Development of visual acuity and contrast sensitivity in children

by

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A thesis
presented to the University of Waterloo
in fulfillment of the
thesis requirement for the degree of
Doctor of Philosophy

in

Vision Science

Waterloo, Ontario, Canada, 2011

AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Purpose: There is little agreement on the age at which visual acuity (VA) and contrast sensitivity (CS) become adult-like. The ultimate purpose of this thesis was to determine whether VA and CS are adult-like at the age of 6-8 or 9-12 years by using both objective and subjective methods in the same individuals. The objective method (sweep visually evoked potentials [sVEP]) has many parameters that may affect the measurement of VA or CS and previously these had not been studied systematically, especially in children. Therefore, a second purpose was to study the effects of these parameters on VA and contrast thresholds and to determine the parameters that give the most repeatable measurements and the greatest number of viable readings in children, to be compared to previous data obtained in adults.

Methods: The effect of five criteria (C0-C4) for choosing the endpoint for the regression line fitting and three luminance levels (25, 50, and 100 cd/m^2) on the sVEP VA and contrast thresholds (at 1 and 8 cpd) was investigated in six 6-8 year old children. Additionally, the effect of these parameters on the number of viable readings obtained from five active electrodes was investigated. C0 was derived from the sVEP software (PowerDiva), C1 used the best fit by eye to determine the range over which the regression line was fitted, C2 used the data point between signal peak and the last data point with an SNR ≥ 1, C3 was similar to C2 but was defined so that the threshold should be within the sweep range, and C4 was similar to C2 except that the SNR should not fall below one at any point within the range used for the regression line fitting. The effects of two electrode placements, three temporal frequencies (6, 7.5, and 10 Hz), sweep direction (low to high and high to low), presence or absence of a fixation target, three stimulus areas (6, 4, and 2° for VA and 15, 10, and 6° for contrast thresholds) and three sweep durations (10, 15, and 20 sec) on VA and contrast thresholds (at 1, 4, or 8 cpd) measured with sVEP were also investigated in six 6-8 year-old children and six adults with normal vision. Additionally, the effect of these parameters on the number of viable readings obtained from five active electrodes was investigated. The sVEP parameters that were found to give the best threshold measurements were employed in a cross sectional study of the development of VA and CS. In this study the objective sVEP technique and two psychophysical techniques were used. The psychophysical techniques were comprised of a two-alternative forced choice (2AFC) staircase for measuring VA and contrast thresholds and signal detection theory (SDT) for measuring contrast threshold. Crowded and uncrowded logMAR VA were also measured with a Bailey-Lovie logMAR chart. The study included three age groups (6-8, 9-12 year olds and adults). The criterion employed by each age group as indicated by the SDT was compared.

Results: There was a significant effect of the criterion for choosing the endpoint for the regression line fitting ($p < 0.05$) on all the measures and a significant effect of luminance ($p = 0.036$) on contrast threshold at 1 cpd. Criterion C2 (in which the range for the regression line fit was defined to include all the data between the signal peak and the last data point [furthest from the peak] with an SNR ≥ 1) consistently gave more viable readings and better thresholds (i.e. higher VA and lower contrast thresholds) than the other criteria. Also C2 was the best criterion in terms of repeatability in children, and repeatability and validity in adults (Yadav et al., 2009). The luminance of 25 cd/m^2 gave higher contrast thresholds than 50 or 100 cd/m^2. There was a significant effect of temporal frequency on the number of viable readings for VA ($p < 0.0001$) and for contrast thresholds ($p = 0.0001$), with more viable readings at 7.5 Hz than at either 6 or 10 Hz. The adults gave more readings with the fixation target than without it ($p = 0.04$) for contrast threshold at 1 cpd. The smallest stimulus area used gave rise to fewer viable readings in both adults and children ($p = 0.022$ for VA and 0.0001 for contrast threshold). The other parameters (electrode placement, sweep direction and sweep duration) did not result in significant differences.

There was a significant effect of age on crowded ($p = 0.0001$) and uncrowded ($p < 0.0001$) VA. The 6-8 year olds gave poorer VA than the 9-12 year olds or adults for both crowded and uncrowded VA. For the grating VA (sVEP and 2AFC staircase) there was a significant effect of age ($p = 0.002$). The 6-8 year olds had poorer VA than the 9-12 year olds or adults. For contrast threshold at 1 cpd, a significant effect of age was found for the 2AFC ($p = 0.008$) and SDT ($p = 0.0003$). The 6-8 year olds gave poorer contrast thresholds than adults with each procedure. For contrast thresholds at 8 cpd, there was a significant effect of age with the 2AFC staircase ($p = 0.036$). The 6-8 year olds gave poorer contrast thresholds than the 9-12 year olds. For SDT, there was a significant effect of age on criterion ($p < 0.05$), with adults being more likely to say “no” in the yes-no SDT procedure than both the 6-8 year olds and the 9-12 year olds for contrast threshold at 1 cpd. Adults were also more likely to say “no” than the 9-12 year olds for contrast thresholds at 8 cpd.

