Sweep Visual Evoked Potential Testing as a Predictor of Recognition Acuity in Albinism

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Objective: To determine if sweep visual evoked potential (VEP) acuity is predictive of recognition acuity in children with albinism.

Methods: A retrospective review was performed in children with albinism who underwent sweep VEP testing from 1992 to 2003. All patients had a complete ophthalmologic examination with either binocular or monocular sweep VEP testing and at least 5 years of follow-up. Positive predictability of sweep VEP acuity was defined as final recognition acuity within 1 Snellen line of initial sweep VEP acuity.

Results: Of the 13 patients included in the study, 11 had nystagmus, iris transillumination defects, and foveal hypoplasia at initial examination. The mean age at initial sweep VEP testing was 3.1 years (range, 0.1-10.0 years).

Five of 13 patients had initial sweep VEP acuity that was predictive of final recognition acuity. Five additional patients had final recognition acuity, which surpassed initial sweep VEP acuity by 2 to 3 lines. Of these 10 patients, the mean duration for recognition acuity to reach VEP acuity was 5.4 years. There was no correlation between predictive VEP acuity and foveal pigmentation, refractive error, strabismus, nystagmus, or longer follow-up.

Conclusions: Sweep VEP testing can be used as a predictive tool for recognition acuity in children with albinism. Predictability was found in a clinical spectrum of albinism.

Arch Ophthalmol. 2007;125:628-633

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ALBINISM, A WELL-DESCRIBED disorder of melanin synthesis, is associated with decreased vision, nystagmus, iris transillumination defects, foveal hypoplasia, and choroidal hypopigmentation. It is thought that the reduced vision is due to nystagmus and foveal hypoplasia. Visual acuity in patients with oculocutaneous and ocular albinism has been reported to range from 20/20 to 20/400 but is frequently below 20/80.[1] It is not clear whether the visual development in these patients progresses normally until the individual's decreased potential is reached or whether it is delayed from birth and progresses at a slower rate until the potential is met. It has been determined that there is a delay in visual development, with studies recording grating acuities significantly lower than published norms.[2,3] The diagnosis is usually made in the first 6 months of life, with the infant's vision being unknown.

Visual evoked potential (VEP) studies in patients with albinism have frequently been reported. Flash VEP acuity data have conclusively demonstrated the excessive decussation of optic fibers at the optic chiasm in humans with albinism. In fact, in several studies, a 100% association of albinism and asymmetric flash VEP acuity has been demonstrated.[4-6] It is often a useful tool in making the diagnosis of ocular albinism, particularly in patients with minimal nystagmus, foveal pigmentation, and no family history of the disorder.

Sweep VEP testing is an important advancement in preverbal acuity assessment in children. Previous techniques of evaluating vision by preferential looking have been unreliable in children younger than 1.5 years.[7] Studies have demonstrated that sweep VEP testing overestimates vision in patients with profound vision loss.[8] In addition, the difference between sweep VEP acuity and Teller card acuity increases with poorer visual acuity.[9] It has also been reported that grating acuity tested with Teller acuity cards overestimates eventual recognition acuity in patients with albinism,[2] though more recently, it was demonstrated that binocular Teller acuity at age 3 years is predictive of letter recognition acuity at ages 4 to 6 years.[10] To this date, there is no study in the medical literature comparing sweep

VEP acuity with future recognition visual acuity in this population.

Our study compares sweep VEP acuity in patients with albinism with recognition visual acuity tested years later. If predictive, it could be used as a guide for the potential development of vision in children with albinism. Clinical signs, such as nystagmus and foveal pigmentation, are also analyzed with VEP results. It is unknown whether or not these signs can be correlated with better predictability of sweep VEP acuity in this population.

