Similarities and differences between behavioral and electrophysiological visual acuity thresholds in healthy infants during the second half of the first year of life

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Abstract

Purpose: Behavioural and electrophysiological methods for visual acuity estimation typically correlate well in children and adult populations, but this relationship remains unclear in infants, particularly during the second half of the first year of life. It has been suggested that the agreement between both methods mostly relies on age and/or subjective acuity factors. The present study aimed at comparing acuity thresholds obtained with both approaches in a sample of healthy infants in a relatively narrow age range, that is 6 to 10 months old.

Methods: Acuity thresholds were assessed in 61 healthy infants aged between 6 and 10 months using the Teller acuity cards (TAC) and sweep visual evoked potentials (sVEP). The TAC stimuli (stationary vertical gratings displayed on laminated cards) ranged from 0.31 to 38 cycle per degree (cpd). The TAC acuity threshold was estimated according to the highest spatial frequency scored by the experimenter as seen by the infant. The sVEP stimuli (high-contrast vertical gratings counter-phased at 12 reversals/s) ranged from 13.5 to 1 cpd. sVEP were recorded at Oz and acuity threshold was estimated using regression linear fitting.

Results: Considering the entire sample sVEP acuity thresholds (8.97 ± 2.52 cpd) were significantly better than TAC scores (5.58 ± 2.95 cpd), although the difference was within 1 octave for 64% of the infants. Neither Pearson nor intra-class correlations between the two methods were significant (0.18 and 0.03, respectively). While age at assessment was not related to any dependent variable (TAC, sVEP, sVEP-TAC difference score), subjective (behavioral) acuity was found to underlie the difference between the two methods. The difference between sVEP and TAC scores decreased as a function of subjective acuity and, at the highest subjective acuity level (> 10 cpd), TAC acuity slightly exceeded sVEP acuity.

Conclusions: The superiority of sVEP acuity often reported in the literature was evident in our infant sample when subjective acuity (TAC) was low or moderate, but not when it was high (> 10 cpd). The relationship between the two estimation methods was not dependent on age, but on subjective acuity.

Keywords: Visual acuity; Teller Acuity Cards; Sweep visual evoked potentials; Infant

Introduction

Maturation of visual acuity (VA) occurs early and rapidly during infancy. Unlike adults, infants cannot explicitly respond to stimuli, making assessment in preverbal or non-responsive infants challenging. Two common techniques are widely used and considered effective for assessing VA in infants and young children. The first one is a behavioral/psychophysical method based on the preferential looking (PL) paradigm and is used to estimate “subjective” VA. The second one is an electrophysiological method that records visually evoked brain responses and is used to estimate “objective” VA.

The PL paradigm is based on the infant preference to look at a stimulus over an area of the same mean luminance as the stimulus when both are presented simultaneously [1,2]. Behavioral VA is defined as the finest grating that elicits a visual preference. A commonly used tool is the Teller acuity cards (TAC) test [3,4]. To obtain an acuity threshold, the infant must demonstrate behaviorally that she/he sees the stimulus (e.g., by turning the eyes toward the stimulus), which is then judged as perceived or not by the experimenter. The rapidity of test administration and the ease of analyzing, interpreting and comparing the results with standardized norms are the main advantages of the TAC test [5,6] . Furthermore, this test is recognized internationally as a reliable and effective assessment tool [7], and has been widely used to asses subjective VA development [6,8]. However, the estimated thresholds of acuity can be altered by non-visual factors, such as eye control, visuo-motor integration immaturity, fatigue and distraction. In other words, the lack of behavioral response to a given acuity card or even to few subsequently administered cards cannot be unequivocally interpreted as an inability of the infant to detect the stripes.

