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The Importance of Labyrinthine Examination in the Prognosis and Therapy for Balance in Spinocerebellar Ataxia

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Abstract

Introduction: Spinocerebellar ataxias (SCAs) are a heterogeneous group of neurodegenerative diseases that are characterized by the presence of progressive cerebellar ataxia. **Objective:** Identify vestibular disorders and demonstrate the importance of labyrinthine examination in the prognosis and therapy for balance in patients with SCAs. **Materials and Methods:** The study had a retrospective cross-sectional design and evaluated 57 patients, mean age of 41.6 years and standard deviation of 13 years. Patients underwent the following procedures: anamnesis, ENT examination and vestibular exam using electronystagmography (ENG). **Results:** The most frequent complaints were gait imbalance (71.9%), dysarthria (49.1%), dizziness (43.8%) and dysphagia (36.8%). 84.2% of the tests showed alterations. The most common tests with alterations were the caloric test (78.9%), slow saccades (61.4%) and the rotating chair test (49.1%). **Conclusion:** The clinical history of the patient and oculomotor alterations in the labyrinthine examination provide sufficient information for the proper use of virtual rehabilitation protocols in the treatment of imbalance, making it the most effective therapy method. It was evident that changes in ENG are related to the severity of the SCA or the clinical stage of the disease. The labyrinthine examination proved to be an important concomitant tool to clinical and genetic study.

Keywords: ataxia; spinocerebellar ataxias; spinocerebellar degenerations; vestibular diseases; nystagmus, pathologic.

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INTRODUCTION

Spinocerebellar ataxias (SCAs) are a heterogeneous group of neurodegenerative diseases that are characterized by the presence of progressive cerebellar ataxia and have initial clinical manifestations such as deterioration of balance and coordination, as well as ocular disorders[1-4]. SCA has a worldwide prevalence of 3 to 4.2 cases per 100,000 people[5]. The most common clinical symptoms in spinocerebellar ataxia dominant (SCAD) present as gait and appendage ataxia (dysmetria, diadochokinesia in limbs, intentional tremors), dysarthria, nystagmus, ophthalmoplegia, dysphagia, hearing loss (in some cases), pyramidal signs, lower motor neuron syndrome, cognitive dysfunction, epilepsy, visual disturbances (pigmentary retinopathy), peripheral neuropathy, dementia and movement disorders (including Parkinsonism, dystonia, myoclonus and chorea)[1,2,6-8].

With advances in molecular genetic techniques through the use of Polymerase chain reaction diagnostics (PCR), several genetic loci and genes have been discovered in different chromosomes, thus enabling a more rational use of genetic clinical classification[9]. The polyglutamine neurodegenerative diseases are characterized by the expansion of a polyglutamine tract in the mutant protein causing the disease. This mutant protein leads to a progressive loss of neuronal function and subsequent neurodegeneration of a specific group of neurons causing the phenotypic forms of each disease, in addition to the patient's ethnic origin, is of paramount importance. The appreciation of different neurological signs in SCAs and genetic study have provided a great aid in genotype-phenotype[2].

The identification of a patient with dominant SCA is made using a variety of clinical means and frequent associations that may occur along the course of the disease. Its etiology is mostly caused by mutations characterized by the presence of an expansive and unstable CAG trinucleotide repeat in the coding region of the tested gene. In Brazil, more specifically in the southern part of the country, we have tested a large number of families suffering from SCA[2,8]. Machado-Joseph disease (MJD), also known as SCA type 3, is the most common form of hereditary ataxia with autosomal dominant inheritance found in major world epidemiological studies[2,10,11].

