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Vision related quality of life in spinocerebellar ataxia

Sachin Kedar [a,b,*], Deepta Ghate [b], Earnest L. Murray [c], James J. Corbett [d], S.H. Subramony [e]

[a] Department of Neurology, University of Nebraska Medical Center, Omaha, NE, USA
[b] Department of Ophthalmology and Visual Sciences, Stanley Truhlsen Eye Institute, University of Nebraska Medical Center, Omaha, NE, USA
[c] Department of Neurology, University of Tennessee Health Science Center, Memphis, TN, USA
[d] Department of Neurology and Ophthalmology, University of Mississippi Medical Center, Jackson, MS, USA
[e] Department of Neurology and the McKnight Brain Institute, University of Florida College of Medicine, Gainesville, FL, USA

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ABSTRACT

Objective: Spinocerebellar ataxia (SCA) leads to abnormal ocular motility and alignment. The objective of this study was to quantitatively assess vision, ocular motility and alignment and its impact on vision related quality of life (VRQOL) in SCA.
Methods: Nineteen genetically diagnosed SCA subjects (11 SCA type 3, 3 SCA type 1 and 5 SCA type 6) participated at two university centers. All subjects completed the National Eye Institute Visual Function Questionnaire (NEI-VFQ), 10-Item Neuro-Ophthalmic Supplement (NOS), scale for assessment and rating of ataxia (SARA) and ophthalmic examination. Twelve subjects seen at one of the 2 sites underwent quantitative ocular motility and alignment assessment.
Results: Composite scores for NEI-VFQ (mean 76.3 ± 13) and NOS (mean 65.2 ± 16.8) were significantly decreased in SCA subjects. NEI-VFQ subscale scores were decreased for general, near, distance and peripheral vision and driving. SCA patients had decreased low contrast sensitivity, stereoacuity and multiple ocular motility defects which included gaze limitation (9/12), nystagmus (5/12), distance esophoria (11/12), near exophoria (12/12) and receded near point of convergence. A significant negative correlation was noted between composite scores and distance convergence fusional amplitude.
Conclusion: VRQOL is significantly decreased in SCA compared to normal population. All SCA patients should be screened for visual disability and referred for neuro-ophthalmic assessment promptly.

1. Introduction

The spinocerebellar ataxias (SCA) are dominantly inherited neurodegenerative diseases characterized by very gradual evolution of cerebellar ataxia and other neurological deficits. SCA are phenotypically and genotypically heterogeneous with more than 30 identified genetic types [1]. Besides SCA-7, which causes rod-cone dystrophy, other SCA types are not associated with defects of afferent visual pathways [2]. Disorders of eye movement, alignment and gaze stability are prevalent in SCA which leads to diplopia, blurred vision and oscillopsia [3,4]. Visual symptoms appear early and often precede neurological deficits by several years [5]. The impact of ophthalmological abnormalities on quality of life in SCA is not known. The objective of this study is to assess vision related quality of life measures in SCA and correlate with disease duration, severity and neuro-ophthalmologic abnormalities.

2. Methods

Subjects were recruited from the neurology clinics at two large centers with dedicated facilities to care for patients with ataxia. The study adhered to the tenets of Declaration of Helsinki and was approved by the institutional review board at both centers. The study design was cross-sectional. Patients were eligible to participate if they had molecularly proven SCA types 1, 2, 3 and 6, had a compatible phenotype for the disease, were of age 18 years or older and agreed to participate in this study. Subjects with alternative causes for ataxia, unrelated ocular pathology or history of amblyopia and strabismus were excluded. Strabismus (also known as “crossed eyes” or “squint”) was defined as a disorder where the two eyes do not line up in the same direction. Informed consent for participation was obtained from all patients.

Abbreviations: SCA, spinocerebellar ataxia; NEI VFQ, National Eye Institute Visual Function Questionnaire; NOS, neuro-ophthalmic supplement; VRQOL, vision related quality of life; SARA, scale for assessment and rating of ataxia; ETDRS, early treatment diabetic retinopathy study; Log MAR, logarithm of minimum angle of resolution; PD, prism diopters; SD, standard deviation.

* Corresponding author at: 988440 Nebraska Medical Center, Omaha, NE 68198-8440, USA.
E-mail addresses: sachin.kedar@unmc.edu (S. Kedar), dghate@unmc.edu (D. Ghate), leemurray100@hotmail.com (E.L. Murray), jcorbettmd@aol.com (J.J. Corbett), s.subramony@neurology.ufl.edu (S.H. Subramony).

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2.1. Clinical methods

Ophthalmological (SK, DG) and neurological examinations (SHS, ELM) were performed by masked investigators. The details of neurological examination, SARA score (scale for assessment and rating of ataxia), functional score and assessment of ambulation using Step activity monitor have previously been described for this cohort in a separate publication [6].

2.1.1. Visual function questionnaire

The National Eye Institute Visual Function Questionnaire—Version 2000 (NEI-VFQ; developed by RAND; funded by NEI, Baltimore, MD) and 10-question Neuro-Ophthalmic Supplement (NOS) were administered and scored using standard guidelines and compared with established normal data [7–9]. The NEI-VFQ comprises a set of 25 vision related questions (representing 11 vision related domains) in addition to a single question pertaining to general health rating. Instructions for questionnaire administration, scoring of patient responses, generation of subscale and composite scores and statistical power computation are described in the NEI-VFQ manual [8]. The NOS is a supplement to the NEI-VFQ and includes 10 items specific to neuro-ophthalmological presentations. The instructions for administration and scoring of NOS, which is similar to the NEI-VFQ, are described in an online supplement to the original publication by the authors of the questionnaire [7]. Items on both NEI-VFQ and NOS are presented in a Likert scale and subjects are asked to rate symptom severity and difficulty performing vision related tasks. The subject responses are then scored on a 0–100 scale and used to generate subscale and composite scores for statistical analysis.