The visual evoked potential (VEP) technique measures neural activity of the visual pathways from the retina to the visual cortex in response to a stimulus. Specifically, the sweep VEP paradigm (sVEP) [9-11] was designed to assess acuity thresholds rapidly and objectively in young infants. Phase reversed gratings are presented at temporal frequencies greater than 4 Hz so that a ‘steady-state’ periodic signal is elicited and a wide range of spatial frequencies is “swept” sequentially upward or downward. VA threshold is typically estimated from an extrapolation based on the peak of the sVEP amplitude spatial frequency function to zero amplitude [12]. The main advantages of this technique compared to other VEP methods are its speed (each spatial frequency is presented briefly) and the necessity for only minimal cooperation and attention. sVEP is preferred for the assessment of VA in infants as well as in patients who are not able to keep visual attention, fixate the stimulus or report their perception verbally (e.g., those with cerebral palsy, cerebral visual impairment) [13-15].

Even though there are no standards for sVEP acuity thresholds, compared to TAC, data from typically developing infants are available in the literature [16,17]. The obtained acuity threshold is considered to be objective, (i.e., independent from an active response of the infant and a decision of the observer based on that response), in contrast to the TAC test. In fact, the VEP is known to primarily indicate the visual pathway response, with a minor implication of higher brain areas (e.g., associative or motor areas) [18]. It can perhaps be argued that the electrical signal of the sVEP reflects the integrity of the visual pathway and activity of the occipital cortex, but not necessarily visual perception

[19,20]. Moreover, there are some practical limitations of the sVEP technique, such as the requirement of relatively high cost equipment, the placement of electrodes, and the necessity of substantial expertise on signal processing in order to compute the acuity. Because of the lack of standard protocol set by the International Society for Clinical Electrophysiology of Vision (ISCEV), investigators use different VEP extrapolation techniques, which can potentially yield variability in data across studies. For example, according to Norcia & Tyler [16], the first zero corresponds to the intercept of the regression line to the *x*-axis, where the amplitude is actually 0 μV. Other authors [21] consider that the use of 0-μV intercept might stretch the regression line, leading to a superior acuity and instead use a signal-to-noise ratio (SNR) of 1 to estimate the VA threshold.

Although the correlation between the two techniques for estimating acuity is generally high in children and adults [22,23], it remains unclear in infants. Moreover, in infants, the acuity threshold obtained from sVEP is generally better than that obtained with TAC. This difference has been linked to methodological, subjective acuity and/or developmental factors. For instance, the PL procedure uses stationary stimuli whereas the sVEP method uses phase alternating gratings [24]. Interestingly, image defocusing using $> +1.5$D lenses drastically decreases subjective (Snellen) acuity but not objective (sVEP) acuity thresholds, suggesting that motion detection and luminosity change could evoke brain responses in the absence of grating detection [25]. In fact, the level of subjective acuity (measured behaviorally by eye chart or PL) could also play a role in the lack of total agreement between sVEP and TAC found by some investigators [26,27]. The general finding is that when subjective acuity is relatively high (good vision), sVEP acuity and subjective acuity are very similar, but when it is low (bad vision), sVEP acuity tends to be better than subjective acuity. This was found in adult and pediatric populations [28,15,27,29-31], although these samples included patients with heterogeneous etiologies, making it difficult to compare the results with those from healthy children. In accordance with these findings, the immature (low) VA in infants also impacts the acuity measurements. First, the development of acuity during the first year of life is associated with unstable or more variable subjective and objective threshold measurements, as reported by Riddell et al. [18] and Sokol et al. [32]. Second, the threshold difference between the two methods decreases with increasing age, stabilizing by about 6-8 months, and converging to similar values around 12-24 months of age [18,32]. Several explicatory hypotheses have been proposed to account for this age-related difference, such as different rates of development in different cortical areas (first the primary visual cortex linked to objective acuity, and then the motor and/or associative areas linked to subjective acuity) [18] (see Table 1 in Almoqbel et al. 2008 [17] for a summary of studies on VA development).

While visual maturation continues until 4 to 6 years of age [29-31], it might be asked what the relationship is between objective and subjective visual acuity thresholds right after the drastic and exponential postnatal development of the visual system that occurs during the first 6 months of life. Interestingly, little attention by previous studies has been paid to the second half of the first year of life, possibly due to difficulty in testing as age increase (e.g., more locomotion and less cooperation) and the major interest in the period of exponential development (the first six months of life). Therefore, it remains unclear how the two VA assessment methods compare during this period.