Subtype prevalence rates vary among geographic regions. For example, the highest prevalence rates of SCA 2 are found in Cuba, India, England, France, and the USA, whereas SCA 3 is most prevalent in Portugal, Brazil, Germany, Japan, and China. Meanwhile, SCA 6 is particularly prevalent in Japan, Australia, and Germany, SCA 7 is most prevalent in Sweden, Finland, the USA, and China, and SCA 10 cases are concentrated in Mexico and Brazil[2,12,13]. Body balance depends on the integrity of the: vestibular system (VS) (labyrinth, vestibulocochlear nerve, nuclei, pathways and connections to the central nervous system - CNS); somatosensory system (sensory receptors located in tendons), muscles, joints and vision[14]. Any disturbance in visual, vestibulospinal, proprioceptive-somatosensory, cerebellar, or musculoskeletal function can lead to postural imbalance and changes in movements such as ataxia[14-17]. Oculomotor abnormalities in patients with cerebellar dysfunction exist and it is known that the cerebellum influences the maintenance of the eccentric portion of the eye, being responsible for smooth eye pursuit movement, the modulation and amplitude of saccades, and visual suppression of caloric induced nystagmus[18].

The VS assessment is carried out using an otoneurological evaluation consisting of a set of procedures for the semiotic exploration of the VS and its relationship to the CNS - especially vestibulo-oculomotor, vestibulocerebellar, vestibulospinal and cervical proprioceptive interrelationships. The result of this assessment will guide the qualified professional in rehabilitative balance therapy through the use of a virtual reality technique that is based on central mechanisms of neuroplasticity[14].

The aim of this study was to identify vestibular disorders and demonstrate the importance of a labyrinthine examination in the prognosis and therapy for improving balance in patients with SCAs.

MATERIALS AND METHODS

The study had a retrospective cross-sectional design. We evaluated 57 patients (26 females and 31 males) with a conclusive diagnosis of SCA. Polymerase chain reaction (PCR) diagnostics indicated that the group included 14 patients with SCA 3, 10 with SCA 2, 1 with SCA 4, 2 with SCA 6, 2 with SCA 7, and 9 with SCA 10[19-21]. It was not possible to determine the subtype of SCA in the remaining 19 patients, who were grouped together as an undetermined type subgroup.

In order to measure the severity of cerebellar ataxia in an easier and more practical way, Schmitz- Hübschet al.[22] proposeda scale for the assessment and rating of ataxia (SARA) which was translated and validated for Brazilian Portuguese by Braga - Neto et al.[23] The SARA has eight items that yield a total score of 0 (no ataxia) to 40 (most severe ataxia); 1: gait (score 0 to 8), 2: stance (score 0 to 6), 3: sitting (score 0 to 4), 4: speech disturbance (score 0 to 6), 5: finger chase (score 0 to 4), 6: nose-finger test (score 0 to 4), 7: fast alternating hand movements (score 0 to 4), 8: heel-shin slide (score 0 to 4). Limb kinetic functions (items 5 to 8) are rated independently for both sides, and the arithmetic mean of both sides is included in the SARA total score[22].

The age of the patients ranged from 18 to 70 years (mean, 41.6 ± 13 years). The duration of the disease ranged from 1 to 18 years (mean, 12.4 ± 4.1 years), as seen in Table 1. Included in the survey were patients without otoscopic alterations, and excluded were patients with musculoskeletal changes that prevented the examination.

Table 1. Summary of patient (P) demographics and genetic diagnoses in dominant ataxia.

