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An Instrument Capable of Grading Visual Function: Results from Patients with Retinitis Pigmentosa

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TAMAI, M., KUNIKATA, H., ITABASHI, T., KAWAMURA, M., SAIGO, Y., SATO, H., WADA, Y. and NAKAGAWA, Y. *An Instrument Capable of Grading Visual Function: Results from Patients with Retinitis Pigmentosa*. Tohoku J. Exp. Med., 2004, **203** (4), 305-312 —— There was no device to grade visual function in patients with retinitis pigmentosa (RP). We have therefore developed an instrument capable of measuring and quantifying the visual capabilities, and here present the results from patients with RP. In total, 118 eyes of 59 patients, 26 men and 33 women, with RP were studied. Seven eyes had hand movement (HM) and eight had light perception (LP) vision, and the others had better visual acuity. The Low Vision Evaluator (LoVE) consists of a pair of goggles with white, light-emitting diodes as the stimulus, a control box, an on-off button to signal the detection of the stimulus, and a printer for permanent records. There are 15 luminance levels of stimuli (combination of 5 intensities and 3 durations). The stimuli are delivered in a random sequence with an audio signal presented 0.3 seconds prior to the light stimulus. Each eye was tested separately, and each stimulus magnitude (intensity × duration) was presented 3 times for a total of 27 stimuli per eye. With 6 catch trials (audio signal without a light stimulus), a total of 60 trials were examined in a full examination. The conventional visual acuity and kinetic visual fields were determined. 59 patients had different visual acuities that ranged from no light perception (NLP) to 1.5 vision, and visual field sizes that ranged from 0.0001 to 3.96 steradians. The visual acuity and visual field size were significantly correlated with the LoVE score (r=0.58 and 0.64, respectively; p<0.01). These results indicate that the LoVE is capable of grading the visual function of RP patients with various visual acuities and visual fields. The testing procedures are simple for the patient and examiner, and this instrument can be used to assess the effectiveness of medical and surgical therapy. ——— retinitis pigmentosa; low vision evaluator; light perception; hand movement; visual acuity

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Until recently, the difficulty in quantifying the residual vision in patients with retinitis pigmentosa (RP), especially those with hand movement (HM) and light perception (LP) vision, was not a major problem even though many patients were interested to know how rapidly their vision was decreasing or whether their vision was improving when new therapeutic procedures were performed. Now, with ophthalmologists treating patients with RP or the other diseases with new drugs or surgical techniques, such as the transplantation of photoreceptor cells or photochips, some measure other than visual acuity and kinetic visual field is needed to document the visual capabilities before and after the treatment (Verin et al. 1986; Berson et al. 1993; Massof and Finkelstein 1993; Horiguchi et al. 1994; Fex et al. 1996; Vingolo et al. 1998, 1999; Abe et al. 2000; Humayun et al. 2000; Chow et al. 2002; Pasantes-Morales et al. 2002; Sagdullaev et al. 2004).

Perimetric and electrophysiological test has been used to assess RP patients, but reliable measurements of their visual capabilities can be difficult to determine when they have poor fixation, early loss of peripheral visual fields or completely no response for light stimulation (Jacobson et al. 1986). Recently, focal and multifocal ERGs with fundus monitoring techniques have been used to assess retinal function (Poloschek et al. 2003).

The equipment to perform electroretinography and kinetic visual field tests (Goldmann Perimeter and Humphrey Field Analyzer) are expensive, and a special room with a technician is required. Furthermore, these instruments are very large and not portable.

In order to overcome these disadvantages, we have developed a relatively simple instrument that can be used to quantify the visual function (Tamai et al. 1999; Yamada et al. 2000; Kunikata et al. 2001; Akiyama et al. 2002). Such a device should have the following properties: a) capable of grading the visual capabilities into a range of scores; b) have good reproducibility; c) be simple and easy to operate; d) examination can be completed in a short time (about 2 minutes); e) examination can be performed without any pre-medications or manipulation of the eyes; f) be compact and easily transported, and can be used in the office or at the bedside; g) can be used by patients or their families at home; h) results are automatically recorded, displayed, and easily understood; i) does not require special lighting or darkened room; and j) can be used in other countries.

The purpose of this study was to develop an instrument with these properties. To confirm that the scores obtained were related to the visual capability of the patient with RP, statistical tests were performed to determine if the scores were correlated with the visual acuity and the size of the visual fields.