While the first exponential growth of VA function occurring in the first 6 months might reflect mostly physiological factors (e.g., maturation of photoreceptors, visual pathways, etc.), the subsequent period is likely to show maturation of higher level, such as which is cortical functions [33]. This research question is also particularly relevant in clinical settings since VA is commonly tested in infants with both techniques, although the TAC is more commonly used. It is also important to know the relationship between the two methods to ultimately be able to predict the score of one method from the other, which can be particularly helpful is some cases. For instance, TAC data might not be possible to collect properly in infants or children with particular neurodevelopmental disorders, so that sVEP is the only option. The aim of this study was thus to compare VA thresholds obtained using both subjective (TAC) and objective (sVEP) methods in a sample of infants with no sign of ocular and/or neurologic impairments, at a period of development in which grating acuity is starting to stabilize but is still increasing, i.e., during the second half of the first year of life.

Methods and materials

Participants

Seventy-two infants were enrolled in the present study. To be included in the study, infants had to be aged between 6 and 12 months, born healthy (without birth defect or neurological dysfunction), without obvious observable ocular abnormality (e.g., congenital cataract, retinoblastoma, etc.), as screened by the red reflex examination test and with normal weight for gestational age. Only infants born full term or moderately to late preterm (i.e., > 32 weeks of gestation) were included. In our sample, four participants (6.5%) were born between 34.2 and 36.6 weeks of gestation and therefore their corrected age, which is obtained by subtracting the number of weeks of prematurity from chronological age at testing time, was considered.

Seventy infants (97.2%) successfully completed the TAC, and sVEP data were acquired for 62 (86.1%) of them. The final sample includes 61 infants (84.7%) (32 males, 29 females) aged between 6.0 and 9.8 months (M = 7.41, SD = 0.93), for whom both TAC and sVEP were available. Both tests were administrated on the same day at the Mother and Child Sainte-Justine University Hospital Center. The TAC test was always administrated before the sVEP for practical reasons, accounting for the finding that sVEP was not conducted in all infants due to tiredness and lack of cooperation. There was no significant difference in age distribution between males and females. Of note, the measures obtained in the premature infants did not differ significantly from full-term infants, which is in agreement with previous studies [18]. The study was approved by the Health Canada Research Ethics Board and the CHU Sainte-Justine ethics committee and adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from the parents of all infants tested after explanation of the nature and possible consequences of the study.

Teller acuity card procedure

Trained research nurses administrated the Teller Acuity Card^{TM} II test to estimate behavioral acuity under binocular viewing. Test duration varied from five to ten minutes. The stimulus set included laminated cards (25.5 x 55.5 cm), containing on one-side vertical black-and-white square wave gratings (12 x 12 cm) with a contrast of approximately 60-70%. Gratings ranged from low (1.3 cpd) to high (38 cpd) spatial frequencies, that is from wide to narrow stripes, varying in approximately 0.5-octave steps (where 1 octave is a halving or doubling of spatial frequency). Each infant was seated on their parent's lap at a distance of 55 cm from the stimulus cards. The cards were presented starting with a low spatial frequency grating (wide stripes) and going progressively to higher spatial frequencies (narrower stripes). The side (left or right) of the grating was arranged in pseudo-random order before testing began and was varied by flipping the card by 180°. The experimenter, masked to the side on which the grating was presented, looked through a small peephole and judged the location (left or right) of the grating based on the child's looking behavior. For each card, if after a 180-degree rotation the experimenter was still unsure about the child's response, the card was presented several additional times (approximately three or four rotations) until a clear judgement was made, as recommended in the TAC test manual. This was done for each card either until the observer judged that the infant had made a clear mistake in the grating location twice in a row or until the behavior became unclear and could not be scored. The highest spatial frequency (narrowest stripes) scored by the experimenter as seen was considered to be the VA threshold.

