Testing the central vestibular functions: a clinical survey

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In vestibular examinations anomalies in the saccade and smooth pursuit tests as well as the fixation suppression after caloric stimulation might indicate central lesions in the vestibular system. Additionally, a high gain in the torsion test is suspicious of cerebellar dysfunction. In this study, 141 patients out of 973 had at least one of these anomalies. For 125 patients we were able to compare the initial findings in the vestibular examination with the final diagnosis by otologists, neurologists and general practitioners. The complaints of 37.6% of the patients with these electronystagmographic (ENG) anomalies appeared to be of central origin. Abnormal saccades, an abnormal smooth pursuit, and an elevated gain in the torsion test were not independently diagnostic for central vestibular disease. The fixation suppression index appeared to be lower for subjects with peripheral vestibular disease. Otologists more often referred their patients to a neurologist if the fixation index was elevated.

Keywords vestibular tests central functions neural disease smooth pursuit saccades fixation index

Patients with complaints suggesting a vestibular disorder, such as dizziness or problems of balance, are usually tested by means of electronystagmography (ENG). Under several test conditions the movements of the eyes are recorded and the nystagmus is analysed. The results are used to assess the functionality of the vestibular system. This indirect method of measuring forms the main limitation of the assessment: between the labyrinths and the eyes several systems, such as the cerebellum, the oculomotor system, the frontal and parietal cortex, and various brainstem nuclei have to function normally. To some extent these central systems are tested by looking at the saccades, the smooth pursuit and the fixation suppression after caloric stimulation. According to Davis et al. abnormal saccades are indicative of central vestibular disease and peripheral vestibular disease does not cause abnormal saccades. They also state that the smooth pursuit test is of the utmost importance in differentiating peripheral from central vestibular disease, although in acute peripheral vestibular disorders smooth pursuit may be impaired. In addition, they indicate that poor fixation after caloric stimulation may be caused by a lesion of the cerebellum or the corticofugal fibres deep in the temporal lobe. Abnormalities in these tests, however, are rarely independently diagnostic of specific disease processes and sometimes even contradictory. They are, however, often used as an indication for further diagnostic tests, such as EEG, computerised tomography (CT) or magnetic resonance imaging (MRI). It has to be noted that the psychophysical condition of the subject also influences the outcome of tests that assess the central vestibular system.

The purpose of this study was to evaluate the clinical significance of ENG anomalies that suggest central nervous system disease. We obtained information on the history and follow-up of 125 patients by reviewing their medical records from the Departments of Otorhinolaryngology and Neurology and by sending questionnaires to their general practitioners.

Materials and methods

PATIENTS

Study patients were drawn from the Audiological Department of the University Hospital of Utrecht. Otorhinolaryngologists from this hospital and some of the surrounding hospitals referred the patients to the Audiological Department for vestibular examination. In a 28-month period...
between 1996 and 1998, ENG was carried out on 973 patients. From this group we selected 141 patients (14.5%) using the criterion that at least one of the following ENG anomalies was found: (1) dysmetric, slow or irregular saccades; (2) abnormal smooth pursuit, including both gain abnormalities and saccadic or ataxic eye movement patterns; (3) poor fixation suppression of caloric nystagmus, or (4) increased gain during sinusoidal vertical axis rotation. By reviewing their medical records from the Departments of Otorhinolaryngology and Neurology we obtained information on the outcome of further diagnostic tests, if any were performed. In addition we sent questionnaires to the general practitioners of the patients who did not have a follow-up in the University Hospital of Utrecht. Seventy-three out of 90 (81.1%) general practitioners responded. We were able to create a dataset of 125 patients, with the results of the ENG test battery and the follow-up data direct from their neurologist, otorhinolaryngologist or via their general practitioner.

VESTIBULAR TESTING

The vestibular system was evaluated via the vestibulo-ocular reflex by means of ENG. Procedures and normal values in this study are in accordance with the guidelines that were adopted by the Committee on Hearing, Bioacoustics, and Biomechanics (CHABA) of the National Research Council in 1992.3 Horizontal eye movements were recorded binocularly. In addition, vertical eye movements of the left eye were recorded. The computerized analysis (Toennies Nystagmolyzer) of the nystagmus was performed on the slow component's velocity (SCV). After calibration, the following tests were performed:

1. Saccades: A light dot on a computer-controlled television screen opposite the patient alternates every 2 s, 20° to the left or to the right side of the patient. The patient is asked to track the dot. The recorded saccades are checked for undershoots, overshoots, and other irregularities. The maximum velocity of the saccades is also calculated. Maximum velocities under 200 µm/°/s are considered abnormal.

