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# **The role of central vision in posture: postural sway adaptations in Stargardt patients**

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## ABSTRACT

The role of central and peripheral vision in the maintenance of upright stance is debated in literature. Stargardt disease causes visual deficits affecting the central field, but leaving unaltered a patient's peripheral vision. Hence, the study of this rare pathology gives the opportunity to selectively investigate the role of central vision in posture. Postural sway in quiet stance was analyzed in 10 Stargardt patients and 10 control subjects, in three different conditions: 1) eyes closed, 2) eyes open, gazing at a fixed target, and 3) eyes open, tracking a moving target. Stargardt patients outperformed controls in the condition with eyes closed, showing a reduced root mean square (RMS) of the medio-lateral COP displacement, while their performance was not significantly different from controls in the antero-posterior direction. There were no significant differences between patients and controls in open eyes conditions. These results suggest that Stargardt patients adapted to a different visual-somatosensory integration, relying less on vision, especially in the medio-lateral direction. Hence, the central vision seems to affect mostly the medio-lateral direction of postural sway. This finding supports the plausibility of the “functional sensitivity hypothesis”, that assigns complementary roles to central and peripheral vision in the control of posture.

**Key Words:** Posture; Stargardt; central vision; central field loss; postural sway; center of pressure (COP); low vision; visual impairment.

## 1. Introduction

Postural control is a perceptual-motor process that integrates information from the visual, somatosensory, and vestibular systems to maintain the body equilibrium [1]. The role of central and peripheral vision in the control of posture is debated. Three different theories can be found in

literature. The first one is the "peripheral dominance theory", which emphasizes that peripheral rather than central vision plays an essential role in the control of posture [2],[3],[4],[5]. The second is known as the "retinal invariance hypothesis" and suggests that central and peripheral vision have the same functional role in maintaining upright quiet stance [6]. Finally, the third theory, the "functional sensitivity hypothesis", holds that there are functional differences and complementary roles for central and peripheral vision in postural control [7],[8],[9],[10]. In particular, it argues that peripheral vision is predominant in the antero-posterior (AP) postural control, while central vision in the medio-lateral (ML) one.

The contradicting findings of previous studies may be explained by various confounding factors. In studies on normal subjects, different kind of visual stimuli, aimed at selectively activating the central or peripheral vision, were used [2],[11],[12]. The methodological dissimilarities regarding the size of the central and peripheral field, as well as the methods of presenting the visual stimuli to these fields may bias the examination of their respective functional roles in postural control [2],[11]. In studies on pathological subjects, the selection of patients presenting visual deficits exclusively in the central or in the peripheral visual field may provide useful insights in ascertaining the complementary roles of central and peripheral vision in the control of posture. To this purpose, Age-related Macular Degeneration (AMD), that causes central field loss, and glaucoma, that causes peripheral field loss, were investigated [13][14][15][16][17]. However, both are late onset diseases, and it is known that, in the elderly, postural control may deteriorate due to a variety of circumstances, including musculo-skeletal, neurological and vestibular deficits, as well as concurrent ocular dysfunctions. The effects of these comorbid degenerations on postural control are not easily estimable, and the old age of patients may bias the analysis of the respective contributions of central and peripheral vision to balance.

Traditionally, posturographic studies test two conditions: eyes open and eyes closed. Frequently, the Romberg's ratio (the ratio between eyes closed and eyes open for each parameter) is used to establish the influence of the visual input on postural balance [18][19]. Typically, in the eyes-open

condition, the subject is asked to gaze at a fixed target. In addition, different kinds of visual stimuli, such as tracking a moving dot, may be included in the study protocol to examine how ocular movements may affect postural sway [20][21][22][23]. In literature, saccadic eye movements (rapid eye movements redirecting the fovea onto an object or region of interest) are known to reduce body sway [22][24]. On the other hand, it remains unclear how smooth pursuit (slower eye-tracking movements) affects postural balance. A previous study compared the influence of a stationary or moving fixation point to the influence of stationary or moving large-field stimulus, systematically documenting the destabilizing effect of eye movements on posture [20]. However, a recent work contradicted this finding, reporting that smooth pursuit eye movements reduce postural sway with respect to fixation [23].