Sweep visual evoked potential procedure

A protocol based on the method described by Norcia and Tyler [16] was used. Infants were seated on their parent's lap at a distance of 85 cm from the stimuli, which were generated using Presentation® software and presented on a CRT monitor (Hewlett Packard, 1280x1024 pixels, 75 Hz). The stimuli consisted of vertical sinusoidal gratings (contrast 80%; luminance 50 cd/m^2) ranging in spatial frequency in 11 logarithmic steps. The gratings were presented from high (13.5 cpd) to low (1.0 cpd) spatial frequency; that is, from narrow stripes to wide stripes (13.5, 12.25, 11.0, 9.75, 8.5, 7.25, 6.0, 4.75, 3.5, 2.25 and 1.0 cpd). The stimuli were swept at 12 reversals/s, with each spatial frequency displayed and recorded in 1-second segments, resulting in a total sweep length of 11 seconds. Sweeps were repeated ≈5 times (from 2 to 6), depending of the infant's cooperation and attention. The gaze of the infant was maintained on the screen using attractive and colorful visual stimuli between trials. When visual disengagement occurred, attention was drawn to the screen using a small noisy rattle. Moreover, when the experimenter seated next to the child judged that the infant gaze was not fixed on the screen, recording was interrupted using a wireless computer mouse and an animal sound was simultaneously emitted from a speaker situated on the top of the stimulus screen.

EEG data was acquired using the V-AMP system (Brain Products, Inc., Munich, Germany) by Ag/AgCl electrodes and recorded at a sampling rate of 1000 Hz with a band pass filter of 0.1 to 100 Hz. In concordance with the ISCEV standard [34], the EEG was recorded from an active electrode placed at the occipital cortex (Oz), referenced at Fz and grounded at AFz (forehead). Electrode impedance was always kept between 5 and under 10 kΩ. The sVEP signals were analyzed using Analyzer® software. Semi-automatic detections were done to reject muscular and ocular (blinks) artefacts. A segment was discarded if 50% or more contained artefacts. sVEP segments were then averaged and the amplitude of the second harmonic as well as the phase of the responses were extracted using a Discrete Fourier Transform (DFT) over a 1000 ms recording epoch. The software calculated mean amplitude value for each spatial frequency and estimated background noise level using the magnitude of frequency components that neighbored the driven frequency component, i.e., 11 and 13Hz.

sVEP VA threshold was estimated using linear extrapolation of the amplitude as a function of spatial frequency recorded at 12 Hz. VA extrapolations were calculated using Matlab® program (MathWorks, Inc.). Briefly, a regression line was fitted to the data using "the peak amplitude" (the last data point where the spatial frequency presented elicited a maximum amplitude response that differed from the background noise) and "the first zero" (the first data point where the spatial frequency presented did not elicit a VEP response). In the present study, two different extrapolation methods were used. First, the one described by Norcia & Tyler [16], where the first zero corresponds to the intercept of the regression line to the *x*-axis, where the amplitude is actually 0-μV. Since this method is known to possibly stretch the regression line, and therefore possibly overestimate acuity threshold, a second method was used where the threshold intercept was calculated at a signal-to-noise ratio (SNR) of 1, i.e., when the noise was equivalent to the signal [21]. To assess VA thresholds, some basic criteria regarding SNR and phase consistency were verified for both extrapolation methods: (1) The SNR of the peak amplitude had to be 3 or greater to minimize false signal alarm rates [16]; (2) If multiple peaks amplitude occurred, the one nearest the highest spatial frequency was selected; (3) The SNR of the first zero had to be 1 or less, since, by definition, a SNR<1 indicates that the sVEP response is not significantly different from the background EEG noise [35]; (4) The phase of the response within the range of spatial frequencies used for the VA estimate had to be either constant or gradually lagging behind the stimulus as spatial frequency increased [17]. Our sVEP extrapolation technique is presented in Figure 1 for a typical participant.

Statistical analysis

Acuity thresholds of the two measures (TAC and VEP) were expressed in cpd, where higher cpd value means better acuity. The differences between those two VA measures were expressed in octaves (1 octave is a halving or doubling of spatial frequency), where higher values correspond to greater differences, and where positive and negative values correspond, in comparison to TAC, to higher and lower VEP, respectively. For statistical analyses, a log-2 transformation was applied to the TAC data to achieve normal distribution, so that all the data were normally distributed (asymmetry and kurtosis values were between -1 and +1). Comparisons between electrophysiological and behavioural VA thresholds were made with paired *t*-tests and ANOVAs. Pearson and intra-class correlation coefficients were calculated to determine the relationship and the agreement between the two methods. All statistical analyses were done using SPSS v22 (IBM Corp. in Armonk, NY) with a significance threshold of $p = 0.05$.