2. Smooth pursuit: A light dot on a computer-controlled television screen is moving slowly and sinusoidally (0.2 Hz) in a horizontal plane with a 30° amplitude. The patient is asked to follow the dot. The gain is calculated and the recorded eye movements are checked for saccadic or ataxic pursuit patterns. The gain is defined as the quotient of the amplitude of the eye movements and the amplitude of the visual stimulus.

3. Torsion test (Sinusoidal earth vertical axis rotation): The patient is sitting in the dark on a chair that is sinusoidally rotated in the horizontal plane with a 120° amplitude (0.1 Hz). The gain and the directional preponderance (DPT) are calculated. The gain is defined as the quotient of the SCV of the nystagmus and the velocity of the rotating chair. Normal values for the gain are between 25% and 90%. In the torsion test, directional preponderance is the difference between the means of the three highest SCVs to the right and to the left, expressed in percentages of the sum of both means. Values >20% are considered abnormal.

4. Caloric stimulation: In the dark, each ear is irrigated with water at 30°C and 44°C for 20 s at the rate of 200 ml/min. The response of each labyrinth is calculated as well as the difference between the responses of the labyrinths and the directional preponderance. For the caloric test, directional preponderance (DPC) values of ≥22% are considered abnormal. Hypofunction of a labyrinth is said to be present when the SCV of the nystagmus after caloric stimulation with warm and cold water is below 10°/s. Unilateral vestibular paresis is said to occur when the difference between the responses of the labyrinths is ≥22%. Eighty seconds after each caloric stimulation the patient is asked to fixate on a light dot for 10 s. The fixation suppression (FS) index is defined as the quotient of the SCV during fixation and the SCV at the culmination phase. FS indices of ≥0.3 are considered abnormal.

All ENG parameters, described above, were included in the analyses. Since the outcome of the central tests is extremely dependent on the alertness of the patient, a parameter that takes the consistency of several test results into account was thought to be more accurate. Therefore, three additional parameters were derived from these registrations for each patient: 1. NCA (Number of Central Test Anomalies): The number of tests that presented ENG anomalies, which suggest central vestibular disease. The maximum number is four (abnormal saccades, abnormal smooth pursuit, elevated FS index, and elevated torsion-gain).

2. PCA (Percentage of Central Test Anomalies): The number of tests that demonstrated ENG anomalies, which suggest retro labyrinthine disease, divided by the number of performed tests. The FS index could only be determined for 80 patients since some patients had bilateral absent caloric responses, and caloric stimulation was not performed on all patients since some had a tympanic membrane perforation. This parameter takes into account whether or not all four tests were performed.

3. TM (Two or More): A binomial indicator, being 1 when two or more of the three following central tests (saccade test, smooth pursuit test, and FS test) were abnormal; otherwise TM is 0. The elevated gain of the torsion test was added more recently to the set of central tests panel, and therefore did not contribute to this parameter.

ANALYSIS

The neurotological findings and demographic features of the patients with confirmed central vestibular disease were compared to those of the other patients. In a similar fash-
ion, patients who consulted a neurologist following their vestibular examination for complaints of dizziness or problems of balance were compared to those who did not seek the opinion of a neurologist. Subsidiary analyses were performed for the following grouping variables: (1) patients > 65 years vs. those under that age; (2) male patients vs. female patients; and (3) patients with a relevant history of optokinetic or ocular disease vs. those without known ophthalmopathy.

Groups were compared using the $\chi^2$ test or Fisher’s exact test for proportions. Student’s $t$-test or one-way ANOVA were used for group comparisons of continuous variables with no significant skewness at the 5% level. All tests were two-sided. Differences between the groups were considered significant at the 5% level.