P	Age/sex (years)	SCA type	Disease duration (years)	Chromosomal locus of abnormality	Gene affected	Mutation type	Protein affected	SARA
1	42/M	SCA3	12	14q32.1	ATXN3	CAG	Ataxin-3	4
2	48/F	SCA3	15	14q32.1	ATXN3	CAG	Ataxin-3	10
3	43/M	SCA3	12	14q32.1	ATXN3	CAG	Ataxin-3	4.5
4	41/M	SCA3	8	14q32.1	ATXN3	CAG	Ataxin-3	10.5
5	48/F	SCA3	10	14q32.1	ATXN3	CAG	Ataxin-3	10.5
6	53/M	SCA3	13	14q32.1	ATXN3	CAG	Ataxin-3	13
7	50/F	SCA3	8	14q32.1	ATXN3	CAG	Ataxin-3	9.5
8	30/F	SCA3	9	14q32.1	ATXN3	CAG	Ataxin-3	11
9	42/M	SCA3	10	14q32.1	ATXN3	CAG	Ataxin-3	7.5
10	45/M	SCA3	15	14q32.1	ATXN3	CAG	Ataxin-3	11
11	51/M	SCA3	7	14q32.1	ATXN3	CAG	Ataxin-3	1.5
12	45/M	SCA3	3	14q32.1	ATXN3	CAG	Ataxin-3	25.5
13	32/F	SCA3	5	14q32.1	ATXN3	CAG	Ataxin-3	10
14	46/F	SCA3	11	14q32.1	ATXN3	CAG	Ataxin-3	7
15	49/M	SCA2	11	12q24.1	ATXN2	CAG	Ataxin-2	33
16	42/F	SCA2	8	12q24.1	ATXN2	CAG	Ataxin-2	21.5
17	54/F	SCA2	11	12q24.1	ATXN2	CAG	Ataxin-2	28
18	38/M	SCA2	8	12q24.1	ATXN2	CAG	Ataxin-2	4.0
19	41/M	SCA2	12	12q24.1	ATXN2	CAG	Ataxin-2	4.5
20	36/M	SCA2	3	12q24.1	ATXN2	CAG	Ataxin-2	21
21	18/M	SCA2	2	12q24.1	ATXN2	CAG	Ataxin-2	18
22	44/F	SCA2	3	12q24.1	ATXN2	CAG	Ataxin-2	21
23	30/F	SCA2	10	12q24.1	ATXN2	CAG	Ataxin-2	4
24	42/M	SCA2	12	12q24.1	ATXN2	CAG	Ataxin-2	9.5
25	43/M	SCA4	5	16q24.qter	SCA4	PLEKHG4?	-	9.5
26	59/M	SCA6	13	19q13.1	CACNA1A	CAG	CACNA1A	17.5
27	57/F	SCA6	5	19q13.1	CACNA1A	CAG	CACNA1A	4
28	49/M	SCA7	13	3p14.1	ATXN7	CAG	Ataxin-7	35
29	47/F	SCA7	10	3p14.1	ATXN7	CAG	Ataxin-7	16
30	52/F	SCA10	16	22q13.3	ATXN10	ATTCT	Ataxin-10	7
31	30/M	SCA10	4	22q13.3	ATXN10	ATTCT	Ataxin-10	9
32	37/F	SCA10	3	22q13.3	ATXN10	ATTCT	Ataxin-10	7
33	49/F	SCA10	6	22q13.3	ATXN10	ATTCT	Ataxin-10	16
34	46/M	SCA10	10	22q13.3	ATXN10	ATTCT	Ataxin-10	13
35	27/F	SCA10	3	22q13.3	ATXN10	ATTCT	Ataxin-10	14
36	70/M	SCA10	13	22q13.3	ATXN10	ATTCT	Ataxin-10	4
37	54/M	SCA10	11	22q13.3	ATXN10	ATTCT	Ataxin-10	10
38	56/F	SCA10	12	22q13.3	ATXN10	ATTCT	Ataxin-10	10
39	63/F	Und.	10	-	-	-	-	7
40	48/M	Und:	18	-	-	-	-	16
41	58/F	Und.	10	-	-	-	-	4.5
42	35/F	Und.	5	-	-	-	-	9
43	45/F	Und.	9	-	-	-	-	9
44	24/M	Und.	2	-	-	-	-	21
45	27/M	Und.	7	-	-	-	-	7
46	20/M	Und.	1	-	-	-	-	9.5
47	32/M	Und.	5	-	-	-	-	18.5
48	22/M	Und.	8	-	-	-	-	9.5
49	22/M	Und.	7	-	-	-	-	16
50	62/M	Und.	3	-	-	-	-	8
51	66/M	Und.	12	-	-	-	-	9.5
52	18/F	Und.	4	-	-	-	-	16
53	23/M	Und.	1	-	-	-	-	10.5
54	37/F	Und.	9	-	-	-	-	10.5
55	48/F	Und.	8	-	-	-	-	11
56	48/F	Und.	8	-	-	-	-	25
57	51/F	Und.	7	-	-	-	-	25.5

SCA: spinocerebellar ataxia; Und.: undetermined; M: male; F: female; SARA: scale for the assessment and rating of ataxia

The study was approved by the Institutional Ethics Committee under the Protocol number 00058/2008 and following authorization through the signing of the informed consent, the patients were subjected to the following procedures:

Anamnesis

A questionnaire was given with an emphasis on otoneurological signs and symptoms.