Results

TAC scores for all subjects (M=5.58; SD=2.95, range from 1.60 to 19 cpd) were within the ±90-99% CI of the norms reported in the literature [36,5,37,6]. Acuity thresholds values obtained using the two sVEP extrapolation methods, 0-μV amplitude [16] and SNR of 1 [21], were highly correlated (r =0.976, p<0.001). However, a paired *t*-test revealed that VA estimates using the 0-μV method were slightly but significantly better

(*M*=10.04; *SD*=2.92; range from 3.67 to 17 cpd) than estimates using SNR of 1 (*M*=8.97; *SD*=2.52; range from 3.2 to 13.95 cpd); $t_{(60)}$= -11.66, *p*<0.001. Since the latter approach better corresponds to the notion of threshold (perceptual limit), the sVEP scores derived using the SNR of 1 method were used in the subsequent analyses. Distribution of TAC and sVEP data as a function of age is shown in Figure 2.

Relationship and agreement between TAC and sVEP thresholds

For the sample as a whole, sVEP scores (*M*=8.97; *SD*=2.52 cpd) were significantly better than TAC scores (*M*=5.58; *SD*=2.95 cpd), $t_{(60)}$ = -7.70, *p*<0.001. sVEP score was actually better than TAC score for 49 infants (80.3%). The remaining 12 infants (19.7%) showed better TAC score than sVEP score. The mean difference between the two measures (sVEP minus TAC, measured in cpd) was 1.05 octave (*SD*=1.25, range -0.50 to 5.26 octaves). Figure 3 presents the distribution of the sVEP-TAC differences in octave units. The two measures agreed within 1 octave (from -0.50 to 0.96 octave) in 39 infants (64%). Among the 12 infants (20%) with a difference of > 2 octaves, 4 showed a large difference, ranging from 3.41 to 5.26 octaves. These differences were not due to sVEP scores (> 7.05 cpd) but to atypically low TAC scores which ranged from 1.60 to 2.40, i.e., to the 5_{th} and 10_{th} percentiles of the TAC data distribution, respectively.

Figure 4 shows the relationship between sVEP and TAC threshold acuities. No significant correlation was found (r_p = 0.18, *p* = 0.18). Of note, there was an overrepresentation of the 6.5 cpd score at the TAC (1/3 of the infants), which reduced data variability and may have affected the power of correlation analyses. The data points that fall on the line of equality (slope = 1) represent participants for whom the values of the two measures are identical. All points below the line of equality represented the participants for whom sVEP scores were better than TAC (80.3%).

Because Pearson correlation does not necessarily reflect data agreement, the intra-class correlation coefficient (ICC) was also calculated [38]. No significant ICC between the two measurements of acuity was found ($r_i = 0.03$, $p = 0.22$). The agreement and systematic error between the two measures is qualitatively illustrated in Figure 5 using the Bland-Altman plot [39,40]. The difference between the two measures is plotted against the mean acuity score of the two measures. The mean difference was 3.39 cpd in favor of sVEP thresholds. Data distribution close to the 0 line indicates that only very few infants had perfect agreement (no difference) between the methods. Most of the data points lie within the upper and lower 95% CI, except for two participants.

Potential influence of age and subjective acuity

We found a significant relationship between the differences of the two assessment methods and the TAC scores ($r = -0.75$, $p < 0.001$), and the sVEP scores ($r = 0.37$, $p = 0.003$). As such, when TAC score was good, the difference between methods was small, and when sVEP score was good, the difference between methods was large (Figure 6a and 6b). Although the age range in our sample was quite limited ($M = 7.41$, $SD = 0.93$, range from 6.0 to 9.8 months), we examined whether age was related to the acuity measures. The TAC (behavioral VA estimates) were not significantly correlated with age ($r = -0.05$, $p = 0.69$) (Figure 6d). However, statistical trends (i.e., p values ≤ 0.1) was observed for the correlation between sVEP VA estimates and age ($r = 0.20$, $p =$

0.1), as well as the correlation between the VA estimate difference (sVEP score – TAC score, in octave) and age ($r = 0.22$, $p = 0.09$) (Figure 6d and 6c, respectively).

