy group. It seems that, within a certain range, higher COP area is correlated with lower COP velocity. Retinopathy showed higher velocity and lower area, whereas laser group showed higher area and lower velocity. Higher COP velocity, exhibited by the retinopathy group, could have helped them in maintain posture with respect to laser group, who showed greatest values in the remaining COP parameters (AP; ML; and Area). Indeed, the effectiveness of the postural control system is generally related to the magnitude of the COP displacement, while COP velocity is associated with activity necessary to maintain postural stability [30]. Importantly, we can suppose that the unbalanced sample size between groups could have influenced the statistical analysis, with no significant differences between retinopathy and laser groups.

The optic flow stimuli used in this study had a characteristic pattern of expansion that simulated a self-motion perception in a forward motion. This could have determined the greatest value of laser group on both left and right tibialis anterior in order to react to visual stimuli. The tonic activity of both tibialis anterior and soleus muscles may contribute to the intrinsic ankle stiffness to keep stability. Indeed, the ankle activation while maintaining posture causes a continuous oscillation in antero-posterior direction requiring the generation of a stronger vertical force to keep postural stability and to avoid falls. In addition to this, a previous study affirms that elderly decrease their body sway by co-activating their muscles around the ankle joint, probably due to postural instability [31]. It can perhaps be assumed that increased muscle

activation of the tibialis anterior results in greater demand for increased ankle dorsi-flexion/extension during standing posture. The greater COP displacement perceived by the laser group might result in a compensatory leg muscle co-contraction in order to reduce COP displacement. The retinopathy group responded to postural perturbation activating predominantly both left and right soleus, whereas the laser group activated both tibialis anterior and soleus muscles. These postural strategies seem to correspond to different levels of retinal functionality evolving into a progressively lower level of adaptability and increased rigidity, with the activation of agonist and antagonist muscles of both legs equally. A disabling consequence of diabetic complication is the progressive reduction of the fine motor control at the ankle level, presumably due to the continuous loss of motor axons with insufficient reinnervation, responsible for both atrophy and muscle weakness [32,33]. The pathophysiology of muscle weakness in the presence of hyperglycaemia may bring to postural alterations. Indeed, due to the lack of blood being supplied to the muscles and the effect of glycosylation, there is more muscle exertion and the fibres take longer to contract to produce the movement [14]. The significant increase in EMG values in patients with retinopathy indicates that higher exertion is required from the lower-limb musculature to produce the appropriate activation to maintain posture, which may result in earlier fatigue. Consequently, identifying muscle characteristics, such as reduced tolerability to fatigue and strength, during the clinical management of the diabetic complications to body extremities is vital for the provision of more effective therapies to improve muscle area and function. Moreover, proprioceptive feedback from the leg and foot will be degraded in patients with such complications. In healthy subjects, restoration of balance following perturbation in quiet standing has been demonstrated to result primarily from movements at the ankle [12]. Moreover, the slightly higher BMI observed for the disease participants is unlikely to affect the neuromuscular balance responses, given that only a BMI higher than 35 kg/m^2 has been associated with higher COP parameters [30].

The postural strategies did not change under different optic flow stimulations, but we found specific postural stabilization strategies related to retinal functional conditions. The absence of a different muscular response to different visual stimuli suggests that the availability of an optic flow stimulation seems not to play a role in triggering the preparatory muscle action; once a structured plan has been acquired, the relevant muscles respond relative to the task of maintaining posture. Previous studies did not find any stimulus effect in changing COP parameters and/or postural muscles activation, so the main role of cortical mechanisms in the maintenance of stance has become increasingly evident [4–6]. Therefore, the total number of neurons in the visual cortex, stimulated by either central or peripheral retinal areas, determined the visual contribution to postural balance [34]. The present findings of an increased in postural body sway with decreasing area of the visual field supports this interpretation [35].

