Repeated visually-guided saccades improves postural control in patients with vestibular disorders

L'esecuzione ripetitiva di movimenti saccadici migliora il controllo posturale dei pazienti affetti da disfunzione vestibolare

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Summary

One of the most recent and promising theoretical hypotheses for compensation of persistent asymmetry of dynamic vestibulo-ocular gain is sensory substitution. As a switch between oculomotor and vestibulo-ocular systems, saccadic eye movements are engaged in humans to compensate the angular displacement of the head towards the labyrinthine defective side thus preserving the foveal fixation of the target. This study focused on the possibility that saccadic eye movements might also compensate for the impaired vestibulo-spinal reflexes and force the postural system to a more effective control on upright stance and verified whether this sway-stabilizing effect could be applied to patients with vestibular disorders and balance dysfunction. In the first experiment, 27 patients with unilateral labyrinthine hypofunction, 24 patients with central vestibular disorders and 24 healthy volunteers were evaluated by static posturography in 3 different visual conditions: a) eye open with fixation of a steady target, b) eye closed, and c) while performing horizontal visually-guided saccades. The percentage of individuals with a decreased body sway area during the oculomotor task was found to be higher in labyrinthine-defective patients as compared to those with central vestibular disorders and controls. In the second experiment, 46 patients with vestibular disorders both of central and peripheral origin, whose postural control improved by eye-tracking, as assessed by posturography, were later submitted to 12 consecutive training sessions based on repeated visually-guided saccades. Both the saccadic performances and postural control improved in all patients but a more pronounced effect was observed in those with peripheral vestibular disorders. Outcome of this rehabilitation technique was also corroborated by a general reduction of the perceived overall impairment from balance disorders as tested by a specific questionnaire.

Key words
Vestibular rehabilitation • Sensory substitution • Postural control • Saccadic eye-movement

Parole chiave
Riabilitazione vestibolare • Sostituzione sensoriale • Controllo posturale • Movimenti oculari saccadici

Riassunto
Una delle più recenti ipotesi interpretative del compenso vestibolare rispetto ad una persistente asimmetria dinamica del guadagno dei riflessi vestibolo-oculomotori conseguente a deafferentazione del recettore labirintico è la sostituzione sensoriale. In una sorta di scambio funzionale tra i sistemi visuo- e vestibolo-oculomotori, alcuni movimenti saccadici di direzione opposta allo spostamento angolare della testa verso il lato del labirinto leso mantengono la fissazione del bersaglio visivo sulla fovea retinica. Questo studio ha esplorato la possibilità che i movimenti oculari saccadici possano inoltre compensare o correggere l’asimmetria dei riflessi vestibolo-spinali e indurre il sistema posturale ad un più efficiente controllo dell’equilibrio statico nei pazienti affetti da disfunzione vestibolare e, in tal caso, se tale effetto di stabilizzazione potesse essere impiegato come tecnica di riabilitazione vestibolare.

Nel primo esperimento, 27 pazienti affetti da deficit labirintico monolaterale, 24 pazienti affetti da disfunzione vestibolare centrale e 24 soggetti sani sono stati sottoposti a posturofonia statica computerizzata in tre differenti condizioni visive: a) ad occhi aperti con fissazione di una mira ferma, b) ad occhi chiusi, e c) durante l’esecuzione di movimenti saccadici guidati da mira luminosa. La percentuale dei soggetti per i quali è stato possibile rilevare una riduzione delle oscillazioni del corpo durante l’esecuzione di tale compito visuo-oculomotorio è risultata maggiore nei pazienti labirintopatici rispetto a quelli con disfunzione vestibolare centrale che al gruppo di controllo. Nel secondo esperimento, 46 pazienti con disfunzione vestibolare sia centrale che periferica, per i quali si era potuto evidenziare un effetto posturale stabilizzante dell’attività visuo-oculomotoria, sono stati sottoposti a 12 sedute consecutive di riabilitazione basata sull’esecuzione di ripetuti movimenti saccadici in risposta a bersagli mobili. Al termine del ciclo riabilitativo, sia la qualità dei saccadi che il controllo posturale hanno dimostrato significativi incrementi, di maggiore rilevanza nel gruppo dei labirintopatici rispetto ai pazienti affetti da disfunzione vestibolare centrale. Tale risultato è stato inoltre accompagnato da una significativa riduzione soggettiva dell’impatto della vertigine sulla qualità della vita, come dimostrato grazie all’impiego di un questionario ad hoc.
Introduction