To better understand the correlation between the acuity score difference (sVEP–TAC) and subjective acuity (TAC), the data distribution of the latter was divided into quartiles in order to run a one-way ANOVA (Figure 7). Four groups were thus created based on the level of subjective acuity: (1) 1.6 to 3.2 cpd (n=18), (2) 4.8 to 6.4 cpd (n=13), (3) 6.5 cpd (n=22) and (4) 9.6 to 19 cpd (n=8). A significant main effect was found, F (3, 57) = 27.56, p < 0001. Post-hoc pairwise comparisons using the Tukey correction indicated that all quartiles were significantly different, except between quartile 2 and quartile 3. The two methods yielded similar acuity values (that is, negligible differences) when TAC scores became > 6.5 cpd. In fact, TAC and sVEP scores were significantly correlated in the fourth quartile only ($r = 0.73$, $p = 0.04$). A Wilcoxon Signed-Ranks Test indicated that TAC scores ($M = 11.20$, $SD = 3.37$ cpd) in the fourth-quartile group were significantly better than sVEP scores ($M = 9.99$, $SD = 1.77$ cpd) ($Z = -2.52$, $p = 0.01$). This pattern (TAC > VEP) was true for 6 out of 8 subjects. Of note, the mean age of the 9.6-19 cpd group (M=7.2, SD=1.1 months) was not significantly different than the mean age of any other group ($ps > 0.05$).

Discussion

All TAC thresholds measured in the present study were within the norms found in the literature and comparable to those from other studies [37,5,7]. However, because the TAC test provides categorical scores, 1/3 of the infants had a visual acuity threshold of 6.5 cpd at the TAC test. This bias, which was not related to age, might have affected the variability of the data and thus the power of the correlational analyses (see Figure 4). The sVEP thresholds, on the other hand, were slightly lower than those found in the literature. Indeed, Prager et al. [26] reported an sVEP threshold mean of 10.39 cpd in 8-month-old infants, whereas other studies found sVEP thresholds up to 20 cpd by the end of the first year of life [41,42,16]. For example, Norcia & Tyler [12] used the 0-μV amplitude method of extrapolation and found an increase from 4.5 to 22 cpd from age 1 to 13 months. When using the SNR of 1 for threshold extrapolation, however, Zemon al. [21] found that half of their subjects were below the 95% confidence limits computed by the Norcia and Tyler. In the present study, we found a mean difference of 1.07 cpd in acuity scores between the two VEP extrapolation methods (0-μV vs. SNR of 1). In agreement with Zemon et al. [21], this suggests that the 0-μV extrapolation approach might overestimate VA. Another factor that could explain our lower sVEP acuity results is the fact that we always used of the mean response of the sweeps, whereas the best sweep among trials, i.e., the one that was associated with the best acuity, is another procedure commonly used [12,43,26]. Finally, the TAC test was always performed before the sVEP test for practical reasons, therefore infants might have been more susceptible to fatigue or inattention while doing sVEP.

Other differences between TAC and VEP testing procedures can be underlined. First, the test distance was not exactly the same (55 cm for TAC and 85 cm for VEP). However, we believe that VA estimates (in cpd, i.e., regardless of the test distance) obtained from both methods can be compared even if different distances were used since infants at this age (6-10 months) are capable of accommodation. Even in very young infants, varying viewing distance from 30 to 150 cm has been found not to affect acuity estimates in 1- to 2- months-old [44]. Second, the stimuli were not identical between TAC and sVEP assessments. In fact, most of VEP studies use sine-wave gratings to assess visual acuity, which confers several advantages, including a better control in terms of spatial frequency (they do not include the additional harmonic frequencies present in square waves due to the sharp edges). Campbell and Robson [45] reported higher contrast sensitivity (about 0.25 increase) when testing with square-waves in comparison to sine-waves. The increase in sensitivity, regardless of spatial frequency, may seem significant, but represents actually only 0.1 log unit increase, which is within response variability commonly observed. On the other hand, the TAC is only commercialized with square-wave gratings. One major potential bias related to square-wave stimuli is that the sharp edges might be used as a detection clue, increasing the subjective VA threshold. However, this bias is probably negligible in infants since the TAC VA scores are systematically lower than VEP acuity.