An important point to discuss is the lack of significant differences between retinopathy and laser groups. This could be due to the unbalanced sample size, with lower number of lasers treated in comparison to retinopathic and healthy participants. Another limitation of our study is the lack of a precise quantification of the dimensions of the residual visual field of both study groups. However, the two groups did not have the same degree of severity of peripheral involvement, with participants in the laser group having the greatest peripheral damage.

Nonetheless, their outcome results on postural stability were comparable. These differed significantly from the results obtained from the control group. This implies that even a mild peripheral retinal damage had a negative impact on postural control. Subjects with a lack of peripheral retinal receptors demonstrated greater postural instability as well as specific patterns of muscle activation, with adaptive motor programs based on the characteristics of visual perception. Quiet standing requires the combination of various body segments, joints, and sensory system integrations to control balance and avoid falls. These results shed light on the motor control system that influences postural responses.

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Legend to figure

Figure 1. Optic flow stimuli. **A.** Fixation on a dark screen (baseline - BASE). **B.** Random dots motion (random - RAN). **C.** Fixation point (FP) to the centre and dots accelerated to the left simulated heading to the left with fixation straight ahead (left direction - LEFT). **D.** FP to the centre and dots accelerated to the right simulated heading to the right with fixation straight ahead (right direction - RIGHT). **E.** Full field radial expansion with the FP simulated heading and fixation straight ahead (full - FULL). **F.** Peripheral stimulation, the blank area in the centre

had a radius of 20° (periphery - PERIP). **G.** Foveal stimulation, the stimulated area had a radius of 7° (fovea - FOV). Arrows represent the velocity and direction vectors of moving dots.

Figure 2. Histograms represent the differences (mean±SEM) between groups (control: black bars; retinopathy: white bars; laser: grey bars) across COP parameters.

Figure 3. Histogram represents the differences (mean±SEM) between groups (control: black bars; retinopathy: white bars; laser: grey bars) across optic flow stimuli during ML direction.
Legend. BASE: baseline; FULL: full; RIGHT: right direction; LEFT: left direction; FOV: fovea; PERIP: periphery; RAN: random; RMS: root mean square; MVC: maximum voluntary contraction; LTA: left tibialis anterior; RTA: right tibialis anterior; LSOL: left soleus; RSOL: right soleus.

Figure 4. Histograms show the muscle activation (% of MVC) between groups (control: black bars; retinopathy: white bars; laser: grey bars) across optic flow stimuli.
Legend. BASE: baseline; FULL: full; RIGHT: right direction; LEFT: left direction; FOV: fovea; PERIP: periphery; RAN: random; RMS: root mean square.

Table 1

Table 1. Group characteristics

	Retinopathy	**Laser**	**Control**	***p* value**
Subjects (N°)	13 (7 males; 6 females)	8 (2 males; 6 females)	15 (10 males; 5 females)	0.078
Age (years)	62±3	58±5	58±2	0.171
BMI (kg/m^2)	28±4	28±3	26±4	0.876
Age at diabetes onset (yrs.)	37±4	30±5	\	0.034*
Disease duration (yrs.)	25±3	29±2	\	0.029*
HbA_{1c} (%)	8.1±1.2	8.4±0.9	\	0.098

Data are means ± SD. Abbreviations: BMI: body mass index; HbA_{1c}: glycated hemoglobin.
* Significant at $p < 0.05$.