ENT evaluation

It was performed in order to rule out any alteration that could affect the test.

Vestibular Assessment

The patients were subjected to the following tests that make up the vestibular examination:

Initially, vertigo and position/positioning nystagmus, spontaneous and semi-spontaneous, were researched.

Then, for a electronystagmography (ENG) a thermosensitive Berger Eletromedicinamodel VN316, made in São Paulo, São Paulo, Brazilunit was used with three recording channels. An active electrode was attached with an electrolytic paste at a lateral angle for each eye and the frontal midline, forming an isosceles triangle, which allows the identification of horizontal, vertical, and oblique eye movements, and especially to allow the calculation of the angular velocity the slow component eye- velocity (SCV) of the nystagmus**.** We used a Ferrante model COD 14200, made in São Paulo, São Paulo, Braziladjustable height swivel chair, a model EV VEC visual stimulator, and air calorimeter model NGR 05, both from NeurograffEletromedicina, São Paulo, São Paulo, Brazil. We compared results with normal standards, obtained from epidemiological studies for the Brazilian population[24-26]. Table 2 shows the criteria used to analyze each test as well as to distinguish central from peripheral vestibulopathy.

The diagnosis of peripheral vestibulopathy is achieved by comparison with normal standards and the absence of pathognomonic signs of central vestibular alterations.

- Calibration of eye movements, at this stage of the examination, the clinical aspect evaluated was the regularity of motion, making the study data comparable.
- Study of spontaneous nystagmus (eyes open and closed) and semi-spontaneous (eyes open). In this stage we evaluated occurrence, direction, inhibitory effect of ocular fixation (IEOF) and the maximum SCV value of the nystagmus.
- Study of pendular tracking for evaluation of occurrence and type of curve.
- Study of optokinetic nystagmus at a speed of 60° per second, horizontally counterclockwise and clockwise. We evaluated the occurrence, direction, maximum SCV counterclockwise and clockwise movements of the nystagmus.

Table 2. Normal standards and criteria used to analyze the vestibular tests and distinguish central from peripheral.

	Normal Vestibular Exam	Peripheral Vestibular Exam	Central Vestibular Exam
Position nystagmus (Brandt & Daroff's maneuver)	Absent	Present (rotatory, horizontal rotatory, and oblique) with latency, paroxysm, weariness, and vertigo	Present (vertical inferior, superior, rotatory, horizontal rotatory, and oblique), without latency, paroxysm, weariness, and vertigo
Calibration of the ocular movements	Regular	Regular	Irregular (alterations in latency, accuracy, and velocity of the saccadic movements)
Spontaneous nystagmus	Present (< 7˚/sec) with closed eyes; absent with open eyes.	Present (> 7˚/sec) with closed eyes; absent with open eyes.	Present with open eyes (vertical inferior, superior, rotatory, horizontal rotatory, oblique, cyclic, dissociated, and retractor)
Gaze nystagmus	Absent	Absent	Present, unidirectional, bidirectional, or mixed; presents a variety of nystagmus types
Oscillatory track	Types I and II	Type III	Type IV (pathognomonic); alterations of morphology and gain
Optokinetic nystagmus	Symmetrical, < 20˚/séc	Asymmetrical, > 20˚/sec, having superposed spontaneous nystagmus with open eyes that justifies this alteration	Asymmetrical, > 20˚/sec, absent and reduced
Rotation test	> 33%, after stimulation of the lateral and superior semicircular ducts	> 33%, after stimulation of the lateral and superior semicircular ducts	> 33%, after stimulation of the lateral and superior semicircular ducts and absence of induced oblique nystagmus
Air caloric test	Absolute value: between 2 and 24˚/sec Relative values: Labyrinth preponderance < 41% Nystagmus directional preponderance < 36%	Absolute value: < 2˚/sec (hyporeflexia), > 24˚/sec (hyperreflexia) and areflexia Relative values: Labyrinth preponderance > 41% Nystagmus directional preponderance > 36% (Jongkees formula)	Absolute value: < 2˚/sec (hyporeflexia), > 24˚/sec (hyperreflexia) and areflexia Relative values: Labyrinth preponderance > 41% Nystagmus directional preponderance > 36% (Jongkees formula). Different nystagmus types may be observed: dissociated, inverted, perverted, and absence of the fast component of the nystagmus
Inhibiting effect of ocular fixation	Present	Present	Absent