Materials and Methods

Low Vision Evaluator (LoVE)

The Low Vision Evaluator (LoVE: TOMEY) is made up of a pair of goggles with white, light emitting diodes (LED: Nichia, NSPW310AS, NICHIA CORPORATION, Anan City, Tokushima), a control box, a hand-held grip with an on-off button, and a printer for permanent records (Fig. 1A). The goggle for each eye has 16 white LEDs set at equal distances along the margins of the goggle, and the light emitted by the diodes is reflected off a concave mirror (radius of curvature=24 mm; 38 mm diameter) for full-field stimulation (Fig. 1B). The reflected light was focused approximately in the plane of the pupil, and thus the light stimulus is maximally transmitted into the eye irrespective of the position of the eye. The goggles are snugly fixed to the skin with a sponge liner and are painted black to reduce any light scatter. The distance between the goggles can be adjusted to the interocular distance and also to fit the orbital margins to block any stray light from the outside (ambient room light) or from the other goggle.

The LoVE instrument is 22×32×12 cm (L×W×H) and weighs 3750 grams. It can be operated with regular line power (100 V, 20 VA). As such, it is portable and can be easily operated in any office or hospital room. Permanent records

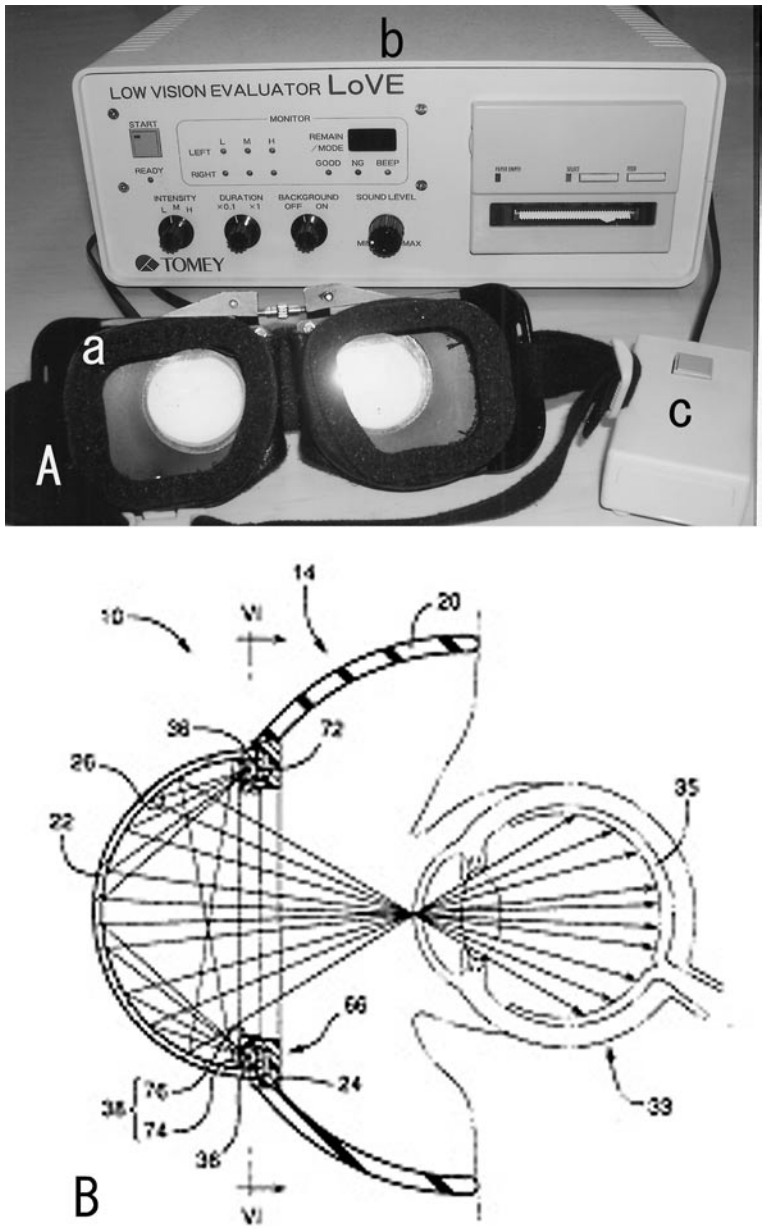

Fig. 1. A: The Low Vision Evaluator. a, goggle; b, control box; c, handle of on-off switch. B: The goggle for full-field stimulation

automatically scroll out from the control box at the completion of the examination documenting the patient's responses. The LoVE score can be obtained as the not-detected trials, and its reliability by the error score. The results can be plotted graphically.