Our study was a retrospective study of patients with ocular and oculocutaneous albinism who had undergone sweep VEP testing since 1992. All patients had a complete ophthalmologic examination by a pediatric ophthalmologist; all sweep VEP tests were performed by a single electrophysiologist at the same institution. The ophthalmologic examination included acuity testing and a slitlamp and dilated fundus examination. The diagnosis of ocular involvement secondary to albinism was based on the presence of several of the following features: nystagmus, decreased foveal pigmentation, iris transillumination defect, and asymmetric flash VEP. Only patients with at least 5 years of follow-up were included in the study. If they were aged at least 12 months, patients were prescribed glasses for any refractive error of more than 2.00 diopters (D) of hyperopia, 1.00 D of astigmatism, and 0.50 D of myopia.

SWEEP VEP STIMULUS AND RECORDING

Visual stimuli were displayed on a high-resolution video display (model 7351 monitor; Conrac Inc, Baldwin, Calif; or IDEK MF 8521; Liyama Ltd, Kitaowaribe, Japan) at a frame rate of 100 Hz. Sinusoidal grating was generated using a personal computer–based pattern generator (VSG2/1 Board; Cambridge Research System Ltd, Kent, England). Horizontal grating bars were shown to patients during testing. A sweep consisted of a 10.24-second period, during which the spatial frequency of the temporally modulated grating increased linearly. The range of spatial frequency was determined by clinical experience and guided by published normative data.[11] A filter was used to compute an estimate of noise from a nearby location in the electroencephalogram frequency spectrum, 2 Hz higher than the second signal frequency. Patients were tested with the appropriate refraction at a viewing distance of 0.5 to 2.0 m to ensure that sufficiently high spatial frequencies could be used.

Testing was first performed under binocular viewing. Monocular testing then followed. One eye was occluded with an adhesive orthoptic eye patch, and testing was repeated. When necessary, the patient's attention was directed toward the stimulus display by dangling small bells or metal rings in front of it.

Sweep VEP acuity was estimated by a method similar to that described by Norcia and Tyler.[11,12] Determination of visual acuity is based on the linear decline in VEP amplitude and the increased implicit time near the acuity cutoff.[11-16] Sweep VEP acuity was defined as the 0-μV intercept of a linear regression line drawn along the decline in amplitude. The single sweep with the highest acuity was taken as the sweep VEP acuity,[16] provided that at least 2 sweep VEP acuities were in relative agreement (within approximately 0.3 octaves of each other). There was good correlation between the acuity estimated from a single sweep and the acuity estimated from the average of 5 sweeps. Sweep VEP acuity was converted to Snellen acuity based on the angular subtense of 1 cycle (eg, 30 cycles/degree=20/20; 10 cycles/degree=20/60). Therefore, the formula used was 600 divided by the actual sweep VEP measurement; that numerical result was used as the denominator in a Snellen acuity measurement.

The timing and frequency of VEP testing was determined by the pediatric ophthalmologist. When patients were old enough to undergo recognition testing, acuity was tested with Allen pictures, the Sheridan Gardiner test, the HOTV test, or Snellen letters. All testing was initially attempted 6.1 m from the vision screen. Refractive correction, if prescribed, was worn. An opaque occluder was used to test monocular acuity. The most rigorous test for the child's age was used. For both sweep VEP and recognition binocular acuity testing, patients were allowed to adopt their preferred head position to achieve their nystagmus null point.

Thirteen patients were included in the study. The mean age at initial examination was 2.1 years; mean follow-up duration was 9.5 years (range, 5.5-14.7 years). All patients with albinism cooperated with sweep VEP testing. Eleven patients had nystagmus, iris transillumination defects, and foveal hypoplasia at initial examination. Two patients had minimal or no nystagmus but had foveal hypoplasia and characteristic asymmetric flash VEP acuity. None of the patients had a normal foveal reflex. Flash VEP tests were performed in 10 of the patients, with all demonstrating abnormal decussation of optic fibers at the chiasm.

Ten patients had strabismus, 2 of which required extraocular muscle surgery. In addition to these 2 patients, 5 patients underwent 4 horizontal rectus muscle recessions for a significant head turn or nystagmus. Nine patients had refractive errors, which were corrected with glasses.