Conclusions: This thesis has shown that VA and CS are not adult-like until the age of 9-12 years by these measures and that children do show differences in criterion compared to adults in psychophysical testing. This difference in criterion indicates the use of SDT or force-choice procedures to avoid this problem in any psychophysical developmental study. It has also shown that criterion for choosing the endpoint for the regression line fitting in the sVEP technique has the greatest effect on VA and contrast thresholds measurements and viable readings, while the other sVEP parameters have little effect on the thresholds.

Acknowledgements

I would like to express my sincere thanks and gratitude to my supervisors, Professor Susan Leat and Professor Elizabeth Irving, for their guidance, support, and encouragement throughout my PhD studies. They helped me develop my research and writing skills through their insightful comments and directions.

I would like to thank my committee members, Professor Trefford Simpson and Professor Marlee Spafford, for their helpful suggestions and comments. I also appreciate the constructive comments of my external examiners, Dr. Dave Ellemberg and Dr. Roxane Itier.

Thanks to Naveen Yadav, my former labmate, for sharing his experience in the sweep VEP software and for all the good times we have spent together. I thank Dr. Liseann Head and Dr. Carolyn Machan for their assistance with the child participants.

I appreciate all the financial support from my employer, King Saud University, and from the Ministry of Higher Education in the Kingdom of Saudi Arabia. I am also thankful to the Saudi Cultural Bureau in Canada for its continuous assistance.

I am grateful and indebted to my mother, my mother-in-law, and my siblings for their prayers and emotional support.

My greatest thanks and appreciation go to my wife, Alanoud, for her enormous encouragement, support, patience and love.

Dedication

To my beloved wife, Alanoud

&

To my children, Abdulaziz and Norah

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Chapter 1
Introduction and literature summary

Different functions of the human visual system mature at different ages through childhood or even into adolescence (Lewis & Maurer, 2005). Visual acuity (VA) and contrast sensitivity (CS) are two of the most extensively studied visual functions. The assessment of these two visual functions can be done subjectively for verbal and cooperative individuals by using visual acuity and contrast sensitivity charts. In the case of infants and nonverbal or uncooperative individuals, an objective (behavioral or electrophysiological) assessment is required. It is important to know when these visual functions become adult-like so that children who do not attain adult-like levels can be recognized, as they may possibly need investigation for the cause of poorer vision. However, the use of different methodologies and stimulus characteristics in the studies assessing VA and CS may have contributed to the disagreement on the timescale for the development of these functions.

In this thesis, a cross sectional study of the development of VA and CS in children, using both subjective and objective methods, is presented. The main aim was to determine whether VA and CS are adult-like at the age of 6-8 or 9-12 years. This chapter describes VA and CS and the subjective (psychophysical) and objective (visual evoked potential [VEP]) techniques used for measuring them. It also provides a review of the literature on the development of VA and CS.

1.1 Visual acuity

VA testing is the most common procedure in an eye examination. A reduction in VA indicates a dysfunction of the visual system (eye, visual pathway, or visual cortex), and triggers the need for further testing to determine what caused the poor VA. Different types of VA have been identified, with different tests having been developed to measure each of them. These types are detection acuity, resolution acuity, recognition acuity and vernier (hyperacuity) acuity (reviewed in Saunders, 1999). Detection acuity is simply the ability of a person to detect the presence of a visual stimulus and it is usually tested when other types of acuity cannot be assessed (Saunders, 1999). An example of a detection acuity test is the Bock Candy Bead test (McDonald, 1986).

Resolution acuity is a measure of the ability of an individual to visually resolve the separation of contours. The smaller the separation of contours the person can see, the better is the VA. An example of resolution acuity is the ability to resolve the separation between the black and white stripes of a grating. The spatial frequency of a grating is described by the number of cycles subtended at the eye per degree of visual angle (c/d) (Duckman, 2006). Each cycle is composed of one black stripe and one white stripe. One test that employs gratings for measuring VA is the Teller acuity card test, which applies the technique of preferential looking in the clinical setting. The preferential looking technique uses the fact that infants prefer to a fixate pattern stimulus over a plain stimulus. In the Teller acuity card procedure the infant is shown a series of grey cards. Each card contains a black and white grating located on the right or left of a small aperture. The spatial frequency of the grating varies from card to card. The observer shows the infant one card at a time, starting from a low spatial frequency and notices (through the aperture) the infant's eye and head movement. The observer decides, based on the infant's looking behavior, which cards contain gratings that can be resolved by the infants. Acuity is estimated as the highest spatial frequency that the observer can accurately determine which side of the card the grating is located (Teller et al., 1986).