A surrounding pattern moving during steady fixation or voluntary saccades generates a similar displacement of images across the retina. In the first case, there is a perception of movement, while in the second, the visual environment appears to be stable. A passive shift of the ocular globe, as obtained by a soft finger touch on the eyelid, causes a perception of torsional movement of the visual scene, but the same counter-rolling of the eyes elicited by a head tilt does not. The perceived stability of the world during saccades, referred to as ‘space constancy’, has been a topic of scientific research since Helmholtz and many theories have been proposed to explain the different processing modalities of visual information during active and passive eye movements. In terms of optical perception of motion (exocentric motion), it is generally held that visual sensitivity (detection and acuity) are actively reduced by the central nervous system during the course of active eye movements (saccadic suppression). In a similar way, different conditions of moving images across the retina exert a different influence on postural stability. A moving surrounding pattern during fixation enhances lateral body sway, but a similar displacement of retinal images generated by voluntary saccades does not. Since the decisive cue for visual stabilization of posture is the detection of retinal target displacement, it is not unreasonable to suspect that its effect depends on whether it is voluntarily or externally produced. It has already been established that vertical saccadic eye movements evoked by asking subjects to periodically track a pair of targets which light alternately, at 0.1-1.3 Hz, result in a reduction of body sway and this phenomenon was defined as “sway-stabilizing effect”. When horizontal eye movements were elicited by pursuing a sinusoidal target, both normal subjects and patients with schizoaffective disorders showed a decreased gravimetric area and a tendency towards postural stabilization and these results suggest interesting neurophysiological observations. The interaction between eye tracking and body sway could be attributed to at least 3 mechanisms:

1. a synergic action between saccadic and vestibular systems on postural control;
2. an indirect action of eye movements on neck dorsal muscles;
3. an increase of the visual feedback control of posture caused by the same central processing involved in visual stability during active eye movements.

The synergistic tendency for saccadic eye movements to improve vestibulo-ocular reflex slow-phase performance is known to achieve a correct final gaze position to a point in space shifted in the direction of head rotation thus suggesting a gaze-stabilizing effect of visual-vestibular interaction. In a similar way, it could be hypothesized that the saccadic and vestibular system co-operate in maintaining an appropriate posture in response to specific motor programmes. In head fixed subjects, a phasic coupling between saccades and dorsal neck muscle activity has been demonstrated. The main type of motor unit discharge pattern in the splenius showed a triphasic profile: a pre-saccadic inhibition, a per-saccadic burst and a post-saccadic tonic discharge that is proportional to eye position. To our knowledge, the interaction of this phasic eye-neck coupling with postural sway has not been further investigated.

The aim of the present study was, therefore, twofold: the first (Experiment A) was to establish whether horizontal saccades performed in an active upright stance position induce substantial changes in body sway in a sample of patients with peripheral and central vestibular disorders and in a population of age-matched healthy volunteers (control group); the second (Experiment B) was to establish whether the presence of a ‘sway-stabilizing effect’, induced by saccadic eye movements, could be employed as a technique of rehabilitation in patients with vestibular disorders who complain of chronic unsteadiness and gait disturbance. Recordings of the parallel evolution of balance and of saccade parameters are described.