Stargardt syndrome is a disease characterized by a morphological and functional alteration of the normal retinal constitution [25]. This hereditary retinal degeneration causes a reduction of central vision, preserving peripheral vision. The loss of vision is due to the presence of yellow spots in the macular region, called "flecks", causing a progressive loss of visual acuity [26]. The disease has an onset at a young age and a genetic etiology [27].

This study aims at analyzing how the central field deficit affecting Stargardt patients influences their postural control. This may be relevant to establish which of the three theories, "peripheral dominance theory", "retinal invariance hypothesis" or "functional sensitivity hypothesis" is more plausible. To the best of our knowledge, there are no other studies investigating Stargardt syndrome in this perspective.

## **2. Materials and Methods**

### 2.1 Participants

Ten patients affected by Stargardt maculopathy were recruited from our Ophthalmic Hospital. Patients were included in the study if they had a genetically confirmed diagnosis, based on the research of the gene ABCA4 that most frequently determines Stargardt disease [28]. The exclusion criteria were the presence of osteoarticular, sensorimotor or vestibular impairments that could affect patient balance, or the presence of other important ocular pathologies other than Stargardt disease. Patients (6 males and 4 females) had a mean age of  $38.4 \pm 15$  years (height:  $1.70 \pm 0.12$  m, weight:  $70.6 \pm 9.9$  kg). They were first diagnosed with significant visual impairment from Stargardt at the mean age of  $15.2 \pm 4.0$  years. When they were enrolled in this study, an average of  $22.5 \pm 12.7$  years have passed since their first diagnosis.

Ten control subjects (6 males and 4 females), with normal visual acuity and no musculoskeletal, vestibular or neurological disorders, were recruited from the local community, matched for age and anthropometric characteristics (age:  $38.4 \pm 13.8$  years, height:  $1.69 \pm 0.13$  m, weight:  $69.1 \pm 13.5$  kg).

Both patients and controls underwent a complete orthoptic and neuro-ophthalmologic examination, to evaluate their visual system. Patients also underwent a retinal microperimetry (with MP-1 NIDEK, Italy) to assess the size of their central scotoma and to quantitatively assess their central field loss [29].

The experimental protocol was approved by the local ethical committee and all participants gave their written informed consent to participate in the study.

## 2.2. Protocol and experimental set-up

Three different conditions were tested: 1) eyes-closed (EC), 2) eyes-open, still target fixation (EO), 3) eyes-open, moving target tracking (EM). In a normally enlightened room, the subject was positioned 2.2 m from the frontal wall, and a target was projected onto the wall, at their eyes level. The target was a 10-cm diameter luminous spot (subtending a visual angle of  $3^\circ$ ), either kept fixed (for EO), or moved along different directions (up/down, left/right and oblique) with a velocity of

0.2 m/s (for EM). Subjects were instructed to fix or track the spot with their eyes only, i.e. without moving their head [20]. All patients could easily see the luminous spot. Five trials were performed for each test condition, hence a total of 15 recordings per patient were acquired. The sequence of trials was randomized among conditions to avoid habituation effects [30].

Subjects were asked to stand quietly on the platform, in upright position, arms along their sides. Footprints were traced on the platform to standardize the foot position (inter-malleolar distance: 4 cm, feet opening angle: 30°) [31][32][33][34]. Each trial lasted 60 seconds. Every two trials the subject rested for 1 minute moving away from the platform.

The force platform used was a Kistler 9286A, and the signals were acquired by the system Step32 (Medical Technology, Italy). The initial sampling frequency was 2 kHz, then the signals were down-sampled to 20 Hz.

### 2.3 Data analysis

In Stargardt patients, the fixation stability was assessed in both eyes. The microperimeter provides the percentage of fixation points inside circles with diameters equal to 2° and 4°, that have as a center the centroid of all fixation points [29]. Normal fixation stability corresponds to 100% of the fixation points within 2°. On each patient's eye, the central field loss was estimated by the formula:

$$\text{Central field loss (\%)} = \frac{100 - \text{average}(\text{fixation stability within } 2^\circ)}{100}. \quad (1)$$

Then the patient's central field loss was calculated by averaging the left- and right-eye values.