As demonstrated by numerous previous studies conducted with infants [3,32,41,18], we found that the sVEP acuity was in general better than the TAC acuity. Several explicatory hypotheses have been proposed to account for this difference, such as variation in the maturation rates of the implicated cerebral areas (i.e., primary visual cortex vs. motor or associative cortices) and methodological factors relative to the subjective test (e.g., staircase vs. classical procedure, printed vs. computer-displayed stimulus presentation, stationary vs. temporal stimulation) or to the objective test (e.g., limitation of the monitors to produce high contrast for high spatial frequency gratings, temporal factors, luminance display, logarithmic vs. linear presentation of the spatial frequencies, threshold criterion across techniques and studies)

[30,18,43,29,25,26,46,24]. In our study, although the correlation between TAC and sVEP VA thresholds was very weak, there was a strong agreement between the two methods within 1 octave for almost 2/3 of the infants (see Figure 3). The absence of correlation between TAC and sVEP scores, which was also reported by other studies [29,47,26], suggests that different aspects of vision are being measured by each technique. Furthermore, the Bland-Altman plot showed that one visual acuity threshold does not necessarily predict the other. The estimated mean difference found in the present study in favor of sVEP thresholds is in accordance with Prager et al. [26] who reported in normal infants a mean difference between sVEP and TAC thresholds (sVEP minus TAC scores) of 0.8 and -0.2 octave at 4 and 8 months, respectively, and with Sokol et al. [24] who found 2 octave difference at the age of 2 months and a 0.5 octave difference at 12 months (see Figure 3 in Sokol et al.).

VA function increases rapidly during the first year of life, with development in the first six months being exponential, after which the rate of improvement levels off by 12-14 months of age [32,18], although it is not until later in childhood that acuity is as good as that of adults [48]. It has been reported that age during infancy can contribute to the sVEP and TAC difference in such a way that greater differences are observed with younger infants while such pattern is no longer present at 12-14 months of age [32,18]. Such an age effect was not detected in our study sample. This result might be due to the fact that the age of the participants was close to the development period where the VA threshold difference tends to stabilize (after 12 months) and/or the age range (6 to 10 months) was too short. In support of the latter hypothesis, no significant correlation was found between age and acuity, either from TAC or sVEP (Figure 6), although the slope of the latter showed a trend toward increasing as a function of age. This result suggests that sVEP might be more sensitive to track visual maturation during the first year of life. In agreement with this notion, it has been shown that the improvement of sVEP acuity is drastic and linear during the first postnatal months but stabilizes quickly after the first year of life [18]. By contrast, TAC acuity is lower in young infants but improves exponentially during the first 6 months, followed by a slower but consistent phase of improvement, reaching adult level at around 4 to 6 years [37]. One possible reason for the different rate of improvement between the two acuity measures might be that the TAC, by contrast to sVEP, requires some processes such as sensory-motor integration that are still immature during the first months of life [32,37]. The convergence of the two measures of acuity around 12 months of age might reflect the maturation of all of those factors limiting visual acuity, both functional (e.g., maturation of sensory-motor integration, attention, orientation capacity) and structural (maturation of the fovea and the visual pathway, myelination of the optic nerve, increase density and agglomeration of the cones) [32,37,49].

Many authors have shown that when acuity reach high value (good vision), electrophysiological VA is better than subjective VA, and when acuity is low or decreased (lower vision), subjective VA is better than electrophysiological VA [29,31,47,50,51,27]. In the present study, we showed that the higher the subjective acuity, the lower the difference between sVEP and TAC thresholds, even becoming insignificant at around 10 cpd (Figure 7). This result in healthy infants agrees with previous studies conducted in visually-impaired children, patients and healthy adults [43,51,25,50]. For example, Arai et al. [29] found in adult patients with various ocular pathologies that as Snellen scores increased, the difference between sVEP and subjective VA measures decreased and reversed when Snellen VA was better than 20/60 (10 cpd).