Results

ELECTRONYSTAGMOGRAPHY

1. In 86 patients out of 125 (68.8%) the results of the saccade test were abnormal. The saccades were either slow or inaccurate.
2. In 107 patients out of 124 (86.3%) we found an abnormal smooth pursuit. This includes both abnormal pursuit patterns and gain anomalies.
3. Caloric stimulation was performed in 114 patients, since the test could not be performed in 11 patients with a tympanic membrane perforation. Unilateral vestibular paresis was demonstrated in 42 patients (36.8%). Ten patients (8.0%), all men, did not produce any nystagmus after caloric stimulation (bilateral vestibular failure). Therefore, no DPC could be calculated for them. An abnormal DPC was found in 19 patients out of 104 (18.3%). Altogether, the results of the caloric test were abnormal in 60 patients (52.6%).
4. The FS index was elevated in 24 patients out of the 80 (30.0%) for whom this index was determined.
5. The torsion test showed an abnormal DPT in seven patients (5.6%) out of 125. A gain of > 90% (hyperfunction) was found in 36 patients (28.8%). Altogether, the results of the torsion test were abnormal in 55 patients (44.0%).
6. The mean of NCA was 2.024 (SD = 0.777).
7. The mean of PCA was 56.0% (SD = 21.0%).
8. The TM was 1 for 84 patients (67.2%), indicating that two or more central tests were abnormal. Thirty-four patients (27.2%) had abnormal results for only one of the three central tests. Seven patients (5.6%) had normal results for the saccade test, the smooth pursuit test, and the FS test; these patients were included in this study because of their elevated torsion-gain.

FOLLOW-UP

In Table 1 an overview is given of the diagnoses that were obtained from the follow-up. According to the diagnosis patients were divided into three groups. A large group was composed of 47 patients (37.6%) with a wide spectrum of central disease. Twenty-nine patients (23.2%) were eventually diagnosed with distinct peripheral vestibular dysfunction. In 49 patients (39.2%) no anatomical or physiological substrate could be found to explain their ENG results. Their complaints were said to be either psychosomatic or unexplainable.

COMPARISON BETWEEN DIAGNOSIS CATEGORIES

In Table 2 some demographic features and the results of the vestibular tests are given for the three groups separately. In patients diagnosed with distinct labyrinthine disease the FS index was less frequently abnormal ($\chi^2 = 6.747$; degrees of freedom = 2; significance = 0.034) than the FS index of the patients in the two other groups. Also, unilateral vestibular paresis was found less frequently in the group with no diagnosis ($\chi^2 = 7.375$; degrees of freedom = 2; significance = 0.025) compared to the two other groups. For the other parameters we found no significant differences between the three groups.

NEUROLOGISTS: CONSULT OR NOT

The patients were also split up according to whether they did or did not consult a neurologist. It appeared that 55 patients (44.0%) consulted a neurologist and 67 patients (53.6%) did not. The general practitioners of three patients (2.4%) did not mention whether these patients had consulted a neurologist or not. In Table 3, demographic features and ENG findings are given for both groups. All variables were evenly distributed over both groups, except for the FS index. The FS index was more often elevated ($P = 0.012$) in the group of patients who consulted a neurologist (41.9%) than in the group who did not (14.3%).

AGE AND SEX

The mean age of the patients was 52.1 years (range: 4.7–81.9 years; SD = 16.6 years). Twenty-nine patients (23.2%) were > 65 years. None of the ENG results of these patients differed significantly from the patients < 65 years.

The group of patients consisted of 67 females (53.6%) and 58 males (46.4%). The difference in age between the sexes was not significant. An elevated gain in the torsion test was more often found ($P = 0.003$) in female (40.3%) than in male patients (15.5%). Abnormal results of the caloric test, however, were more often found ($P = 0.040$)
in men (63.5%) than in women (43.5%). These findings might be caused by the high number (10) of male patients with bilateral absent caloric responses, which relatively decreases the number of male patients with an elevated gain. In a subsidiary analysis, excluding those 10 men, the abnormally large torsion gain was no longer significantly more often found in female patients ($P = 0.056$). Other ENG anomalies, including unilateral vestibular paresis and abnormal DPC, were equally distributed over both sexes.