Figure 2

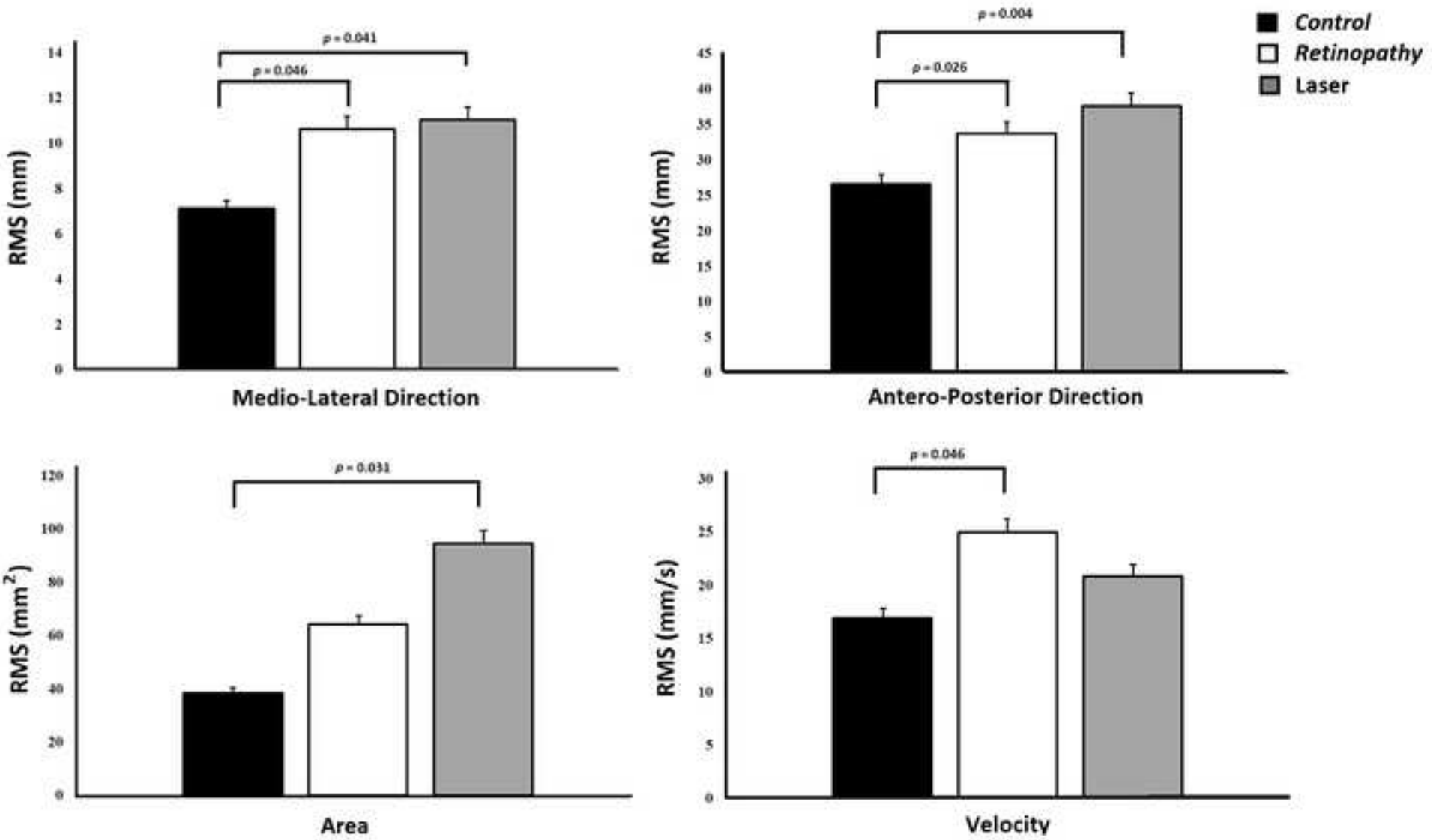

p = 0.041
p = 0.046
RMS (mm)
Medio-Lateral Direction
p = 0.004
p = 0.026
RMS (mm)
Antero-Posterior Direction
Control
Retinopathy
Laser
p = 0.031
RMS (mm²)
Area
p = 0.046
RMS (mm/s)
Velocity