Patients

There were 118 eyes of 59 RP patients (26 men and 33 women) that were examined. The mean±S.D. deviation age was 48.3±15.3 years. The visual acuity of these patients ranged from no light perception (NLP) to 1.5. There were 7 eyes with HM vision, and 8 with LP vision who were RP patients being followed in the Congenital Retinal Diseases Clinic of the Tohoku University Hospital. Before the LoVE test, the kinetic visual field was determined with the V4e target by the

Goldman Perimeter (GP) and the field size was expressed in solid angle steradians (Weleber and Tobler 1986).

After the purpose and procedures of the examination were explained, an informed consent was obtained from all, and the procedures were performed to conform to the tenets of the Declaration of Helsinki.

Procedures

The stimulus intensity was changed to five levels: 0.1 cd/m^2 (C), 1 C, 10 C, 100 C, and 1000 C; and three durations of 0.01 seconds (S), 0.03 S, and 0.1 S. Thus, 15 different stimulus levels could be presented, and a 5 log unit range of stimulus intensities could be tested from the weakest (0.1 C×0.01 S) to the strongest (1000 C×0.1 S) stimulus. For the comfort of the patients and to reduce testing time, the stimulus intensities were divided into a low intensity set (0.1 C, 1 C and 10 C), an intermediate intensity set (1 C, 10C and 100 C), and a high intensity set (10 C, 100 C and 1000 C) with the same 3 durations.

The only task for the patient was to push the button when they detected a light flash. Each eye was independently stimulated three times at each intensity, and if a patient responded correctly in 2 out of the 3 trials, he was scored as having detected that stimulus. The stimulus was preceded by a sound 0.3 S before the stimulus to alert the patient. In addition, 6 sound stimuli were presented without a light stimulus as catch trials. False positive responses to catch trials and any responses prior to the light stimulus were treated as error scores. The error scores were used to assess the reliability of the subject. An examination with more than one error score was treated as unreliable.

In one complete set of examination, each eye was randomly stimulated 30 times and maximally 60 times for the two eyes. The stimulus intensity-duration combinations were ranked from –1 to –15 with rank –1 the weakest stimulus (0.1 C and 0.01 S) and rank –15 the strongest stimulus (1000 C with 0.1 S). If a patient did not respond to the strongest stimulus, he was ranked –15, and if he responded to all stimuli correctly his rank was 0.

To shorten the examination time, an initial screening mode was placed in the program in which a patient was tested twice with a selected intermediate stimulus level. If the patient detected this stimulus correctly, stimuli 2 steps brighter than the stimulus were omitted, and if not detected, stimulus intensities 2 steps weaker than the stimulus omitted. With this strategy, the trials were reduced to less than 30, and the examination time was shortened from about 5 minutes to about 2 minutes.

All examinations were performed in a regular examination office without dark-adaptation and pupillary dilation.

To examine the reproducibility of the LoVE score, 2 RP patients were admitted to the University Hospital and tested in the morning and evening (10:00 and 17:00 hour) for 9 days. At each testing period, the patients' subjective estimation of their vision on a 1 to 5 scale with a score of 1 being poor and 5 being excellent was recorded.

Statistical analyses

The coefficient of correlations of the LoVE scores to the conventional visual acuity and solid angle of the visual field size (steradians) were analyzed with the Peason's correlation coefficient.

Results

Case reports

Case 1 was a 41-year-old woman with advanced autosomal recessive RP (ARRP) who had decreased vision (0.02 OD, 0.03 OS) and a ring scotoma with restricted visual field although she still retained her peripheral field. Her visual field size was 0.33 Steradians (Sr) in the right eye and 0.24 Sr in the left eye. Her LoVE score was -5 in the right eye and –4 in the left eye (Fig. 2A).

Case 2 was a 20-year-old woman with ARRP who still had good vision (1.0 OD and 1.0 OS) and almost full visual fields. Her visual field size was 3.5 Sr in the right eye and 3.7 Sr in the left

eye. Her LoVE score was 0 in both eyes (Fig. 2B).

Case 3 was a 54-old-year woman with very advanced RP and her vision was HM in the both eye. She could not recognize the V4e target of the GP. Her LoVE score was –7 in the right eye, and –8 in the left eye (Fig. 2C).

Case 4 was a 69-old-year woman with very advanced RP and her vision was LP in the both eye. She could not recognize the V4e target of the GP. Her LoVE score was –9 in the right eye, and –13 in the left eye (Fig. 2D).

Correlation of LoVE Scores to visual acuity and visual fields

In eyes with 0.01 vision or better, the LoVE scores were correlated with the visual acuity (r=0.57, p<0.01). For eyes with worse vision, we designated HM vision as 0.001, LP vision as 0.0001 and NLP as 0.00001. Using these values, we found that the LoVE scores were correlated with the visual acuity (r=0.58, p<0.01, Fig. 3A).