Sweep VEP tests were performed on all patients (**Table**). Monocular and binocular VEP acuities were obtained, depending on the child's ability to cooperate with the test. The mean age at initial sweep VEP testing was 3.1 years (range, 0.1-10.0 years). Excluding patients who were tested for VEP and recognition acuity at the same visit, the mean time between initial VEP and recognition acuity was 2.4 years. The mean time between initial VEP acuity and final recognition acuity testing was 8.6 years (range, 5.5-11.3 years). Positive predictability of sweep VEP acuity was defined as final recognition acuity in either eye within 1 Snellen line compared with sweep VEP acuity. Final recognition acuity was obtained using Snellen letters. Because sweep VEP testing was performed at different ages in the various patients, VEP acuity at a defined age could not be used for the initial acuity. Instead, the initial sweep VEP acuity for each patient was used as the target with which future recognition acuity was compared (**Figure**).

Five of 13 patients (patients 2, 7, 10, 12, and 13) had initial sweep VEP acuity that was predictive of their eventual recognition acuity. The mean age of initial VEP testing was 3.5 years (range, 0.3-5.4 years), and the mean duration for recognition acuity to reach VEP acuity was 6.9 years. However, an additional 5 patients (patients 1, 3, 6, 8, and 11), whose initial sweep VEP acuity was not predictive of final acuity, had overlap of VEP acuity with recognition acuity. In all 5 patients, the final recognition acuity was actually better than initial VEP acuity.

Table. Initial Sweep VEP Acuity and Final Recognition Acuity in Patients With Albinism

Patient	Age at Initial VEP Testing, y	Initial VEP Acuity OD	Initial VEP Acuity OS	Initial VEP Acuity OU	Age at Final Recognition Acuity, y	Final Recognition Acuity OD	Final Recognition Acuity OS	Final Recognition Acuity OU
1	0.1	20/300	20/300	20/300	8.9	20/100	20/250	20/160
2	0.3	20/100	20/100	20/80	7.8	20/100	20/80	20/70
3	0.3	20/150	20/150	20/120	11.3	20/70	20/60	20/60
4	0.4	20/85	20/85	20/85	10.7	20/125	20/125	20/200
5	0.5	20/120	20/150	20/90	5.9	20/320	20/320	20/320
6	1.2	. . .	. . .	20/180	12.2	20/80	20/70	20/60
7	2.4	20/100	20/60	. . .	13.4	20/60	20/60	20/60
8	10.0	20/150	20/150	. . .	17.9	20/100	20/70	20/70
9	3.4	20/85	20/85	20/65	9.1	20/100	20/125	20/100
10	4.3	20/80	20/80	20/60	15.7	20/100	20/80	20/60
11	6.4	20/60	20/60	. . .	13.4	20/40	20/40	20/30
12	5.4	. . .	. . .	20/100	15.3	20/125	20/125	20/80
13	5.0	20/30	20/60	. . .	10.4	20/30	20/50	20/30

Abbreviation: VEP, visual evoked potential. Ellipses indicate that the investigator was unable to complete the test owing to a lack of patient cooperation.

Three of these 5 patients had subsequent sweep VEP acuity that did correlate with final acuity. The other 2 patients underwent only 1 VEP test. This VEP result correlated with recognition acuity, though not with final recognition acuity. The mean age of predictive VEP acuity testing was 1.8 years, and the mean time for both acuities to become equivalent in these 5 patients was 3.6 years. Four of the 10 aforementioned patients were noted to have increasing foveal pigmentation as their recognition acuity improved. All 4 of these patients were followed-up for at least 7 years. Both patients with minimal nystagmus had predictive sweep VEP acuity. Statistical analysis was not performed to assess VEP acuity predictability with different phenotypes because of the small patient number and variable characteristics among the patients. There appeared to be no correlation between predictive sweep VEP acuity and increased foveal reflex, lower refractive error, absence of strabismus or nystagmus, or longer duration of follow-up.