Recognition acuity requires the person to identify a letter, a number, shape or picture. These are generally called optotypes. This test is the most widely-used clinical VA test, and is suitable for older children and generally people who can identify the objects on test chart, either verbally or by matching

Vernier acuity is a measure of the eye's ability to perceive that a misalignment exists between the elements of the stimulus, when compared with a stimulus without such misalignment (Duckman, 2006).

Thresholds for the different types of VAs differ considerably. The detection threshold for a line width is around 0.5 second of arc, the resolution threshold is between 0.5-1 minute of arc, the recognition threshold is 0.5-1 minute of arc and the vernier threshold is between 3-6 second of arc (reviewed in Saunders, 1999). Although resolution and recognition acuities have the same threshold on average, they do not correlate very well. Resolution (grating) acuity is better than recognition acuity in patients with ocular disorders (Mayer et al., 1984; Rydberg et al., 1999 and Stiers et al., 2004).

1.2 Contrast sensitivity

VA testing involves visual stimuli that decrease in size, but the visual system's ability to detect a visual stimulus depends on another stimulus feature, its contrast. A sufficiently large visual stimulus that can be detected when it has a high contrast with regard to its background becomes very difficult to detect when its contrast is reduced. Contrast of an object is defined by the difference in luminance between the object and its background in relation to the background. If L_B denotes the luminance of the background of a letter chart and L_T denotes the luminance of the letter, the contrast of the letter is defined by the Weber contrast as: $(L_B - L_T) / L_B$ (Alexander et al., 1995).

The Michelson contrast is used when black and white stripes (gratings) are employed to measure contrast threshold – the minimum amount of contrast required to detect an object. If L_{max} denotes the luminance of the bright stripes and L_{min} denotes the luminance of the dark stripes, the Michelson contrast is defined as (Michelson, 1927):

$$\text{Contrast} = L_{max} - L_{min} / L_{max} + L_{min}$$

The reciprocal of contrast threshold is contrast sensitivity (CS), which gives an indication of "the ability to detect, discriminate, or recognize objects that vary slightly in relative luminance" (Citek, 2006).

The contrast sensitivity function (CSF) represents the contrast sensitivity of the eye with respect to spatial frequency (Figure 1-1). The reciprocal of the minimum contrast to detect a grating is determined and, when plotted against spatial frequency this gives rise to the curve in figure 1-1. The human adult CSF typically reaches a peak at 3-5 cpd and decreases on either side of this peak. The decreased sensitivity at low spatial frequencies (i.e. the low spatial frequency cut) is thought to be due to lateral inhibition at the ganglion cells, while the decrease at high spatial frequencies is considered to be due to the limited ability (due to optical aberrations and photoreceptors spacing) of the visual system to resolve details (reviewed in Schwartz, 2004). The point where the curve in figure 1-1 meets the horizontal axis (high frequency cut-off) corresponds to the subject's grating VA (Daw, 2006).

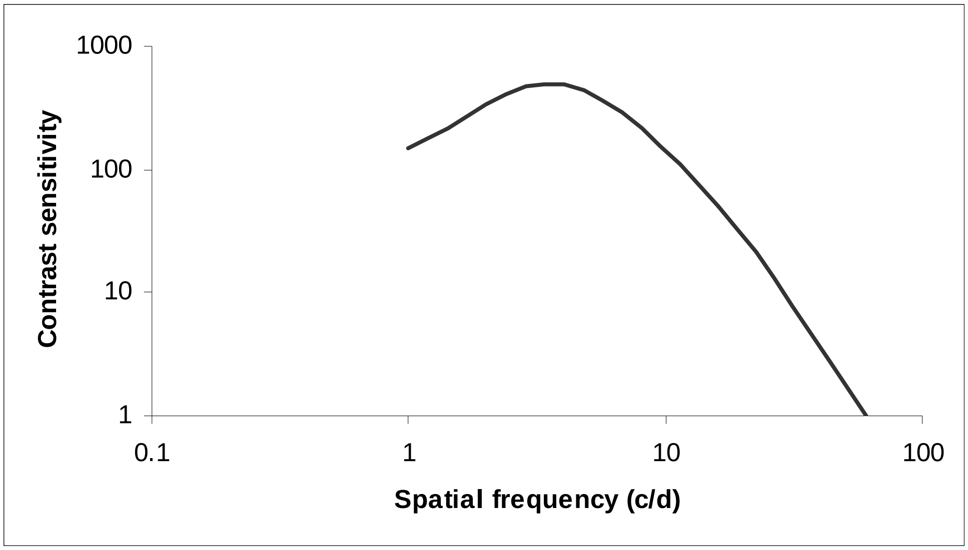

Figure 1-1: Contrast sensitivity function.