### Table 2. Comparison between diagnosis categories

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Central ($n = 47$)</th>
<th>Peripheral ($n = 29$)</th>
<th>No diagnosis ($n = 49$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (SD)</td>
<td>55.1 (15.0)</td>
<td>53.0 (16.2)</td>
<td>48.7 (17.9)</td>
</tr>
<tr>
<td>Female patients</td>
<td>46.8%</td>
<td>65.5%</td>
<td>53.1%</td>
</tr>
<tr>
<td>Patients with abnormal saccade test</td>
<td>76.6%</td>
<td>55.2%</td>
<td>69.4%</td>
</tr>
<tr>
<td>Patients with abnormal smooth pursuit</td>
<td>89.4%</td>
<td>82.2%</td>
<td>85.4%</td>
</tr>
<tr>
<td>Patients with elevated FS index</td>
<td>43.3%</td>
<td>9.5%*</td>
<td>31.0%</td>
</tr>
<tr>
<td>Patients with abnormal caloric tests</td>
<td>61.4%</td>
<td>61.5%</td>
<td>38.6%</td>
</tr>
<tr>
<td>Patients with unilateral vestibular paresis</td>
<td>43.2%</td>
<td>50.0%</td>
<td>22.7%*</td>
</tr>
<tr>
<td>Patients with caloric directional preponderance (DPC)</td>
<td>17.9%</td>
<td>33.3%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Patients with torsion directional preponderance (DPT)</td>
<td>4.3%</td>
<td>6.9%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Patients with elevated gain in torsion test</td>
<td>23.4%</td>
<td>34.5%</td>
<td>30.6%</td>
</tr>
<tr>
<td>NCA: mean no. of central ENG anomalies (SD)</td>
<td>2.2 (0.82)</td>
<td>1.8 (0.73)</td>
<td>2.0 (0.75)</td>
</tr>
<tr>
<td>PCA: mean percentage of central anomalies (SD)</td>
<td>59.8% (21.5%)</td>
<td>48.3% (18.6%)</td>
<td>57.0% (21.1%)</td>
</tr>
<tr>
<td>TM: no. of patients with ≥ 2 abnormal central tests</td>
<td>76.6%</td>
<td>51.7%</td>
<td>67.3%</td>
</tr>
</tbody>
</table>

* $P < 0.05$. 

OPHTHALMOPATHY

Twenty patients out of 121 (16.5%) had a positive history of optokinetic or ocular disease. Their ENG results were not significantly different from those without eye disease. The general practitioners of four patients (3.2%) did not indicate whether the patients had a relevant history of eye disease or not.

CORRELATING ENG PARAMETERS

In a subsidiary analysis of the ENG parameters, we found that individuals with an elevated FS index more frequently \( (P \leq 0.004) \) have an elevated gain in the torsion test than individuals with normal FS. Patients with a strong DPC have more often \( (P \leq 0.019) \) a strong DPT as well.

Discussion

In this study we compared the outcome of central vestibular tests with the final diagnosis given by a neurologist or otolaryngologist to investigate the clinical importance of these tests. A prospective study, in which the same neurological and vestibular tests would be performed on all patients with both peripheral and central vestibular disorders, would be the best method to evaluate the clinical significance of ENG parameters that suggest central vestibular disease. Since only 14.5% of our entire population fitted the criterion that one or more of these parameters had an abnormal value, the costs, logistics and ethics of such a study would find that method impracticable. The current study has tried to take advantage of data already available for a large number of patients.

An abnormal saccade test alone, or an abnormal smooth pursuit test alone appeared not to be indicative of central vestibular disease. In theory, these tests should be able to differentiate between central and peripheral disorders of the vestibular system.\(^{14,18}\) In normal practice, however, it appears that the outcome of these tests depends on the alertness of the patient. This might be the reason for our findings.

The FS index proved to be significantly lower for patients with peripheral vestibular disease. The FS index, however, did not differentiate between patients in the central group and the group with no diagnosis. The latter group probably consists of patients with central and peripheral disease, which however, could not be demonstrated. It is not surprising, therefore, that the FS index is not significantly different between these two groups. The parameters NCA, PCA and TM appeared not to be significantly different in any of the three groups. Therefore, these parameters cannot be used to differentiate between a central or peripheral vestibular lesion.