Experiment A

Material and methods

SUBJECTS

A total of 27 unilateral labyrinthine-defective patients (22 with vestibular neuritis, and 5 with Ménière’s disease in the intercritic period) and 24 patients with central vestibular disorders (12 patients with multiple sclerosis, 12 patients with cerebral vasculopathy) were selected in the ENT Clinic Centre for Vestibular Testing, University of Modena and Reggio Emilia. This series comprised 20 males (39.2%) and 31 females (58.8%) of comparable age (males: range 38-57 years, mean: 50.2; females: range 35-60 years, mean: 48.2). Patients’ data were compared with those obtained from 24 healthy subjects, well-matched for sex (9 males, 37.5%; 15 females, 62.5%) and age (males: range 36-60 years, mean: 48.8; females: range 33-58 years, mean: 46.7). Healthy subjects were recruited on the basis of normal vestibular examination and none reported a history of vertigo or balance disorders. All subjects had normal binocular vision and visual acuity sufficient to clearly identify the red diode used for visual tracking at a distance of 150 cm. The experimental proto-
col followed the recommendations of the Declaration of Helsinki for Human Experimentation and informed consent was obtained from each participant before examination.

**Electro-oculography**

A computerized electro-oculography (EOG) examination (Saccadic Analysis System, Toennies Ltd., Wurzburg, Germany) was performed in all cases to evaluate oculomotor (saccades and smooth-pursuit) and optokinetic functions. The EOG battery included tests for spontaneous and gaze nystagmus, 3 cycles of sinusoidal rotation testing with a maximum speed of 60°/sec for vestibulo-ocular reflex and bithermal irrigation of both ear canals for labyrinthine activity. A 30% right/left excitability difference on caloric testing was the necessary requirement for a significant labyrinthine hypofunction. The neuro-otological examination was completed by cerebral magnetic resonance in all cases.

**Static-platform posturography and visual eye tracking device**

Static posturography was performed with the subject standing on a stable force-plate sensitive to vertical force. The force-plate was mounted on 3 strain-gauge force transducers which are positioned at the vertices of an equilateral triangle, providing description of body sway in terms of displacement of the centre of pressure (COP) of the patients (i.e., roughly the projection of the centre of mass to the ground). The stabilometric platform (S.Ve.P. Amplifon) is positioned, in our laboratory, in front of a diode bar which provides both fixed and moving targets. Visual background was a full-field grating pattern of 25 cm-wide white and grey vertical stripes. Stabilometric recordings were performed in standardized conditions. The subjects were instructed to maintain a relaxed, motionless upright stance, the head fixed to the trunk by a special helmet (Fig. 1) under 3 different conditions:

1. during steady fixation (SF) of a red diode at their eye level, at a distance of 150 cm;
2. during the execution of horizontal visually-guided saccades (GS) elicited by a diode target which is lit alternatively at 1 Hz, at a distance of 30° of arc on a horizontal bar;
3. with eye closed (EC), in total darkness. In both visual conditions, the illumination of the laboratory was set at 2000 lx, thus preventing the deterioration of dynamics and visual guided targeting saccades in darkness. The duration of each test was 52 seconds.

**Stabilometric parameters and statistical analysis**

Stabilometric data were sampled at 5 Hz in each test. Body sway was computed by calculating an elliptic area which corresponds to 90% of the COP positions over time. This procedure is designed to eliminate 10% of the more extreme positions of COP which could be due to involuntary perturbations of quiet stance. Three parameters were used to determine the weighting of fixed visual input and of visually-guided saccades on static postural control in patients and controls: a. b. c.

a. mean amplitude of body sway area in SF, GS and EC conditions;
b. ratio [(EC/SF)×100], which corresponds to a posturographic Romberg’s quotient;
c. ratio [(GS/SF)×100], which reflects the difference between the two visual conditions.

Both patients and controls were divided into 3 groups according to an interval scale of the ratio [(GS/SF)×100]:
- Group 1 if [(GS/SF)×100] is > 120;
- Group 2 if [(GS/SF)×100] is between 80 and 120;
- Group 3 if [(GS/SF)×100] is < 80.