Stimuli in the psychophysical or behavioral studies of CS are usually stationary gratings (i.e. have a 0 Hz temporal frequency), while in VEP studies the stimuli are temporally-modulated. The CSF resulting from temporally modulated gratings is distinguished from the CSF obtained with stationary gratings by lacking the low spatial frequency cut (Atkinson et al., 1977).

1.3 Psychophysics

Psychophysics has been defined as "the scientific study of the relationship between stimulus and sensation" (Gescheider, 1997, p. vii). One of the first attempts to measure sensation was made by Gustav Fechner in 1860. Psychophysical procedures consist of a set of methods that quantify the relationship between the physical properties of stimuli and the sensory status of the system under study. The quantification of the sensory status is usually inferred by measuring sensory thresholds. The term threshold refers to the smallest amount of stimulus intensity necessary to barely detect a stimulus (absolute threshold) or the stimulus intensity required to detect a difference in a readily detectable stimulus (difference threshold). The reciprocal of the threshold is termed sensitivity.

1.3.1 The classical psychophysical methods

Gustav Fechner introduced three basic psychophysical methods for measuring thresholds: the method of constant stimuli, the method of limits, and the method of adjustment (Gescheider, 1997). In the method of constant stimuli, repeated presentations of a set of stimuli whose intensities span the estimated threshold are carried out. The stimuli are presented in a random order with the same number of presentations for each stimulus intensity. The subject typically reports whether or not s/he sees the stimulus. Plotting the percent of "yes responses" against the stimulus intensity typically shows a psychometric function with an ogival shape. Classically, the threshold is usually specified as the stimulus intensity that is seen on 50% of the trials.

In the method of limits (Gescheider, 1997), the experimenter presents a stimulus that is well below or well above the estimated threshold. Then, the stimulus intensity is either increased until the subject reports seeing the stimulus (if started below threshold = ascending method of limits), or decreased until the subject reports not seeing the stimulus (starting above threshold = descending method of limits). Any transition point from seen to not seen or vice versa can be taken as an estimate of the threshold, but usually a number of ascending and descending series are performed and the threshold is calculated as the average of threshold values from these series. The method of limits may suffer from two errors: habituation and expectation. The error of habituation occurs when the subject maintains the same response from trial to trial regardless of seeing or not seeing the stimulus. This will result in an increase of the threshold on ascending trials and a decrease of the threshold on descending trials. The error of expectation, on the other hand, will have the opposite effect (a decrease of the threshold on ascending trials and an increase of the threshold on descending trials). This occurs when the subject expects (anticipates) the appearance or disappearance of the stimulus on ascending or descending trials, respectively (i.e. s/he anticipates the stimulus appearance or disappearance and responds too soon). A modification of the method of limits is the staircase method (Gescheider, 1997). In this method a series of stimuli which increase or decrease in intensity are presented. If, for example, the stimulus series starts with a stimulus to which the subject responds by saying "yes" (I can detect it), the stimulus intensity is then decreased by one step. This continues until the subject says "no" (I cannot detect it), and at this time the series is reversed by increasing the stimulus intensity by one step at a time. This procedure continues with decreasing the intensity if the subject's response is "yes" and increasing the intensity if it is "no" until sufficient number of response-transition points (reversals) has been obtained. The threshold is then taken as the average of the stimulus intensities for a number of reversals.

The method of adjustment involves setting the stimulus intensity either well below or well above the threshold and asking the subject either to increase the intensity until the stimulus is just detectable or to decrease the intensity until the stimulus is just undetectable. The average of a number of ascending (starting below threshold) and descending (starting above threshold) settings is then taken as the threshold. An advantage of the method of adjustment is that the subject usually does not get bored as the task requires the subject's continuous participation as s/he increases or decreases the stimulus intensity.

A potential disadvantage that all the classical psychophysical methods have in common is that they do not take into consideration the subject's response bias or criterion (Celesia, 2005). Some subjects may be biased toward responding "yes I saw the stimulus", which result in a decrease in the threshold. On the other hand, some subjects may be biased toward responding “no I did not see the stimulus”, which causes the threshold to increase. This response bias precludes the measurement of an accurate threshold.