Figure 3_revision#1

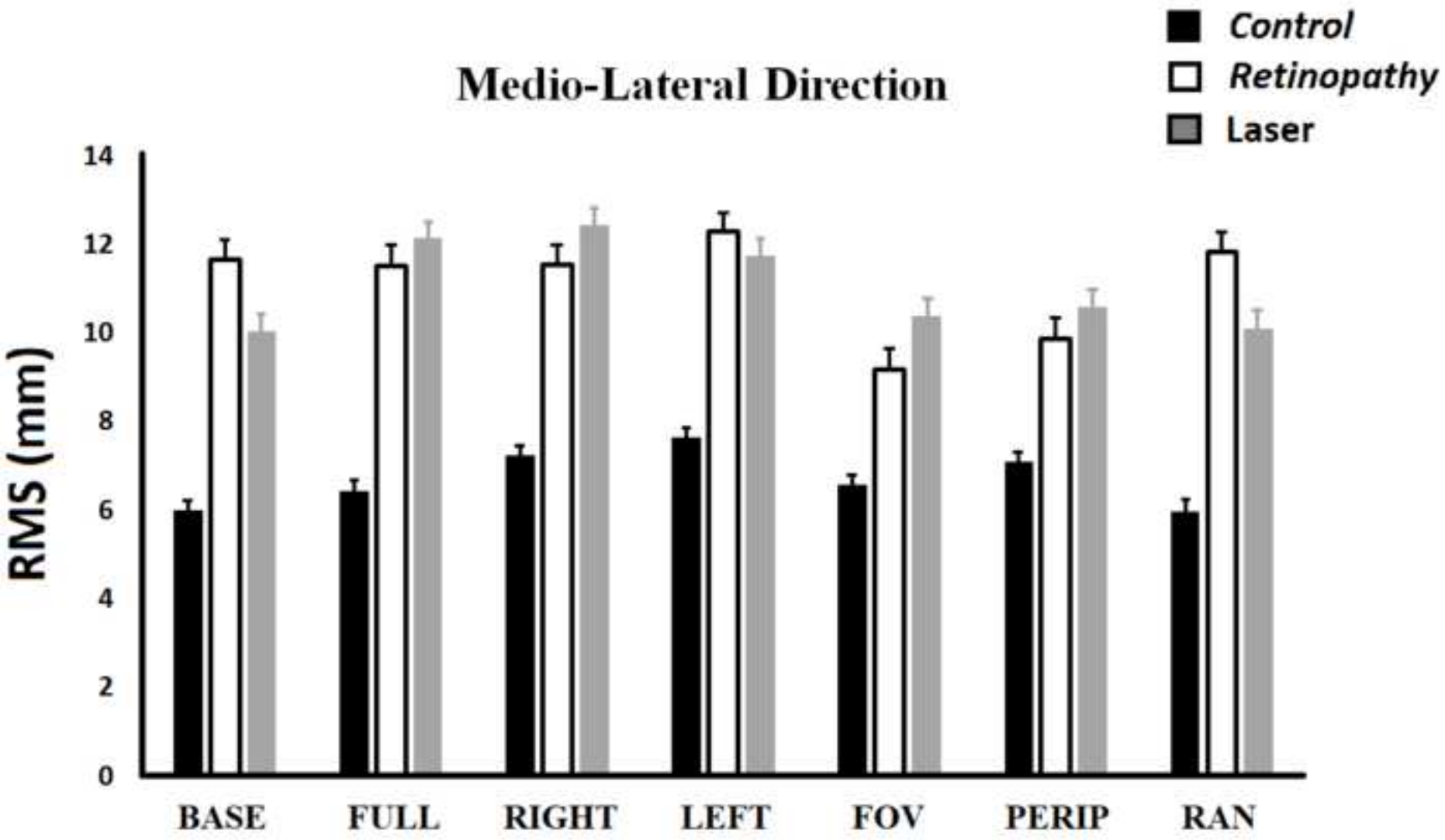
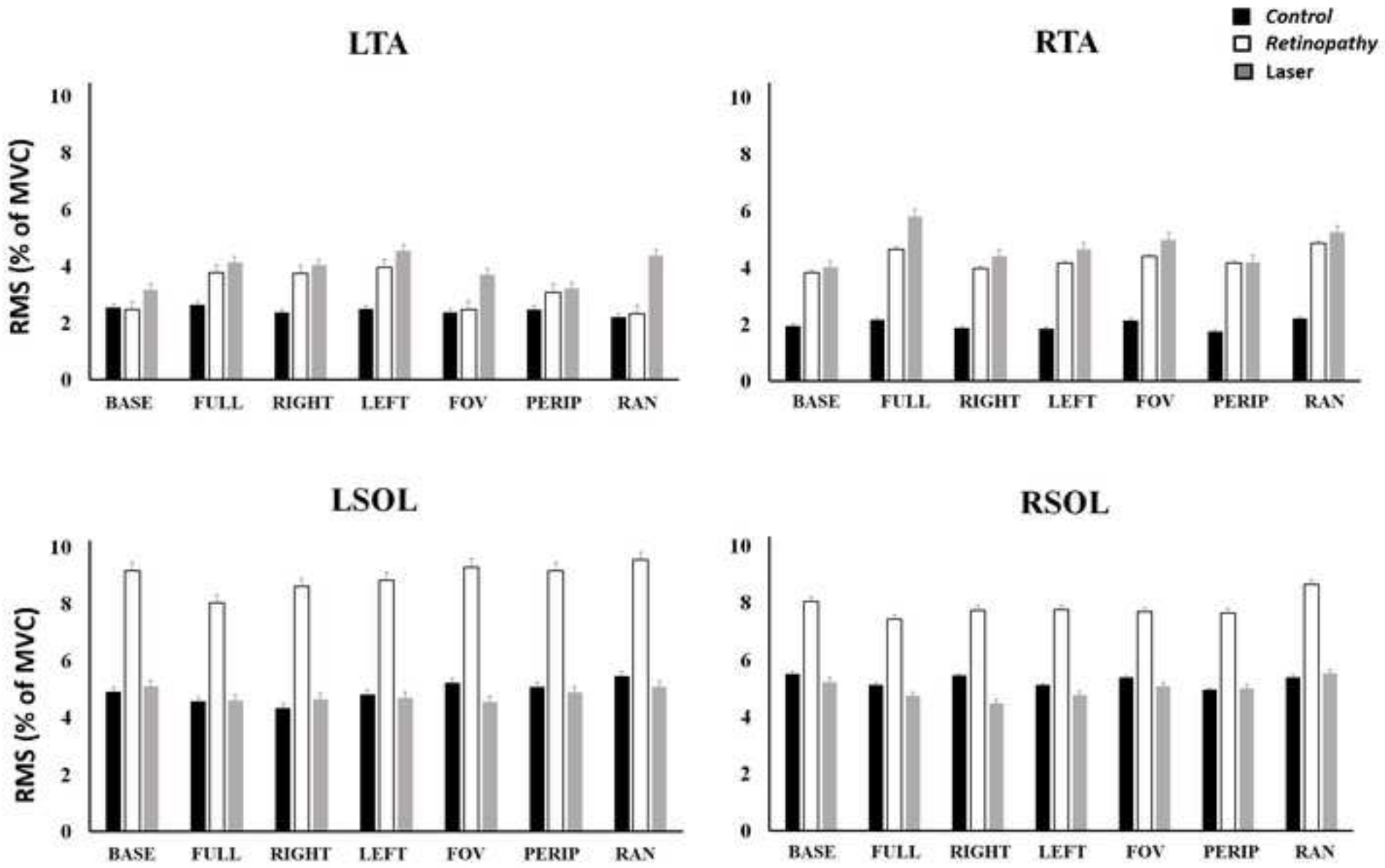


Figure 4


LTA
RTA
LSOL
RSOL
Control
Retinopathy
Laser
RMS (% of MVC)
0
2
4
6
8
10
BASE
FULL
RIGHT
LEFT
FOV
PERIP
RAN