The subjects in Group 1 are destabilized by visually-guided saccades, subjects in Group 2 are indifferent and subjects in Group 3 show a stabilizing effect of eye tracking on body sway area. Pearson chi-square was used to test the null hypothesis that subjects with the ‘stabilizing effect’ are not distributed equally over pathological categories and controls. Analysis of variance (ANOVA) and post-hoc analysis with
Bonferroni test were used to test the null hypothesis that means of body sway area in the three conditions (SF, GS, and EC) and of both ratio [(GS/SF) x 100] and [(EC/SF) x 100] were not different between labyrinthine-defective patients, patients with central vestibular disorders and controls. A value of p < 0.05 was considered significant in all statistical tests.

Results

Regardless of pathological category, Group 1 comprised 4 subjects (5.3%), Group 2, 21 subjects (28%) and Group 3, 50 subjects (66.7%) (Fig. 2). Subjects with a sway-stabilizing effect of visually-guided saccades (Group 3) were differently distributed over patients and controls (F = 4, p < 0.05). The percentage of these subjects was higher in labyrinthine-defective patients, in comparison both with patients with central vestibular disorders and controls. The percentage of subjects with no relevant saccadic interference on body sway (Group 2) was higher in patients with central vestibular disorders and in controls than in labyrinthine-defective patients. These latter had no subjects in Group 1, while only two subjects of Group 1 were present both in controls and in patients with central vestibular dysfunction. These data clearly indicate that postural sway is decreased by visually-guided saccades in a large percentage of cases and also indicate that labyrinthine-defective patients are the pathological category most frequently conditioned by this phenomenon (Fig. 3).

Visual stabilization of posture: static versus dynamic fixation

No differences in mean values of the body sway area were found, either in SF or GS conditions, between patients and controls (F = 0.456, p = 0.636; F = 2.118, p = 0.128). In the EC condition, body sway showed a significantly greater increase in patients with central vestibular disorders than in labyrinthine-defective disorders (p < 0.05) and in controls (p < 0.005). A difference of body sway area, in EC condition, was found also between the two latter samples (p < 0.05). The mean value of [(EC/SF) x 100] was significantly increased in patients with central vestibular disorders in comparison with labyrinthine-defective (p = 0.048) and normal subjects (p = 0.004), and this finding confirms the heavy influence of visual cues on postural control in patients with central vestibular dysfunctions. The sway-stabilizing effect is more effective on the postural control of labyrinthine-defective patients than those with central vestibular disorders (p < 0.05), while no difference was found when the latter were compared with controls (p > 0.05) (Tables I-III).

![Fig. 2. ‘Sway stabilizing effect’ in entire sample. Group 1 is composed of 4 subjects (5.3%), Group 2 of 21 subjects (28%) and Group 3 of 50 subjects (66.7%).](image_url)
Experiment B

Materials and methods

SUBJECTS

A total of 33 labyrinthine-defective patients (11 bilateral and 22 unilateral defective patients) and 23 patients with central vestibular disorders (18 with cerebral vasculopathy and 5 presenting multiple sclerosis) were selected in the ENT Clinic Centre for Vestibular Testing, University of Modena and Reggio Emilia. The study population comprised 30 males (53.6%) and 26 females (46.4%) of similar age (males: age range 46-60 years, mean: 53.2; females: 42-62 years, mean: 49.9). Inclusion criteria for the rehabilitation programme were:

1. complaints of chronic unsteadiness (lasting more than 6 months);
2. evidence of abnormal postural control (as demonstrated by static posturography);
3. presence of a well-documented ‘sway-stabilizing effect’ \( [(GS/SF) \times 100] < 80 \) during posturographic examination.
REHABILITATION OUTCOME IN ENTIRE SAMPLE

Body sway area, as expressed by COP, was significantly reduced by therapy both in SF and EC (p < 0.005). The stabilometric Romberg quotient, on the other hand, was increased (p < 0.005). As far as the saccadic analysis is concerned, MPV and ACC were improved after training (p < 0.005) with the exception of DEL which remained unchanged (p > 0.05). The self-rated assessment of quantitative characteristics of dizziness and of its impact on quality of life was significantly decreased (p < 0.005) (Table IV).