For each trial, the postural sway in the medio-lateral (ML) and antero-posterior (AP) directions was estimated from the Center of Pressure (CoP) trajectory, calculating the root mean square (rms) of the  $ML(n)$  and  $AP(n)$  time series [35]:

$$ML_{rms} = \frac{1}{N-1} \sum_{n=1}^N (ML(n) - \overline{ML})^2 \quad (2a)$$

$$AP_{rms} = \frac{1}{N-1} \sum_{n=1}^N (AP(n) - \overline{AP})^2. \quad (2b)$$

For each visual condition, the values of the two stabilometric parameters were obtained by averaging five trials.

A 1-way MANOVA was applied to establish if there were significant differences between patients and controls, considering 6 dependent variables: 3 test conditions (EC, EO, EM)  $\times$  2 direction of sway (AP and ML). Post-hoc comparisons were performed between groups (two sample *t*-test, 2 tails,  $\alpha=0.05$ ) and conditions (paired *t*-test, 2 tails,  $\alpha=0.05$ ), for the AP and ML parameters.

In addition, the Romberg's ratio was calculated as the EC condition measure divided by the EO measure [36]:

$$ML \text{ Romberg's ratio} = \frac{ML_{RMS} \text{ with eyes closed}(EC)}{ML_{RMS} \text{ with eyes open}(EO)} \quad (3a)$$

$$AP \text{ Romberg's ratio} = \frac{AP_{RMS} \text{ with eyes closed}(EC)}{AP_{RMS} \text{ with eyes open}(EO)}. \quad (3b)$$

This is an index that is usually used to establish the influence of the visual input on postural control. When its value is close to unity, this reflects the fact that there is a negligible difference between EC and EO conditions, meaning that the visual input is almost uninfluential. Differences in Romberg's ratios between patients and controls were estimated by two sample *t*-tests (2 tails,  $\alpha=0.05$ ).

### 3. Results

The residual visual acuity and fixation stability of Stargardt patients is reported in Table 1.



Globally, the postural sway of the Stargardt group differed from that of controls (MANOVA Wilk's lambda test:  $p=0.04$ ). Figure 1 shows the average ML and AP postural sway, for Stargardt patients and controls, in the three test conditions (EC, EO, EM).

Post-hoc comparison (see Table 2) showed a reduced ML postural sway in the Stargardt group, under eyes-closed condition (EC), with respect to controls ( $p=0.03$ ).

In the Stargardt group, ML postural sway was not significantly different across the three conditions, while AP postural sway was greater in EC with respect to EO condition ( $p=0.001$ ). In the control group, greater postural sway, in both the ML and AP directions, was observed under eyes-closed condition (EC) with respect to EO and EM conditions (ML:  $p<0.001$ ,  $p=0.003$ ; AP:  $p<0.001$ ,  $p<0.001$ ). No significant differences were observed between EO and EM conditions, in both groups.

In the Stargardt group, ML Romberg's ratio was close to unity ( $1.04\pm 0.09$ ), a value significantly smaller with respect to controls ( $1.23\pm 0.12$ ) ( $p=0.001$ ). In the AP direction, the Romberg's ratio of patients ( $1.26\pm 0.16$ ) was close to that of controls ( $1.37\pm 0.08$ ), with  $p=0.07$ .

To study the correlation between the degree of visual deficit and a patient's balance performance, we represented a scatter plot of each patient's central field loss against their ML and AP Romberg's ratios (Fig. 2). The average Romberg's ratios in controls was also represented for reference (controls did not show any central field loss). The results indicated a significant correlation between the central field loss and ML Romberg's ratio (Pearson's correlation coefficient  $R = -0.74$ , 95%-confidence interval:  $[-0.2; -0.9]$ ). Although the same tendency holds for AP Romberg's ratio, the correlation in this case may not be considered as statistically significant ( $R = -0.51$ , 95%-confidence interval:  $[-0.9; 0.2]$ ).

#### **4. Discussion**

Control subjects swayed more under eyes-closed condition with respect to both open-eye conditions. The finding of an increased postural sway under eyes-closed condition with respect to eyes open (gazing at a fixed target) is in agreement with many studies on healthy subjects [18][19].