1.3.2 Forced-choice method

In the forced-choice method, the subject is presented with two or more observations (alternatives) in each trial, with only one containing the stimulus (Gescheider, 1997). These alternatives may be shown simultaneously but separated spatially (spatial forced-choice), or may be shown one after another in the same spatial location (temporal forced-choice). When the forced-choice paradigm is used with the method of constant stimuli, a psychometric function can be constructed by plotting the percentage of the subject’s correct responses against the stimulus intensity. The threshold is then taken as the stimulus intensity that results in a percentage correct value that lies midway between chance performance and perfect performance. Chance performance is the reciprocal of the number of alternatives (e.g. for two alternative forced-choice, chance performance is ½ or 50%). An advantage of the forced-choice technique is that it minimizes the effect of the subject’s bias toward saying yes or no by forcing him/her to choose between alternative choices. The assumption is that when there is no response bias toward one or more of the observation intervals, the subject will choose the observation interval that contains the largest sensory observation (Gescheider, 1997) and even if one subject is more inclined to say “yes” than another, both subjects will still choose the interval which gives the strongest sensation. The bias toward one or more of the observation intervals can be minimized by randomizing trials, but none of these can control the attention of the subject.

1.3.3 The threshold

As opposed to the old view of threshold as a fixed stimulus intensity that serves as barrier to perception, threshold came to be considered to vary over time due to the variability inherited in the stimulus or in the sensory system. As a result, a visual stimulus of certain intensity may be seen by a subject on some trials and not seen on others. Therefore, a measure of the threshold can be achieved by plotting a psychometric function that shows the percentage of the trials in which the subjects correctly reports seeing the stimulus against the stimulus intensity. Threshold is then taken as the stimulus intensity that is reported to be seen on a given percentage of the trials.

According to Gescheider, early psychophysicists assumed that the subject is unbiased when giving a response to a stimulus presentation during a detection task (Gescheider, 1997). That means s/he would say "yes" only when s/he detects the stimulus and "no" only when s/he does not detect it in a reliable and unbiased manner. However, the results of some psychophysical experiments revealed two non-sensory factors that were found to affect the performance (and the threshold as a result) in a detection task (Gescheider, 1997). The first one is the probability of stimulus occurrence. In a yes/no experiment, in which the stimulus is presented on some trials and no stimulus is presented on other trials, there are four possible outcomes (table 1-1). When the stimulus is presented, the subject may say yes (hit), or say no (miss). When no stimulus is presented, the subject may say yes (false alarm) or no (correct rejection).

Table 1-1: Stimulus-response matrix

Trial \ Response	Yes	No
Stimulus	Hit	Miss
No stimulus	False alarm	Correct rejection

It has been found that the more often the stimulus is presented, the greater the likelihood that the subject will say "yes, I detected the stimulus". This is true for weak, moderate, and strong stimuli. The fact that the subject tendency toward saying "yes, I detected the stimulus" is affected by the probability of stimulus occurrence makes the psychometric function vary and, as result, the measured sensory threshold varies as well. The second non-sensory factor that was found to affect the threshold is the consequences, if any, related to the subject's response. If the subject is to be rewarded when s/he makes a "hit", s/he will say "yes, I detected the stimulus" more often to achieve a high hit rate. As a result, the hit rate will increase but also the false alarm rate will increase. On the other hand, if the subject is to be punished when s/he makes a "false alarm", s/he will say "no, I did not detect the stimulus" more often. In this case, the false alarm rate will decrease but also the hit rate will decrease.

1.3.4 Signal detection theory (SDT)

The assumption of an unbiased response by the subject in a detection task was confronted by the signal detection theory (SDT) proposed by Tanner and Swets (Tanner & Swets, 1954). SDT assumes that stimuli (signals) to be detected by the subject are not pure – they are always contaminated by background activity (noise). The noise may be either external to the subject or internal, but only if the signal exceeds the noise level can the stimulus be detected. SDT emphasizes the decision strategies that the subject employs when s/he is required to detect a signal in the presence of noise and makes no assumptions of a sensory threshold.