There were 3 patients (patients 4, 5, and 9) whose VEP results overestimated future recognition acuity. The follow-up time between initial VEP acuity and final recognition acuity ranged from 5.5 to 10.3 years. Two of these patients had multiple subsequent VEP recordings that did not correlate with recognition acuity. All 3 patients had absent foveal reflexes with choroidal hypopigmentation in both eyes. The first patient had more than 30 prism diopters of exotropia (which improved with refractive correction) and more than 3 D of astigmatism. The other 2 patients were siblings. They both had marked nystagmus for which they underwent surgical recession of 4 horizontal rectus muscles. One of them developed a consecutive exotropia, which required advancing bilateral medial rectus muscles. None of these patients developed foveal pigmentation during follow-up.

COMMENT

Assessing visual acuity in infants and young children with albinism can be challenging. Because albinism is often associated with decreased vision, nystagmus, and refractive errors,[17] recognition visual acuity may vary depending on null point–induced head position, accuracy of glasses prescription, and experience of the visual acuity tester. Reliance on fixation preference testing, such as Teller acuity cards, to assess vision has been required for patients younger than 2 years. Sweep VEP testing is a novel technique that can be used to assess visual acuity in preverbal patients with albinism.

Previous studies have indicated that visual acuities can be estimated with good accuracy using swept spatial frequency VEP testing. Gottlob et al[16] compared sweep VEP acuity to optotype acuity in 135 children with various visual disorders. High correlation coefficients (0.94-0.96) between the optotype acuity estimated on each patient from either a single sweep or from an average of several sweeps confirmed previous findings in healthy infants. The study by Gottlob et al[16] concluded that sweep VEP testing was a valid method to provide estimates that correlate well with optotype acuity and that it was useful in the clinical management of patients with visual disorders.