On the other hand, Stargardt patients postural stability did not deteriorate in the absence of vision, in the ML direction. Under eyes-closed condition, Stargardt patients showed a reduced postural sway with respect to controls, in the ML direction, but not in the AP direction. Since in the ML direction they showed no change in the closed-eyes with respect to open-eyes conditions this suggests that they rely less on the visual system to maintain balance in this direction. On the contrary, in the AP direction, they showed an augmented postural sway under eyes-closed condition with respect to the condition with eyes open gazing at the fixed target, a behavior similar to that of controls. This is confirmed by the analysis of the Romberg's ratio. In fact, the Romberg's ratio was significantly correlated to the central field loss of Stargardt patients, in the ML, but not in the AP direction. Hence, our results suggest that the higher was the patient visual impairment, in terms of central field loss, the greater their ability to maintain the ML balance in upright stance without relying on vision.

Previous studies showed that blindness or low-vision may lead to a compromised balance control [37],[38],[39]. In older adults with open-angle glaucoma, a greater visual field loss was associated with reduced postural stability [16]. Our study showed that, Stargardt patients performed similarly to controls in open-eyes conditions, while they outperformed controls under eyes-closed condition. This may be explained by the fact that Stargardt disease has an early onset: patients most probably had the time to gradually find balance compensative strategies and a different visual-somatosensory integration, strategies that might become difficult to achieve at an older age.

Stargardt disease selectively impairs the visual central field, leaving unaltered peripheral vision. The fact the Stargardt patients differ from controls especially in the ML postural sway, where they seem to rely less on vision to maintain upright stance, suggest that ML body sway is directly affected by central field loss. This supports the plausibility of the “functional sensitivity

hypothesis”, that assigns complementary roles to central and peripheral vision in the control of posture. More specifically, our findings seem to confirm that peripheral vision may be predominant in the antero-posterior (AP) postural control, while central vision in the medio-lateral (ML) one.

Previous research extensively investigated how postural responses are influenced by artificially generated optical flow patterns [19][20][40][41], as well as examined the mechanisms underlying visually induced body sway [42]. In the present study we analyzed a single smooth pursuit eye-tracking condition, using a relatively small dot (angle of substance  $3^\circ$ ) rather than a large-field stimulus. This smooth pursuit target tracking did not alter body sway with respect to gazing at a fixed target, in both Stargardt patients and controls. Hence, our finding fall in between with respect to what was found by Laurens et al. [20], that documented the destabilizing effect of eye movements on posture, and the work by Rodrigues et al. [23], that reported a reduced postural sway in presence of smooth pursuit movements with respect to fixation. A limitation of the study is the small sample size. This is due to the fact that Stargardt disease is a rare pathology, and it has been difficult to collect even a small sample of patients sharing the same genetic expression of the disease.

## **5. Conclusions**

Stargardt patients, suffering from visual impairment in the central but not in the peripheral field, showed better performance than controls especially in the medio-lateral postural sway, in closed eyes conditions. This was interpreted as an adaptation to their central field deficit, requiring them to rely less on vision in the maintenance of upright stance. This adaptation is statistically significant only in the medio-lateral direction, supporting the theory that central and peripheral vision have functionally different and complementary roles in posture.

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Table 1 - Visual deficits in Stargardt patients

Patient	Visual acuity						Fixation stability (%) <sup>4</sup>				Central field loss (%) <sup>5</sup>
	Decimal scale <sup>1</sup>		MAR <sup>2</sup>		LogMAR <sup>3</sup>		< 2°	< 4°	< 2°	< 4°	
	Right	Left	Right	Left	Right	Left	Right	Left			
1	0.2	0.2	5.0	5.0	0.7	0.7	87	100	95	100	9.0
2	0.2	0.2	5.0	5.0	0.7	0.7	100	100	35	94	32.5
3	0.25	0.25	4.0	4.0	0.6	0.6	75	96	94	98	15.5
4	0.15	0.1	6.7	10.0	0.82	1	97	100	97	100	3.0
5	0.05	0.04	20.0	25.0	1.3	1.4	96	100	22	94	41.0
6	0.05	0.04	20.0	25.0	1.3	1.4	17	51	45	85	69.0
7	0.04	0.04	25.0	25.0	1.4	1.4	84	100	47	94	34.5
8	0.06	0.08	16.7	12.5	1.2	1.1	85	99	22	59	46.5
9	0.04	0.08	25.0	12.5	1.4	1.1	52	94	47	89	50.5
10	0.1	0.1	10.0	10.0	1.0	1.0	92	100	71	95	18.5

<sup>1</sup>Far vision acuity was measured at a 2m-distance. Normal visual acuity corresponds to 1.