In 50 eyes, the visual field could be determined by the GP, and the LoVE scores were also strongly correlated with the visual field size (r=0.64, p<0.01; Fig. 3B).

Reproducibility

The LoVE scores of the 2 cases that were tested for 9 days are plotted in Fig. 4. One case (Case 5) was a 62-old-year woman and her vision was 0.02 in the right and 0.06 in the left eye. The mean of the LoVE scores was –3.78±0.55 for the right eye and –3.44±0.51 for the left eye, and the 95% confidence interval were –3.51 to –4.05 (OD) and –3.19 to –3.70 (OS) (Fig. 4). The other case (Case 6) was 67-old-year man and his vision was LP in the both eye. The mean of the LoVE scores

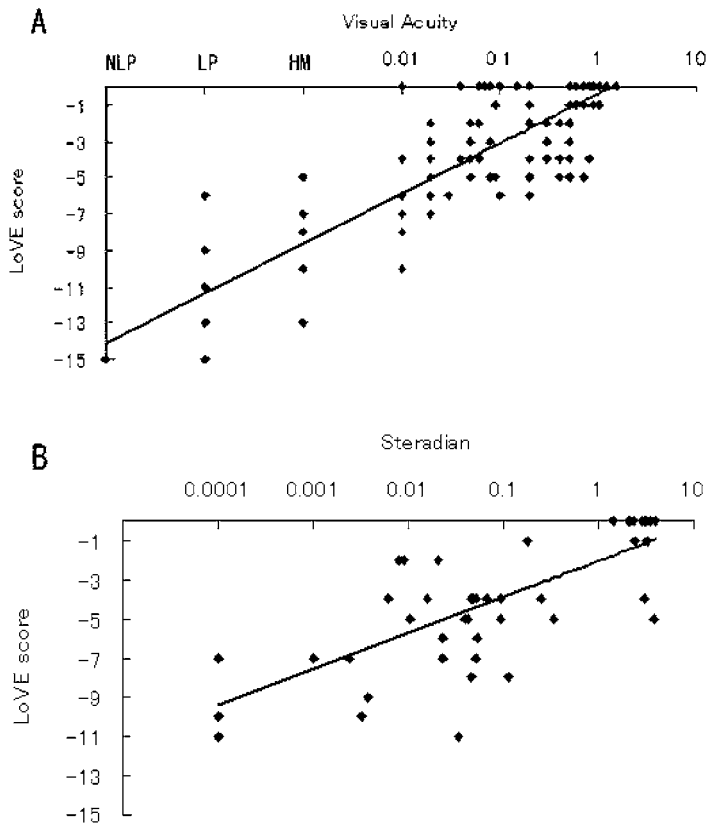

Fig. 3. A: Correlation of LoVE Scores to the visual acuity. B: Correlation of LoVE Scores to the size of the visual field (Steradian)