Our finding suggests that the differences and similarities between sVEP and TAC acuity estimates in relation to subjective acuity is not restricted to visually impaired individuals or adults, but is also present in healthy individuals as early as the first year of life. Therefore, although it is not clear why, relative to TAC, sVEP tends to be better in individuals with subjective acuity lower than 10 cpd, and to be lower it in those with a subjective acuity higher than 10 cpd [29], it seems that this effect occurs in individuals with or without ocular or neurological diseases and, as suggested by our data and by the work of Orel-Bixler [43], is not dependent on age, which in our sample is during the second half of the first year of life.

Conclusion

We showed that sVEP were generally better than TAC thresholds, until the subjective acuity reached a spatial resolution of 10 cpd, at which point the two methods provide similar results. To our knowledge, even though some limitations are present in this study, it is the first to show such a pattern in healthy infants, previously reported only among adult or children populations. The weak correlation between the two VA assessment methods in infants suggests that they may not reflect the same neural processing and, therefore, should not be used interchangeably. The two methods are thus complementary, providing different information about visual acuity function. Given its major advantages (easier, quicker, etc.), subjective VA assessment is often performed first in clinical settings. Our results suggest that if unclear results are observed and/or when a pathology is suspected (e.g., amblyopia, optic nerve disorder), VEP should be prioritized given their methodological advantages (finer scale compared to TAC, independent from sensory-motor capacities, etc.).

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Compliance with ethical standards

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Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Figure captions

Fig. 1 a) Fourier amplitude as a function of spatial frequency for one infant (male, 7.1 months old). The responses show an initial increase in amplitude followed by a coherent decrease in relation to an increase in spatial frequency. The acuity limits were estimated at 11.39 and 10.10 cpd, using the 0-μV and the SNR of 1 extrapolation methods, respectively. For this particular example, 7 data points were used to fit the regression line, specifically between 2.25 and 9.75 cpd. **b)** The phase angle is relatively constant up to 7.25 cpd and becomes inconsistent at higher values.

Fig. 2 Distribution of TAC and sVEP VA thresholds (in cpd) as a function of age (in months). Error bars = ±1 standard error of mean (SEM).

Fig. 3 Range of the differences between sVEP and TAC VA thresholds expressed in octave from the whole sample.

Fig 4. VA thresholds determined from sVEP and TAC (cpd). The solid line represents the best-fit function of the data, $y = 0.25x + 3.30$. The dashed line (equality line) represents the agreement between the two measures. Data points above the equality line represents better TAC than VEP, and data points below represents better VEP than TAC. The wide data distribution exceeding the equality line indicates the inconsistency between measures.

Fig. 5 The Bland-Altman plot shows the difference between the two measures as a function of their average (in cpd). The solid line at 0 value represents perfect agreement, the solid gray line the mean difference value (3.39 cpd) and upper/lower dashed lines, respectively positioned at 10.27 and -3.49 cpd, account for the 95% CI. The lower part of the plot (below the zero solid line) contains data from infants with better TAC than VEP scores and the upper part contains data from infants with better VEP than TAC scores.

Fig. 6 Relationship between score difference (sVEP – TAC in octaves) and (a) subjective acuity (in cpd), (b) objective acuity (in cpd) and (c) age (in months). Relationship between (d) subjective/objective acuity (cpd) and age (in months). In each plot, the regression line corresponds to the best-fit function, (a) $y = -0.29x + 2.66$, (b) $y = 0.17x - 0.43$, (c) $y = 0.13x + 0.09$ and (d) $y = -0.22x + 7.24$ (TAC) and $y = 0.54x + 4.97$ (sVEP).

Fig. 7 Score difference (sVEP – TAC in octaves) as a function of subjective acuity (in cpd) in each quartile. The negative values on the *y*-axis indicate that TAC thresholds are better than VEP thresholds. The bars represent the mean difference score for each quartile; Error bars = ±1 standard error of mean (SEM).