<sup>2</sup>Minimum angle of resolution (MAR), expressed in minute of arc. Normal visual acuity corresponds to 1 minute of arc.

<sup>3</sup>Logarithm of the minimum angle of resolution. Normal visual acuity corresponds to 0.

<sup>4</sup>Percentage of fixation points within 2° and 4°. Normal fixation stability corresponds to 100% of the points within 2°.

<sup>5</sup>Central field loss was estimated as:  $[100 - \text{average (fixation stability} < 2^\circ)]/100$ , where the average between the right and left eyes was considered.

Table 2 – Postural sway in ML and AP directions, for both populations.

Condition1	Group	Medio-lateral direction (ML)		Antero-posterior (AP)	
		Mean (SD) <sup>2</sup>	Range	Mean (SD) <sup>2</sup>	Range
EC	Stargardt	2.2 (0.6) *	1.2 - 3.3	3.2 (0.9) §	2.1 - 4.5
	Controls	2.9 (0.6) *†‡	2.0 - 3.8	3.7 (0.5) †‡	3.0 - 4.9
EO	Stargardt	2.1 (0.5)	1.1 - 3.0	2.5 (0.5) §	2.0 - 3.3
	Controls	2.3 (0.5) †	1.5 - 3.0	2.7 (0.5) †	2.1 - 3.7
EM	Stargardt	2.1 (0.6)	0.9 - 3.2	2.7 (0.5)	1.9 - 3.6
	Controls	2.4 (0.6) ‡	1.5 - 3.1	2.9 (0.3) ‡	2.3 - 3.2

<sup>1</sup>EC: eyes closed; EO: eyes open, still target fixation; EM: eyes open, moving target tracking.

<sup>2</sup>Mean and standard deviation over the population. Significant differences between Stargardt patients and controls are indicated by an asterisk (\*) (p<0.05). Significant differences between EC and EO are indicated by (§) for patients, and by (†) for controls (p<0.05). Significant differences between EC and EM are indicated by (‡) for controls (p<0.05). No significant differences were found between EC and EM, in patients, or between EO and EM in both populations.