Close correlations were found between [(EC/SF) x 100] and [(EC before rehabilitation/SF after rehabilitation) x 100] and [(EC before rehabilitation/EC after rehabilitation) x 100] between patients with peripheral and central vestibular dysfunctions. A Pearson’s coefficient was also used to correlate parametric variables and a p value of < 0.05 was considered statistically significant.

Table I. Mean values for stabilometric parameters (body sway area) in steady fixation (SF), with visually guided saccades (GS) and with eye closed (EC) conditions and of the two ratio [(EC/SF)x100] and [(GS/SF)x100].

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Conditions</th>
<th>Controls (0)</th>
<th>Peripheral (1)</th>
<th>Central (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF</td>
<td>Mean</td>
<td>230.38</td>
<td>260.15</td>
<td>289.75</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>97.07</td>
<td>255.32</td>
<td>213.89</td>
</tr>
<tr>
<td>GS</td>
<td>Mean</td>
<td>178.63</td>
<td>136.33</td>
<td>257.33</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>127.41</td>
<td>73.10</td>
<td>165.03</td>
</tr>
<tr>
<td>EC</td>
<td>Mean</td>
<td>257.15</td>
<td>316.38</td>
<td>495.00</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>203.36</td>
<td>214.05</td>
<td>319.00</td>
</tr>
<tr>
<td>[(EC/SF)x100]</td>
<td>Mean</td>
<td>119.85</td>
<td>143.19</td>
<td>220.79</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>55.07</td>
<td>89.06</td>
<td>160.65</td>
</tr>
<tr>
<td>[(GS/SF)x100]</td>
<td>Mean</td>
<td>65.50</td>
<td>58.19</td>
<td>81.33</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>36.44</td>
<td>20.46</td>
<td>29.70</td>
</tr>
</tbody>
</table>

Table II. One-way analysis of variance and significance levels of statistical difference (p < 0.05) between stabilometric parameters (body sway area) in steady fixation (SF), with visually-guided saccades (GS) and with eye closed (EC) conditions and of the two ratios [(EC/SF)x100] and [(GS/SF)x100].

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ANOVA</th>
<th>F</th>
<th>t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF</td>
<td></td>
<td>0.456</td>
<td>0.636</td>
</tr>
<tr>
<td>GS</td>
<td></td>
<td>2.118</td>
<td>0.128</td>
</tr>
<tr>
<td>EC</td>
<td></td>
<td>6.155</td>
<td>0.003</td>
</tr>
<tr>
<td>[(EC/SF)x100]</td>
<td></td>
<td>5.852</td>
<td>0.004</td>
</tr>
<tr>
<td>[(GS/SF)x100]</td>
<td></td>
<td>4.094</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Table III. Test post hoc (Bonferroni) for differences between samples (0 = controls, 1 = labyrinthine-defective patients, 2 = patients with central vestibular disorders).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Samples (I)</th>
<th>Differences between means (I-J)</th>
<th>SD</th>
<th>t test</th>
</tr>
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<tbody>
<tr>
<td>EC</td>
<td>2 0</td>
<td>178.63</td>
<td>53.41</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>2 1</td>
<td>237.85</td>
<td>65.18</td>
<td>0.046</td>
</tr>
<tr>
<td>[(EC/SF)x100]</td>
<td>2 0</td>
<td>100.93</td>
<td>30.56</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>2 1</td>
<td>77.60</td>
<td>31.45</td>
<td>0.048</td>
</tr>
<tr>
<td>[(GS/SF)x100]</td>
<td>2 0</td>
<td>23.15</td>
<td>8.21</td>
<td>0.019</td>
</tr>
</tbody>
</table>
PERIPHERAL VERSUS CENTRAL VESTIBULAR DYSFUNCTION