In the basic SDT approach, the subject is required to make a decision after each trial of whether the trial contained a stimulus (i.e. a signal added to the background noise [SN]) or no stimulus (i.e. just the noise [N]). Because the N is randomly fluctuating, SN also fluctuates from trial to trial. The result of the subject's decision is one of the four possible outcomes mentioned earlier: hit, miss, false alarm, or correct rejection. Over many trials, N and SN trials result in a range of perceptual experiences that vary randomly. On average, the SN trials evoke perceptual experiences that are greater than those produced by N trials. SDT describes the relationship between these two perceptual experiences as two overlapping distributions (Figure 1-2). The SN distribution results from adding the signal (which is assumed to be constant) produced by the stimulus to the noise distribution N. The mean of N depends on the noise intensity and the mean of SN depends on the noise plus the signal intensity. The subject can distinguish the signal plus noise from the noise alone more easily as the signal intensity increases (i.e. the detectability increases). The detectability measure of the SDT is termed *d'*. The *d'* is the distance between the mean of the N distribution and mean of the SN distribution (Figure 1-2). The calculation of *d'* requires a transformation of the hit rate (*H*) and the false alarm rate (*F*) to z scores. The *d'* then can be calculated as follows (Macmillan & Creelman, 2005):

$$d' = z(H) - z(F)$$

where, *H* is the proportion of SN trials to which the subject responded "yes" and the *F* is the proportion of the N trials to which the subject responded "yes".

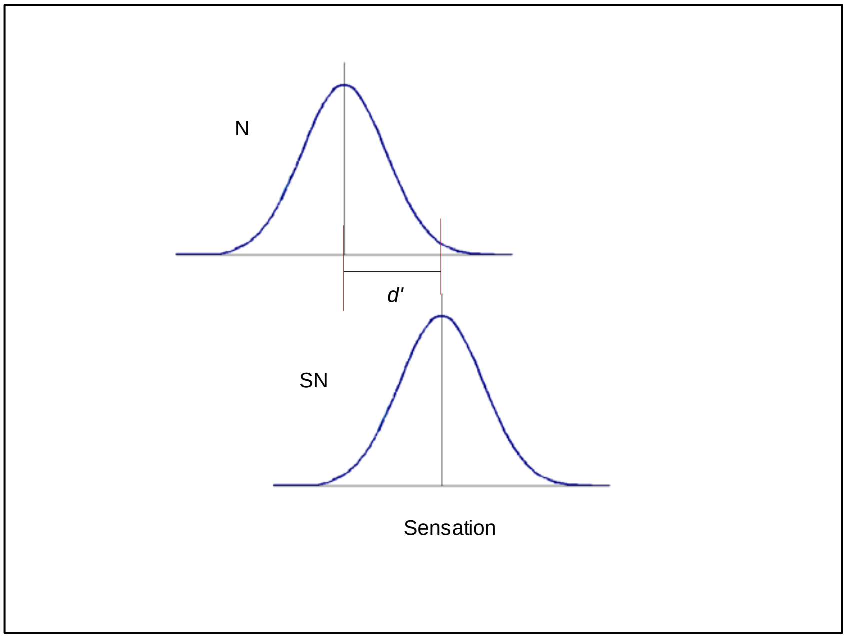

Figure 1-2: Distributions of noise (N) and signal plus noise (SN) showing d'.

The value of d' will be negative if $F > H$, zero if $F = H$, and positive if $H > F$. As detectability increases, the d' value increases positivity. On the other hand, as detectability decreases, the d' decreases and may give negative values. Negative values of d' may result from sampling error or response confusion (i.e. saying no when intending to say yes, and vice versa) (Stanislaw & Todorov, 1999).

Along the continuum in figure 1-3, the subject chooses to place a cutoff point that s/he uses to make a decision after each observation (i.e. trial) of whether the observation is a result of noise alone or a signal added to the noise. This cutoff point is called the criterion. Any observation that exceeds the criterion will be considered as representing the presence of a signal, and any observation less than the criterion will be considered as representing noise alone.