2.1.2. Ophthalmological procedures

The following ophthalmological procedures were performed for all patients. Distance visual acuity was measured using Revised 2000 Series ETDRS Charts (Precision Vision, La Salle, Illinois) in a retro-illuminated cabinet at 4 m. Monocular as well as binocular testing was performed using available refractive correction. The total number of letters read correctly in each row was recorded and converted to the log MAR value using established guidelines [10]. Near acuity was tested using Rosenbaum near vision card at 14 in Snellen equivalent of the smallest row of letters read correctly was recorded. Low contrast letter acuity was tested with retro-illuminated 1.25% and 2.5% Sloan Translucent Low Contrast Charts (Precision Vision, La Salle, Illinois) using available correction in binocular state at distance of 2 m. Letters read correctly in each row was recorded and the total number of letters was used for statistical analysis by comparing with established control data [11]. Testing was done in a binocular state because none of our patients demonstrated interocular differences for distance and near acuity and we had excluded patients with ophthalmological diseases that could affect vision. Color vision was tested using Roth 28- Hue test (Richmond Products, Albuquerque, NM). Each subject was asked to sort the color caps in a circular sequence starting with the reference color cap. The sequence of the color caps as sorted by the subject was recorded on the score sheet provided by the manufacturer. Color vision was considered normal if there were two or fewer sorting errors and sequence line did not cross the center [12]. Stereo-acuity was tested using Randot test (Stereo Optical Co. Inc., Chicago IL) at 40 cm and recorded as arc-seconds (normal ≤40 s) [13,14]. Confrontation visual field was performed using a 5 mm circular red target to assess the kinetic boundary and Amsler grid to assess the central field [15,16].

Examination of ocular motility and alignment was performed on twelve patients seen at site one by an experienced neuro-ophthalmologist (SK). Seven subjects evaluated at the second site did not undergo this examination due to lack of expertise. The range of ocular motility was assessed by observing the corneal and scleral light reflex during horizontal and vertical gaze with the penlight kept at a distance of 25 cm from the nasion. Adduction was considered normal if 1/3rd of adducting cornea extended beyond an imaginary line from the superior to inferior puncta; abduction was normal if corneo-scleral limbus extended to lateral canthus. Vertical versions were normal if supraducted eye demonstrated a corneal light reflex beyond the pupillary margin and infraducted eye demonstrated scleral reflex, 10 mm superior to limbus [17]. Cover-uncover and prism tests were used to study ocular alignment and fusional amplitudes. The following were used as abnormal values for fusional amplitudes: divergence <5 prism diopters, convergence <15 prism diopters at 20 ft; convergence and divergence <20 prism diopters at 25 cm [18]. Near point of convergence was measured using Krimsky accommodation rule (Richmond Products, Albuquerque, NM) and was normal if ≤10 cm [17].

2.2. Statistical analysis

Statistical analysis was performed using IBM SPSS statistics Version 19. Outcome measures were composite and subscale score on NEI VFQ and NOS. Summary data included mean and standard deviations for continuous variables and frequency tables for categorical variables. Bivariate analysis was performed to evaluate factors that influenced scores on NEI visual function questionnaire and neuro-ophthalmic supplement questionnaire. Independent samples *t*-test was used for group comparisons. Multivariate analysis was not performed due to small sample size.

3. Results

Nineteen subjects (15 females; 4 males) were enrolled. The cohort included 11 SCA type 3, 3 SCA type1 and 5 SCA type 6. No eligible SCA type 2 subjects were found. The mean age of the cohort was 56.16 ± 10.66 (SD) years and the mean disease duration was 9.05 ± 6.18 (SD) years. Table 1 summarizes disease severity and visual measures ($n = 19$). The mean age at examination was 56.16 years (SD 10.66; range 38–75 years); the mean age at onset was 47.16 years (SD 10.63; range 23–63 years). The mean disease duration was 9.05 years (SD 6.18; range 2–24 years). Ten patients (52.7%) were ambulating independently while nine (47.3%) needed wheelchair assistance or cane at the time of study assessment.

3.1. Neuro-ophthalmological findings

Table 1 provides a summary of the ataxia scores (SARA score and functional score) as well as ophthalmological measures. Distance visual acuity was better than 20/40 in all subjects while near acuity with correction was 20/25 Snellen equivalent or better in all patients. Low contrast sensitivity was significantly reduced in SCA ($p < 0.001$ independent samples *t*-test) compared to the established normal reference [11]. The values for contrast sensitivity were less than 2 SD in 11 subjects for the 2.5% chart and 8 subjects for the 1.25% contrast sensitivity chart compared to established normal reference. Color vision was normal in all except one patient who demonstrated a pre-existing tritan defect. Stereo acuity was normal in 7/19 (36.8%) subjects. Visual field testing by confrontation method was normal in all patients.

The results for the ocular motility and alignment performed in 12 subjects are listed in Table 1. All 12 subjects had more than 1 abnormality of ocular movement and/or alignment. Gaze limitation was observed in 9/12 patients. Distance convergence fusional amplitude was decreased in 10/12 patients while distance divergence fusional amplitude was decreased in 6/12 patients. Near convergence and divergence fusional amplitudes were decreased in 10/12 (83%) and 8/12 (67%) patients respectively. Nystagmus was observed in 5/12 patients and all had end-gaze nystagmus. None of these patients complained of oscillopsia and all had visual acuity 20/25 or better.

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