Louwagie et al[10] conducted a retrospective study, which demonstrated a correlation between binocular grating acuity and future letter recognition acuity in patients with ocular and oculocutaneous albinism. In 40 patients who had Teller grating acuity measured at 1, 2, and 3 years of age and letter recognition acuity measured at 4 to 6 years of age, mean binocular grating acuity obtained at 3 years of age appeared to be similar to mean binocular letter recognition acuity at ages 4 to 6 years. In addition, grating acuity measured at 1 and 2 years of age underestimated future letter recognition acuity. It was hypothesized that there were 3 explanations for the underestimation of recognition acuity when tested at a younger age. First, the orientation of the grating bars on the Teller cards may have been suboptimal for the direction of patients' nystagmus. If patients with horizontal nystagmus were tested with horizontal grating bars, they may have achieved better acuity measurements.[18] Second, there
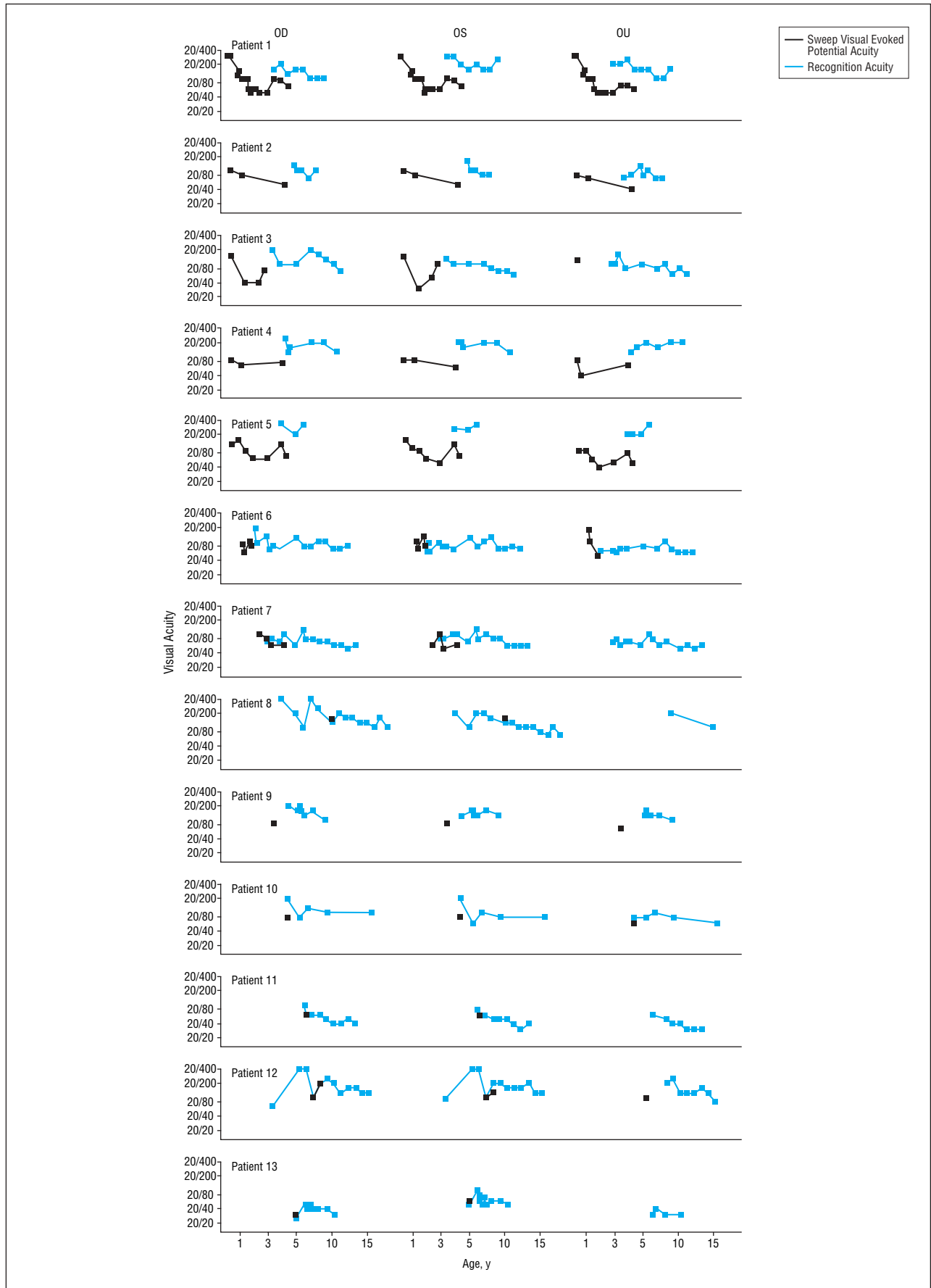
Figure. Sweep visual evoked potential acuity and recognition acuity over time.

is an expected improvement in grating acuity with increasing age. Perhaps the acuity at age 3 years better correlated with future recognition acuity simply because of further visual development at an older age. Third, children learn to adopt a head posture to dampen their nystagmus to optimize visual acuity. It may be possible that the 3-year-old children used a beneficial head posture while undergoing grating acuity testing while the younger children did not.

In our study, 5 patients had an initial sweep VEP acuity that underestimated future recognition acuity. Three of these patients underwent VEP testing when they were younger than 2 years (range, 0.1-1.2 years), which may explain why their Snellen acuity surpassed their VEP acuity results. Assessment of their serial VEP results demonstrates that their recognition acuity was predicted by a VEP acuity test performed between the ages of 1 and 3 years in all 3 cases. This is consistent with expected visual development in a child, as visual acuity at a later age correlates with future acuity. However, the 2 additional patients whose initial VEP acuity underestimated recognition acuity were aged 6.4 and 10 years at the time of their VEP testing.