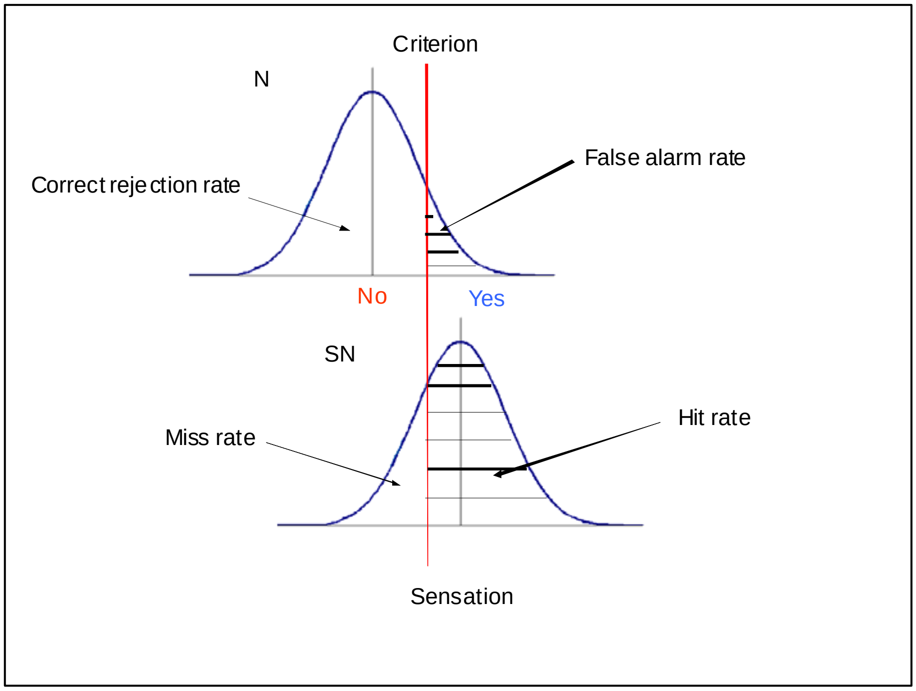

Figure 1-3: Distributions of noise (N) and signal plus noise (SN) showing the subject's criterion and the four possible outcomes in a yes-no experiment that includes signal plus noise (SN) trials and noise (N) trials.

A very conservative subject will place his/her criterion line toward the right in figure 1-3. As a result, the false alarm rate will decrease but also the hit rate will decrease. On the other hand, a very liberal subject will place his/her criterion line toward the left in figure 1-3. This will increase his/her hit rate but also will increase his/her false alarm rate. Thus, reducing the overlap between the SN and the N distributions is the only way to increase the hit rate while decreasing the false alarm; hence increasing *d'*. This makes the sensitivity index (i.e. *d'*) independent from the response bias index or criterion and that is the major advantage of SDT. For example, when a subject is to be presented with the same stimulus on two occasions and is asked to respond "yes" if the stimulus is detected and "no" if it is not, if the subject is being conservative in one occasion and liberal in the other, his/her hit and false alarm rates will change accordingly as mention before but his/her detectability index *d'* will be the same on both occasions.

The invariability of *d'* as the hit rate and false alarm change can be understood in terms of the receiver operating characteristic curve (ROC) (Figure 1-4). To generate ROC curves, the Hit rate (*H*) is plotted on the y-axis against the False alarm (*F*) on the x-axis. For each value of false alarm rate the plot shows the hit rate that would be required to obtain a particular detectability (*d'*) level (Macmillan & Creelman, 2005).

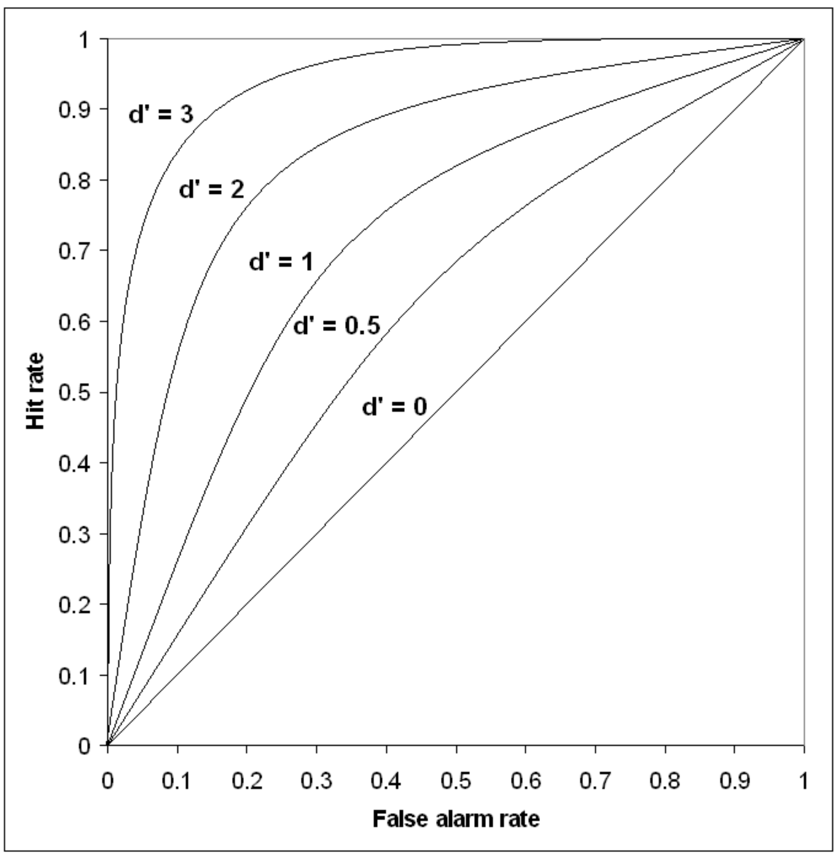

Figure 1-4: Receiver operating characteristic (ROC) curves corresponding to *d'* values ranging from 0 to 3.