It was confirmed that \((\text{GS}/\text{SF}) \times 100\) is higher in patients with vestibular peripheral deficit than in those with central vestibular dysfunction \((p < 0.005)\) and it was observed that both \((\text{SF before rehabilitation}/\text{SF after rehabilitation}) \times 100\) and \((\text{EC before rehabilitation}/\text{EC after rehabilitation}) \times 100\) are greater in the first pathological sample than in the second (albeit, significance level was reached only for \((\text{EC before rehabilitation}/\text{EC after rehabilitation}) \times 100\)) (Table VI).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pathology</th>
<th>Mean values</th>
<th>SD</th>
<th>t test (Sig.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>((\text{GS}/\text{SF}) \times 100)</td>
<td>Peripheral</td>
<td>31.23</td>
<td>19.99</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Central</td>
<td>49.97</td>
<td>21.36</td>
<td></td>
</tr>
<tr>
<td>((\text{SF before rehabilitation}/\text{SF after rehabilitation}) \times 100)</td>
<td>Peripheral</td>
<td>317.93</td>
<td>194.66</td>
<td>0.171</td>
</tr>
<tr>
<td></td>
<td>Central</td>
<td>226.55</td>
<td>133.22</td>
<td></td>
</tr>
<tr>
<td>((\text{EC before rehabilitation}/\text{EC after rehabilitation}) \times 100)</td>
<td>Peripheral</td>
<td>326.40</td>
<td>233.97</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>Central</td>
<td>165.87</td>
<td>80.25</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

As suggested in previous investigations, the present data confirm that visually guided saccades interact with static postural control. The general effect is directed to a stabilization of body sway during upright stance but is not present in a large percentage of normal subjects or in patients with central vestibular disorders (33% and 42%, respectively). On the other hand, the stabilizing effect is present in a large percentage of patients with peripheral vestibular disorders (88%). This result was corroborated by a significantly increased ‘sway stabilizing effect’ in peripheral vestibular patients, in comparison with normal subjects and with patients with central vestibular disorders. Since all subjects were examined under standardized conditions, the source of this different reduction of body sway may account for a supplementary synergy between oculomotor (namely saccades) and vestibulo-spinal reflexes in the multiple sensory strategy that compensate postural instability as a consequence of a peripheral vestibular failure. The ‘sway stabilizing effect’ was not correlated with the ‘weight’ of static visual cues on postural control, either in pathological or normal populations. This finding suggests that the reduction of body sway induced by active eye movements occurs independently of individual weighting of static visual cues in the control of balance. Further investigations are necessary to identify the physiological mechanism of this interaction that, hypothetically, can be identified in a similar central process both of visual and postural stability or in a supplementary somatosensory cue (for example, from extra-ocular muscle proprioception) which becomes more consistent and reliable in the recovery of postural stability whereas labyrinthine information is defective. The presence of a well-documented ‘sway stabilizing effect’ can be employed in vestibular rehabilitation and has been demonstrated to be useful in the reduction both of actual postural sway and perceived overall impairment from chronic balance disorders in patients with various vestibular dysfunctions. The positive outcome of this technique is greater in labyrinthine-defective patients than in patients with central vestibular dysfunction and is directly related to the reduction of body sway induced by visually-guided saccades, while it is not correlated with the Romberg’s quotient either. This result confirms that the positive interaction between saccadic eye movements and vestibulo-spinal reflexes in the recovery of postural control does not depend on the same mechanism of static visual stabilization of body sway. In contrast, improvements both of saccadic performances and of Romberg’s quotient were observed after rehabilitation that are probably due to the technique itself that is based exclusively on repeated visual-oculomotor stimulation that could lead both to a different selection of sensory orientation strategy and to an improvement in neural plasticity of the cerebral structures involved in saccadic generation.

The most striking result of this study is the rapid improvement in saccade parameters and of postural control obtained in upright-standing subjects with head fixation and without sensory conflict while previous experiments in primates and humans have demonstrated that the adaptive mechanisms for vestibular deficit are more efficient in opposite conditions. A possible interpretation of this discrepancy could be referred to the different activation of cortical and sub-cortical neural networks during vestibular, optokinetic and saccadic eye movements which could lead to different patterns of the recovery process.

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