There have been recent reports of the use of sweep VEP testing for vision screening in young children. Simon et al[19] demonstrated that sweep VEP predicted clinical amblyopia in infants and young children with high accuracy. In children aged 0.5 to 5.0 years, the sensitivity of sweep VEP testing was found to be 0.973; the positive predictive value was 0.706. Thompson et al[20] evaluated the correlation of recognition acuity to sweep VEP acuity in patients aged 4 to 16 years who underwent lensectomy for congenital cataract at a young age. There was a strong correlation between VEP estimation and recognition acuity in the patient group. Lauritzen et al[21] demonstrated excellent test-retest reproducibility with sweep VEP testing in 92 infants aged 6 to 40 weeks. The visual acuity estimate from VEP testing performed on 2 separate visits had a correlation coefficient of 0.91.

Our study demonstrates that sweep VEP testing can be used as a predictive tool for recognition acuity in patients with albinism. Of the 10 patients in which initial VEP acuity was equal to or lower than final recognition acuity, the mean duration in which the recognition acuity "caught up" to the VEP acuity was 5.4 years. Because this was a retrospective study, sweep VEP testing was not performed on all patients at the same age. Many patients had VEP testing performed at an age in which they were verbal but not able to consistently demonstrate recognition acuity in the clinical setting. The characteristics of the 10 patients varied. Eight patients had nystagmus, only 4 had foveal pigmentation (which increased with age), and 6 had refractive errors primarily for hyperopic astigmatism.

Only 3 of 13 patients did not have VEP acuity that correlated with future recognition acuity. Because of the small patient number, clinical factors, such as foveal hypopigmentation and significant nystagmus, could not be associated with the 3 patients. It was interesting that a pair of siblings fell in this category, both having similar initial VEP acuity of 20/85 OU. Although they both had long follow-up (>10 and >5 years), their recognition acuity remained 2 to 3 Snellen lines behind the VEP acuity estimate. However, the trend of the recognition acuity is such that they both may reach the VEP acuity prediction in the next few years. It is possible that some patients will eventually meet their VEP acuity estimate with longer follow-up.

It has been reported that Teller acuity overestimates recognition acuity in children with albinism.[2] In 27 children with mostly oculocutaneous albinism, recognition acuity was tested when the children were 3 years of age or older; the recognition acuity was compared with Teller grating acuity at ages 1, 2, and 3 years. The mean age of the patients at the time of recognition acuity testing was unreported, and grating acuity overestimated recognition acuity. A more recent report of 64 patients suggests that grating acuity at age 3 years predicts letter recognition acuity at age 4 to 6 years.[10] Perhaps there is variability of grating acuity predictability that depends on individual characteristics, such as foveal development or severity of nystagmus. Because albinism is a rare diagnosis, most published studies that compare grating with recognition acuity involve small patient numbers. Using statistical analysis to identify phenotypic characteristics associated with poor visual development predictability is difficult. Although the 3 patients in our study whose VEP acuity overestimated recognition acuity all had an absent foveal reflex, no statistical analysis could be properly performed with such a small total patient number.

A prospective study needs to be undertaken with sweep VEP testing at specific intervals (ie, at 6, 12, 18, and 24 months) to evaluate the optimal timing of sweep VEP testing in predicting future recognition acuity in patients with albinism. This data could then determine how many years it would take for recognition acuity to reach the predictive VEP acuity in this patient group. It could potentially serve as a tool in predicting acuity in a patient population whose prognosis of an individual's visual potential is currently unknown.

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Ophthalmological Numismatics

Jose Ignacio Barraquer (1916-1998) was born in Barcelona, Spain, the eldest son of the renowned ophthalmologist Ignacio Barraquer. He established the Barraquer Institute of America in 1965 in Bogota, Colombia, but is best remembered as the inventor of refractive keratoplasty in 1949. Because he was the cofounder of the International Society of Refractive Keratoplasty (now the International Society of Refractive Surgery), the annual Barraquer Award Medal has been presented in his honor and now in his memory since 1987.

The medal is a 77-mm bronze depicting Barraquer facing right. It is inscribed Prof Jose Ignacio Barraquer/Barcelona 1916.

Courtesy of: Jay M. Galst, MD, 30 E 60th St, New York, NY 10022.