Source: Based on Padovan and Pansini [24], Mangabeira-Albernaz,Ganança, and Pontes[25] and Ganança, Ganança, Souza, Segatin, et al.[26]

- Study of pre-and post-rotatory nystagmus in swivel chair testing, stimulating the lateral, anterior and posterior semicircular canals. For stimulation of the lateral (horizontal) semicircular canals, the head was bent forward 30°. In the next step, to sensitize the anterior and posterior (vertical) semicircular canals, head positioning was 60° backward and 45° to the right, and then backward 60° and 45° to the left, respectively. The occurrence, direction, counterclockwise and clockwise rotation frequency of the nystagmus was observed.
- Study of pre and post-caloric nystagmus, performed with the patient positioned so that the head and trunk are inclined 60° backward for adequate stimulation of the lateral semicircular canals. The irrigation time of each ear with air at 42°C and 20°C lasted 80 seconds for each temperature and the responses were recorded with eyes closed and then with eyes open to observe the IEOF. In this evaluation, the direction, the absolute values of the SCV and the calculation of the relationship of directional preponderance and labyrinthine preponderance of post-caloric nystagmus were observed.

Statistical Analysis

The difference in proportions test was used to determine the most relevant symptoms, see what tests showed the most alterations, and compare that with the results of the vestibular exam (analyzing normal and abnormal results and the gender variable). 0.05 or 5% was set as the rejection level of the null hypothesis.

RESULTS

The most frequent complaints in anamnesis were: gait imbalance (71.9%), dysarthria (49.1%), dizziness (43.8%) and dysphagia (36.8%), as shown in Table 3. The difference in proportions test revealed that gait imbalance balance was the symptom with the largest proportion of cases, and was statistically significant ($p = 0.0142$*). In the assessment of vestibular function the caloric test, saccadic movements, as well as positional, spontaneous, semi-spontaneous, optokinetic, and rotational nystagmus presented alterations in the SCAs, as shown in Table 4. The difference in proportions test revealed a significant difference between bilateral vestibular hyporeflexia and the absence of rotational nystagmus ($p = 0.0138$*). Comparing saccadic movements with bilateral vestibular hyporeflexia ($p = 0.2370$) and the absence of rotatory nystagmus ($p = 0.1858$) was observed to have no statistical significance.

Among the evidence of alterations in all SCAs, the highest prevalence occurred in the caloric test (78.9%), which demonstrates a labyrinthine hypofunction in saccades (61.4%), indicating difficulty in tracking motion. Next was the optical rotation test (49.1%), which demonstrates a lack of response from lateral, anterior and posterior semicircular canals. And finally semi-spontaneous nystagmus (45%), as shown in Table 4.

Table 3. Symptoms in 57 patients with dominant SCA.

Symptons	No. patients	Frequency (%)
Gait imbalance	41	71.9
Dysarthria	28	49.1
Dizziness	25	43.8
Dysphagia	21	36.8
Dysphonia	19	33.3
Hearing Loss	18	31.5
Headaches	14	24.5
Falling	14	24.5
Tingling in extremities	14	24.5
Diplopia	13	22.8
Tinnitus	13	22.8
Depression	12	21.0
Anxiety	11	19.2
Pain. irradiated to shoulder. arm	10	17.5
Double vision	10	17.5
Tremors	9	15.7
Pain. difficulty in neck movement	9	15.7
Insomnia	8	14.0
Fatigue	8	14.0
Migraine	5	8.7

Regarding the results of the vestibular exam, in 41 cases (72.0%) there was central vestibular dysfunction, including 6 patients with SCA 2, 11 with SCA 3, 2 with SCA 6, 2 with SCA 7, 6 with SCA 10, and 14 with SCAs of undetermined types. In 7 cases (12.2%) had peripheral vestibular dysfunction, 1 with SCA 2, 3 with SCA 3, and 3 with SCAs of undetermined types. The vestibular exam was normal in 9 cases (15.8%), 3 with SCA 2, 1 with SCA 4, 3 with SCA 10, and 2 with SCAs of undetermined types, as described in Table 5.