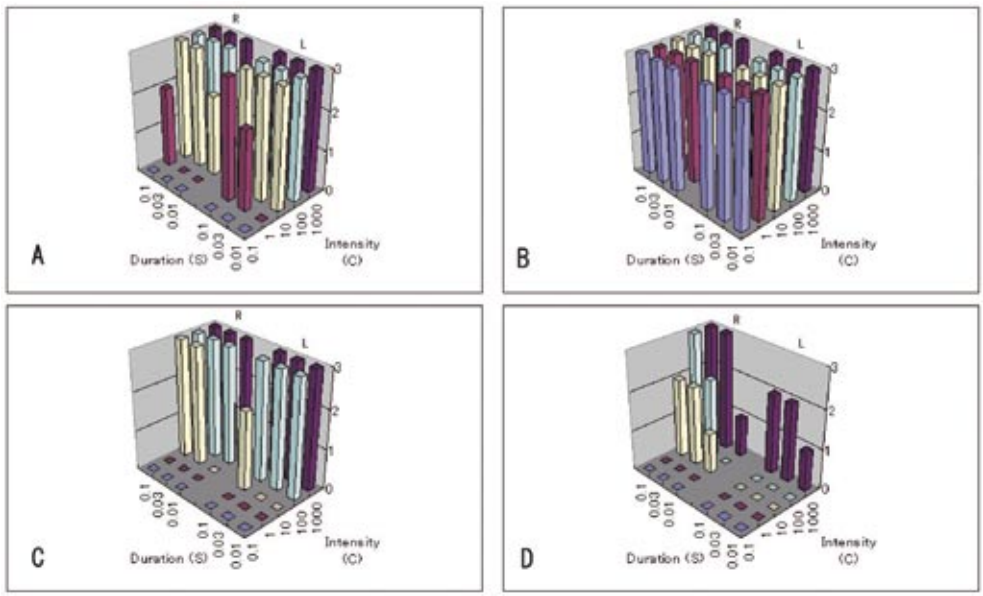

Fig. 2. Graphical results of the LoVE score.
(A) Case 1. The LoVE score is –5 in the right eye and –4 in the left eye. (B) Case 2. The LoVE score is 0 for both eyes, i.e., a perfect score. (C) Case 3. The LoVE score is –7 in the right eye, and –8 in the left eye. (D) Case 4. The LoVE score is –9 in the right eye, and –13 in the left eye.

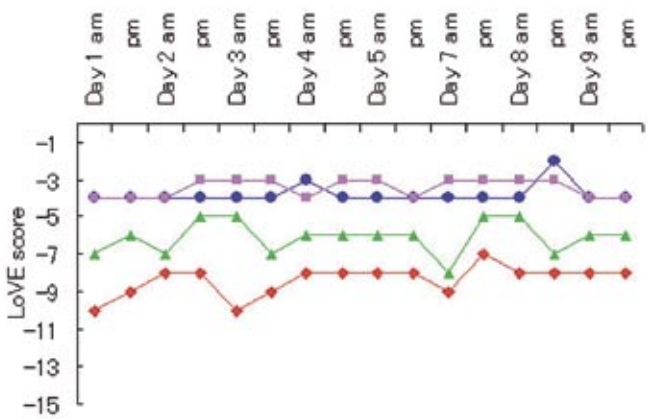

Fig. 4. Reproducibility, the LoVE scores of 2 cases that were tested for 9 days. A 62-old-year woman (Case 5) and her visual acuity was 0.02 in the right eye and 0.06 in the left. The mean of the LoVE scores was –3.78±0.55 for the right eye and –3.44±0.51 for the left eye. A 67-old-year man (Case 6) and his vision was LP in the both eye. The mean of the score was –6.13±0.89 for the right eye and –8.38±0.81 for the left eye.
—●—, OD Case 5; —■—, OS Case 5; —▲—, OD Case 6; —◆—, OS Case 6.

was –6.13±0.89 for the right eye and –8.38±0.81 for the left eye, and the 95% confidence interval were –5.66 to –6.60 (OD) and –7.95 to –8.81 (OS) (Fig. 4). This patient (Case 6) showed no change in the score following 30 min dark-adaptation on the evening of the 8th day (–7 → –7, OD; –8 → –8, OS).

Reliability

The error score was less than 1 in all 59 patients. Thus, there were no unreliable LoVE results in all of the RP patients.

Patients' subjective estimation of vision

The two patients' subjective estimation of their vision on a 1 to 5 scale with a score of 1 being poor and 5 being excellent was recorded along with their LoVE scores. No significant correlation was found between the LoVE score and this parameter.

Discussion

These results demonstrated that the LoVE could grade the visual function of RP patients with different visual acuities and visual field sizes. In addition, our results of two cases showed that repeatable scores could be obtained with this instrument. There were no unreliable LoVE results in all of the RP patients, and we can conclude that the reliability of the LoVE scores for these patients was very high. From our use of this instrument on 59 RP patients, we conclude that it meets all of the requirements set forth.

Most importantly, the LoVE scores were significantly correlated with the visual acuity and the visual field size. This confirms our expectation that the LoVE score represents the visual function of an eye.

Although only eight eyes with LP and seven eyes with HM vision were tested, their LoVE scores were different and ranged from –6 to –15 in the eyes with LP vision, and –5 to –13 in the eyes with HM vision. In case 6, the visual acuity of both eyes were LP vision, and the kinetic visual field could not be determined by the GP. However, the LoVE scores demonstrated that the right visual function was better by 2 to 3 scores than left with high reproducibility (Fig. 4).

When case 6 was dark-adapted for 30 minutes, the LoVE scores were the same in the both eyes. In patients with very low vision such as HM or LP as in patients with severe RP, the dysfunction of photorecepter cells might be severe and, if the patient was dark-adapted, the sensitivity of retina for light did not increase.

There were, however, some limitations of LoVE. The detection of the stimulus is based on a minimum visible and not on a minimum separable, i.e., visibility and not resolution. So, ideally, this instrument might be used for the HM and LP classification.

In conclusion, our results have shown that the LoVE is a simple and easily used instrument. It was effective in grading RP patients with different visual acuities including those with LP or HM vision, and those with different visual fields sizes. Additional patients of different ages and different retinal diseases are being tested.

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