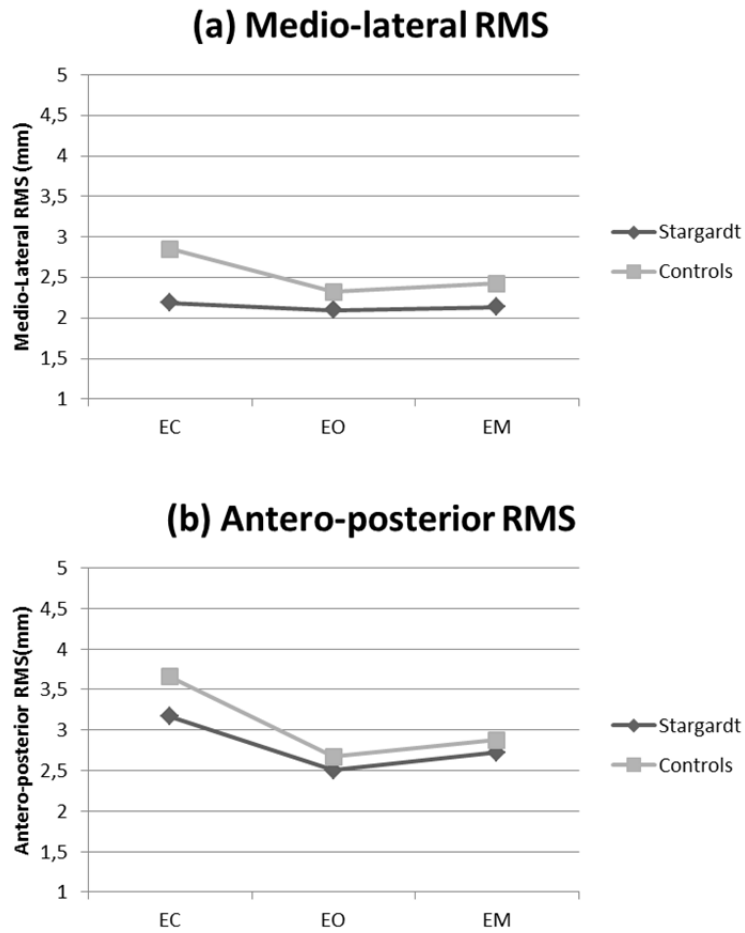


Fig. 1 – Postural sway in (a) Medio-Lateral and (b) Antero-Posterior directions for Stargardt patients and controls.

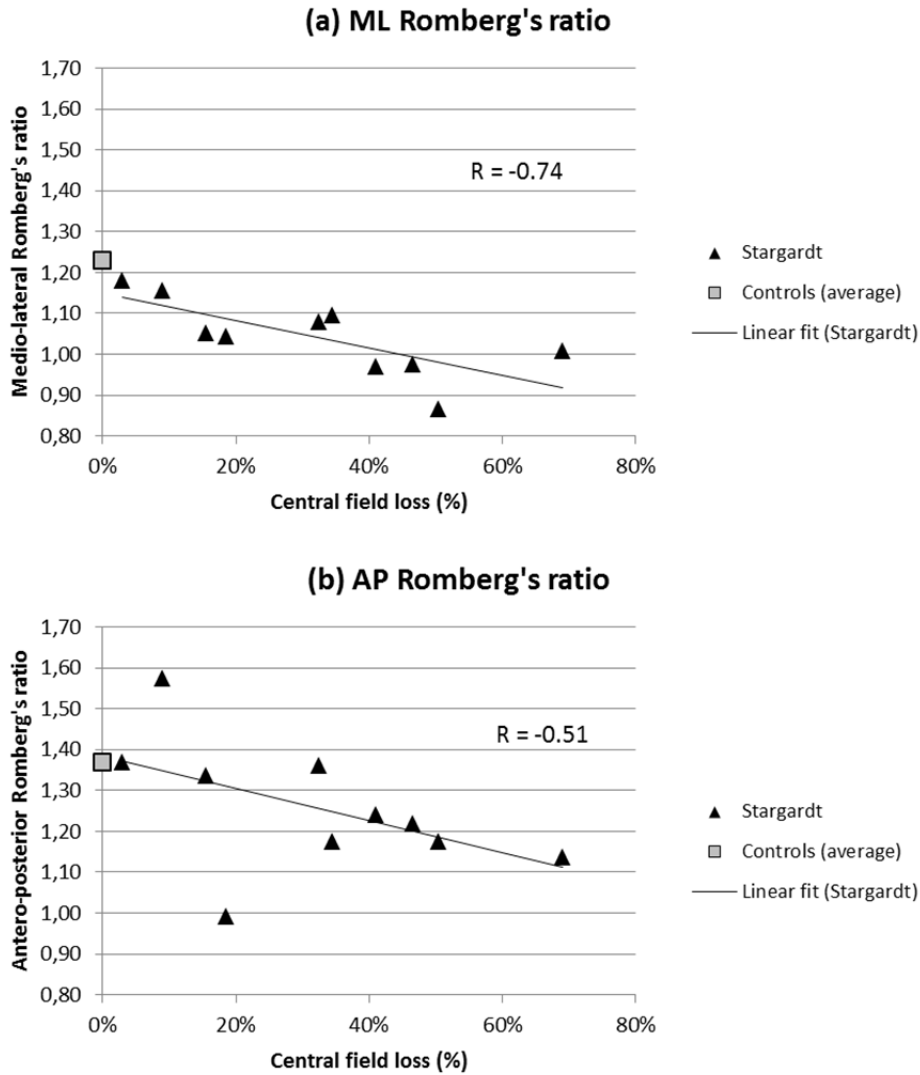


Fig. 2 – Scatter plot of the Romberg's ratio (EC condition measure divided by the EO measure) against central field loss, in Stargardt patients, in the Medio-Lateral (a) and Antero-Posterior (b) directions. The average Romberg's ratio, across controls, is also represented for reference.