The difference in proportions test revealed significant differences between central and peripheral vestibular dysfunction ($p = 0.0040$*). The results of the vestibular exam related to gender, is shown in Table 6. The difference in proportions test revealed a significant difference between the result of normal and abnormal vestibular test ($p = 0.0001$*) in both sexes, male ($p = 0.0025$*) and female ($p = 0.0004$*).

DISCUSSION

The symptoms most commonly reported by patients were also the most common symptoms observed by the authors[2,7,27]. Because of SCA's multidisciplinary clinical form, various events may occur with the progression of the disease. Gait imbalance alterations, nystagmus, decreased muscle tone, dysarthria, vertigo, dysphagia, and dysphonia, are frequent symptoms described in several studies[2,28,29].

The cerebellum receives afferent information from different structures such as: visual, auditory, vestibular, brainstem somatosensory, somatosensory receptors in limbs and motor areas, premotor and prefrontal areas of the cerebral cortex. The cerebellum has three anatomical regions: the medial zone (cerebellar vermis and core meridian), which is responsible for the control

Table 4. Frequency of abnormal findings in the vestibular evaluation in 57 patients with dominant SCA.

Altered Results	SCA 2		SCA 3		SCA 4		SCA 6		SCA 7		SCA 10		UnD		SCADT	
	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n
Bilateral labyrinthine hyporeflexia	50.0	13	92.8	-	0.0	2	100.0	2	50.0	13	92.8	-	0.0	2	100.0	2
Dismetric saccades	70.0	9	64.2	-	0.0	1	50.0	1	70.0	9	64.2	-	0.0	1	50.0	1
Rotational nystagmus absent	50.0	9	64.2	-	0.0	1	50.0	2	50.0	9	64.2	-	0.0	1	50.0	2
Multiple gaze nystagmus	0.0	4	28.5	-	0.0	1	50.0	1	0.0	4	28.5	-	0.0	1	50.0	1
Optokinetic asymmetrical nystagmus	20.0	8	57.1	-	0.0	-	0.0	2	20.0	8	57.1	-	0.0	-	0.0	2
Bidirectional gaze nystagmus	0.0	2	14.2	-	0.0	-	0.0	-	0.0	2	14.2	-	0.0	-	0.0	-
Positional nystagmus	10.0	-	0.0	-	0.0	1	50.0	-	10.0	-	0.0	-	0.0	1	50.0	-
Unidirectional gaze nystagmus	20.0	1	7.1	-	0.0	1	50.0	-	20.0	1	7.1	-	0.0	1	50.0	-
Unilateral labyrinthine hyporeflexia	10.0	-	0.0	-	0.0	-	0.0	-	10.0	-	0.0	-	0.0	-	0.0	-
spontaneous nystagmus with open eyes	0.0	1	7.1	-	0.0	1	50.0	-	0.0	1	7.1	-	0.0	1	50.0	-

SCA: spinocerebellar ataxia; Und: undetermined; SCADT: spinocerebellar ataxia dominant total n: patients; %: frequency

Table 5. Frequency of the vestibular exam results in 57 patients with dominant SCA.

VESTIBULAR EXAM	SCA 2		SCA 3		SCA 4		SCA 6		SCA 7		SCA 10		UnD		SCADT	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Central vestibular dysfunction	6	60.0	11	78.5	-	0.0	2	100.0	2	100.0	6	66.7	14	73.7	41	72.0
Peripheral vestibular dysfunction	1	10.0	3	21.5	-	0.0	-	0.0	-	0.0	-	0.0	3	15.8	7	12.2
Normal vestibular exam	3	30.0	-	0.0	1	100.0	-	0.0	-	0.0	3	33.3	2	10.5	9	15.8

SCA: spinocerebellar ataxia; Und: undetermined; SCADT: spinocerebellar ataxia dominant total; n: patients; %: frequency

Table 6. Frequency of the vestibular exam results in 57 patients with dominant SCA.