The complaints of 37.6% of the patients with at least one ENG anomaly that suggested central vestibular disease turned out to be of central origin. This finding justifies further diagnostic tests for central nervous system disease, such as EEG, CT or MRI for these patients. In this study, patients with an elevated FS index were more often referred to a neurologist by their otolaryngologist than patients with a normal FS. Since it appeared that the FS index is an indicator for central disease this is good practice. It must, however, be noted that, due to the fact that patients with a high FS index are more often referred to a neurologist, it is likely that neurological disease is found more often in this group of patients.

An elevated gain in the torsion test merely proved not to be indicative of central vestibular disease. However, the number of patients with an elevated gain but with normal

| Table 3. Comparison between patients who consulted a neurologist and those who did not |
|-------------------------------|------------------|------------------|
| Baseline variables | Consulted neurologist (n = 55) | Did not consult neurologist (n = 67) |
| Mean age in years (SD) | 53.4 (17.0) | 51.0 (16.5) |
| Female patients | 58.2% | 50.7% |
| Patients with abnormal saccade test | 72.2% | 65.7% |
| Patients with abnormal smooth pursuit | 83.3% | 88.1% |
| Patients with elevated FS index | 41.9%* | 14.3% |
| Patients with abnormal caloric tests | 50.9% | 51.7% |
| Patients with unilateral vestibular paresis | 41.5% | 29.3% |
| Patients with caloric directional preponderance (DPC) | 13.7% | 24.0% |
| Patients with torsion directional preponderance (DPT) | 1.8% | 9.0% |
| Patients with elevated gain in torsion test | 29.1% | 28.4% |
| NCA: mean no. of central ENG anomalies (SD) | 2.2 (0.76) | 1.9 (0.76) |
| PCA: mean percentage of central anomalies (SD) | 58.0% (20.8%) | 53.9% (20.5%) |
| TM: no. of patients with \( \geq 2 \) abnormal central tests | 76.4% | 59.7% |

*\( P < 0.05. \)
saccades, normal smooth pursuit and normal FS was rather small. More patients with such a combination of test outcomes are needed to confirm our finding. It has to be stressed that the gain in the torsion test is one of the contributing parameters of the PCA indicator and therefore cannot be omitted as one of the parameters.

Peripheral vestibular lesions are sometimes said to cause changes in the results of central ENG tests, such as asymmetrical optokinetic nystagmus and abnormally slow smooth pursuit to the side opposite the side of a lesion. When comparing the central ENG results of the 42 patients with unilateral vestibular paresis to those of the 62 patients with symmetrically functioning labyrinths, no significant differences were found. Therefore, the effect of peripheral lesions on central ENG tests could not be demonstrated.

Age is a factor that should be taken into account when interpreting ENG results. Especially the smooth pursuit tends to be more often abnormal in the elderly. In this study, however, no such effect could be demonstrated, despite the large population and the wide range of ages of the examined patients. Because the differences between the sexes were no longer significant after exclusion of the patients with bilateral vestibular failure, we consider the differences between the sexes as coincidental findings which are not relevant.

Patients with optokinetic or ocular disease did not experience more difficulty in performing vestibular tests such as saccades and smooth pursuit. Although it remains important to realize that normally functioning eyes are a prerequisite of ENG testing, it is often possible to perform reliable ENG tests in patients with eye disease.

Directional preponderance indicates an imbalance of tone arriving at the oculomotor nuclei, resulting from an imbalance of vestibular tone between the two sides of the vestibular system. In patients with unilateral canal paresis such a directional preponderance can be found. Typically, this bias of the nystagmus is directed toward the side opposite the lesion. This ‘rule of thumb’ is valid for both caloric stimulation and rotational testing. Therefore, the correlation between DPC and DPT found in the present study, was expected.

Conclusions

1. Of all patients that underwent vestibular examinations, 14.5% had at least one ENG anomaly that suggested central vestibular disease.
2. Eventually, the complaints of 37.6% of the patients with these often accidental ENG findings turned out to be of central origin.
3. Abnormal saccades, abnormal smooth pursuit, and an elevated gain in the torsion test were not independently diagnostic for central vestibular disease.
4. The parameter PCA (percentage of central anomalies) was significantly lower for the patients with peripheral vestibular disease.
5. The FS index was significantly lower for the patients with peripheral vestibular disease.
6. Otolaryngologists more often referred their patients to a neurologist if the FS index was elevated.
7. Patients with known ophthalmoopathy do not necessarily perform worse in the saccade and smooth pursuit test.

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