EXAM RESULT	DOMINANT SCA					
	Male		Female		Total	
	n	%	n	%	n	%
Abnormal	27	87.0	21	81.0	48	84.2
Normal	4	13.0	5	19.0	9	15.8
Total	31	100.0	26	100.0	57	100.0

SCA: spinocerebellar ataxia;n: patients; %: frequency

of posture, balance and movement; the intermediate zone (intermediate hemisphere and interposital nuclei), responsible for the control of movement and discrete ipsilateral limb reflexes; the lateral zone (lateral hemisphere and dentate nucleus), responsible for motor planning and the complex movements of the limbs guided by vision[30]. Several studies have found the specific involvement of the VS in SCAs[31,32]. The authors[33] reported that the combinations of vestibular dysfunction in the presence of cerebellar atrophy can contribute significantly in the appearance of gait instability, which is an initial symptom of SCAs. Regarding the ENG examination, there was a higher prevalence of vestibular dysfunction (78.9%), alterations in saccadic movements (61.4%), in the rotatory test (49.1%), and semi-spontaneous nystagmus (45.5%) as noted in Table 3. Cerebellar vermis lesions cause ataxia of the upper limbs, head twitching, eye movement dysmetria and trembling – which shows electrical activity along the extent of the eye muscles and neck. Some evidence suggests that lesions in the cerebellar vermis cause vertical dysmetria, while more lateral lesions cause horizontal dysmetria. Moreover, the more anterior the lesions, the more intense the dysmetria in looking upward. The more posterior the lesion, the more intense the dysmetria in looking downward[34]. The most prevalent changes[14], were the presence of positional nystagmus, irregular eye movement calibration, rebounding spontaneous nystagmus, multiple semi-spontaneous, optokinetic abnormality, pendular tracking, vestibular hypofunction, and absence of the eye's ability to remain fixed.

Vestibular hypofunction is known to be related to damaged neuronal structures, but little is known about when and why it occurs[35,36]. The authors[37] evaluated two patients with SCA 3 after genetic confirmation of the disease and onset of disease symptoms (one year after onset for case 1 and 3 years after for case 2) and found that in both cases there was no response to the caloric test. Studies[38] have reported that spinocerebellar ataxia is one of the clinical entities in VS disorders.

Yoshizawa et al.[37] reported a reduction in the size

of the tegmentum of the pons and medulla, seen via MRI, thereby demonstrating that this area is the location for the vestibular nuclei, perihypoglossal nuclei (intercalated nucleus, prepositus nucleus, and the nucleus of Roller) and neurons in the paramedian tract that are related to the VS. Premature degeneration of these structures can lead to a brainstem atrophy. Studies by Zeigelboim et al.[14] reported that the loss of hair cells of the ampullary crests and defilements, the decline in the number of nerve cells in the vestibular ganglion (Scarpa), the degeneration of the otoliths, a reduction in labyrinthine blood flow, the progressive depression of neural stability, and a reduction in compensation capacity of vestibulo-ocular and vestibulospinal reflexes all contribute to reducing eye pursuit speed and rotational movements, as well as caloric hypoactivity in the peripheral and central vestibular system, features present in SCAs.

In SCA 3, an MRI reveals cerebellar atrophy, with or without involvement of the brainstem (olivopontocerebellar atrophy)[21,39,40]. Pathological studies[41] of the vestibular complex and the combination of their fiber bundles in four patients with SCA 3 revealed that the five nuclei of the vestibular complex (interstitial, lateral, medial, upper and lower), suffered neurodegeneration resulting from the disease, demonstrating that all the bundles of related fibers (ascending tract of Deiters), the juxtarestiform body, medial and lateral vestibulospinal tract, medial longitudinal fasciculus, and the vestibular portion of the eighth cranial nerve suffer widespread neuronal loss and atrophy causing demyelination of the structures. These lesions may explain the changes in the brainstem, postural instability with imbalance, oculomotor deficits (deficits in optokinetic nystagmus, slow saccadic eye movements and absent caloric response) and the presence of a pathological vestibular-ocular reflex (VOR)[31].

SCA 2 is characterized by cerebellar atrophy and a loss of Purkinje cells and granular olivary neurons of the substantia nigra and ventral horn neurons in the spinal cord[21]. A neurological examination showed slow saccadic eye movements, twitching of the face and limbs, dysarthria, and ataxia. SCA 4 is a rare form of ataxia, characterized by cerebellar ataxia associated with peripheral neuropathy and pyramidal tract involvement. Neuropathological studies show a reduction of Purkinje cells and the ganglion cells of the dorsal root and dorsal column of the spinal cord[42]. The authors[43], after post- mortem studies in an SCA 4 case, reported severe neuronal loss in: the Purkinje cell layer of the cerebellum; the nucleus of the meridian; the red, trochlear, lateral vestibular and lateral reticular nuclei; the tegmental pontine reticular nucleus and subhypoglossal nucleus (of the Roller). Bearing in mind the functional role of the affected nuclei and related fibers are accounted for in this way by the symptoms that occur during the course of the disease (ataxia, dysarthria, somatosensory deficit, diplopia, evoked nystagmus, hearing impairment, auditory evoked potential changes, saccadic pursuit, and depreciated somatosensory functions).

For SCA 6, studies[44] show that there is a reduction in Purkinje cells and gliosis of the inferior olivary complex. It is reported that patients complain of severe episodes of vertigo that precede the onset of ataxia, causing the presence of spontaneous nystagmus, which is seen as a predominant sign[45]. SCA 7, from the neuropathological view, has olivopontocerebellar degeneration associated with a reduction of retinal ganglion cells and pigmented macula dystrophy[46]. Accompanying pyramidal signs, ophthalmoplegia, Parkinsonism, and slow saccadic movements, in particular[19].

SCA 10 studies demonstrate the presence of pan-cerebellar atrophy without abnormalities in other regions[47] and the presence of direction and variable-type nystagmus[2]. SCAs are genotypic and phenotypically very heterogeneous. Several authors have suggested that the detailed analysis of abnormal eye movements may help identify key SCAs (types 2, 3 and 6). Abnormalities in eating habits, changes in amplitude and speed of saccades, nystagmus and commitment VOR are all more common in certain types of SCA[48]. Degenerative diseases can produce a variety of abnormal findings in ENGs. The authors[49] evaluated 72 patients with brain degeneration and observed a high incidence of saccadic pursuit and eye dysmetria upward. Also observed were moderate incidences of horizontal eye dysmetria, rebound nystagmus, vertical positional nystagmus and visual suppression.

The studied literature, current studies used in this study, reported major changes in the tests that make up the inner ear examination, noting labyrinthine changes indicating VS dysfunction in 72% of patients and peripheral vestibular dysfunction in 12.2%, revealing a significant difference between dysfunctions. Regarding the results of the vestibular exam, 84.2% had alterations. This study showed that patients with SCA have significant impairment in dynamic equilibrium, which has a direct impact on their ability to function, especially in relation to self-care in areas of transfer and locomotion. Moreover, balance and the ability to function are influenced by the severity of the ataxia. Neuroplasticity refers to the ability of the CNS has to modify some of its morphological and functional properties in response to changes in the environment and in response to morphological and functional changes in the brain tissue itself. It is important to stimulate, through exercises, the central mechanisms related to neuroplasticity to improve labyrinthine rehabilitation. Such exercise results in multifactorial neural adaptations, sensory substitution, functional recovery of the vestibular-ocular reflex (VOR) and vestibulospinal reflex (VSR), as well as improved overall conditioning, and lifestyle. In this way, patients with SCA can see improved motor coordination and consequently better body balance.

CONCLUSION

It was evident that changes in ENG are related to the severity of the SCA or the clinical stage of the disease.

Using the clinical history of the patient, alterations in oculomotor tests found in the vestibular examination, and its overall result, whether peripheral or central in origin, we have enough information to know which protocol to use for patients in treatment for vestibular disorders and thus apply the most effective therapy. The labyrinthine examination proved to be an important tool concomitant to the clinical and genetic study.

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