While the detectability index *d'* depends on the difference of *H* and *F* (in z scores), the response bias index or criterion depends on the sum of *H* and *F*. The basic bias index in SDT is called *c* (for criterion) (Macmillan & Creelman, 2005) and is defined as:

$$c = -0.5\ [z\,(H) + z\,(F)]$$

Positive values of *c* arise when *F* is lower than the miss rate (1 – *H*) and indicates a tendency to say "no", whereas negative values arise when it exceeds it and indicates a tendency to say "yes". When *F* and (1 – *H*) are equal, *c* equals 0 (Macmillan & Creelman, 2005).

The next two sections review the studies of the development of visual acuity and contrast sensitivity that have used psychophysical techniques.

1.3.5 Development of visual acuity

Subjective studies of the development of grating acuity had to rely on preferential looking (PL) for infants but used classical psychophysical techniques for older children. Table 1-2 summarises the results of subjective studies of the development of VA. Using Operant preferential looking (OPL) and a 60% criterion for correct responses, Mayer and Dobson (1980) studied the development of grating acuity in children between the age of 6 months and 2 years. They found that by 2 years of age grating acuity was close to that achieved by adults. Based on a 75% criterion for threshold, acuity of the 2-year-olds was within a factor of 2 of adult acuity. Using the same technique (i.e. OPL) Mayer and Dobson (1982) extended the age range to infants and children aged between 5 months and 5 years. They concluded that acuity becomes adult-like between the ages of 3 and 5 years. Birch et al. (1983) also used OPL and a 75% criterion for correct responses to estimate acuity in children between 7 months and 5 years. Their results showed that acuity of the 5-year-olds was 30 c/d (6/6), which is almost the same as the mean adult acuity measured in their study (30.61 c/d). In another study, Birch and Hale (1988) found acuity of 32 c/d in the 5-year-old children using OPL with slightly higher (0.12 octave) binocular acuity than monocular acuity. Using the method of limits, Ellemberg et al. (1999) found an adult-like grating acuity in the 6-year-olds children. On the other hand, Atkinson et al. (1981) used a two-alternative forced-choice staircase procedure and a 70% correct threshold to measure acuity in preschool children (3-5 years old) and found that grating acuity was lower in this age group compared to adults, although the children achieved acuity better than 30 c/d (i.e. 6/6). They concluded that the lower acuity in children could be due to a combination of cognitive and sensory developments. Using a new version of Teller Acuity Cards (TAC), Courage and Adams (1990) provided visual acuity norms for infants and children between the ages of 1 week to 3 years. The grating acuity attained by the 3-year-old children was found to be 18 c/d, which was 0.75 octave less than that attained by adults. Mayer et al. (1995) provided monocular acuity norms for the TAC between the ages of 1 month to 4 years. Monocular grating acuity of the 4-year-old children was 25 c/d, but no comparison was made with the acuity of adults in this study. Stiers et al. (2003) reported grating acuities in 5 year olds which were significantly lower than those in adults (36 vs. 50.41 c/d). Overall, therefore, these studies are inconclusive or do not agree regarding when grating acuity becomes adult-like.

Table 1-2: Subjective studies of the development of visual acuity

Study	Method	Participants age range/group	Results
Mayer and Dobson (1980)	OPL for infants. Constant stimuli with yes-no response for adults	6 months – 2 years (n= 6) and adults (n= 7)	Acuity at 2 years was within a factor of 2 of adult acuity based on a 75% criterion for correct responses, and close to adult based on the 60% criterion
Mayer and Dobson (1982)	OPL	5 months – 5 years (n= 50) and adults (n= 6)	Adult-like between 3-5 years
Birch et al. (1983)	OPL	7 months – 5 years (n= 297) Adults (n= 9)	Adult-like at 5 years
Ellemberg et al. (1999)	Method of limits with yes-no responses	4-, 5-, 6-, and 7-year-old and adults (n= 24/age group)	Adult-like at 6 years
Atkinson et al. (1981)	Alley running with 2AFC	3 – 5 years (n= 20) and adults (n= 6)	Not adult-like at 5 years
Courage and Adams (1990)	TAC	1 week – 3 years (n= 140)	Not adult-like at 3 years
Mayer et al. (1995)	TAC	1 month – 4 years (n= 460)	Monocular acuity was 25 c/d at 4 years but no comparison with adult was made
Stiers et al. (2003)	2AFC for grating acuity. 4AFC for optotype acuity with Ladolt Cs	2.5 – 6 years (n= 205) and adults (n= 12)	Not adult like at 6 years (both grating and optotype)

1.3.6 Development of contrast sensitivity

There is no general agreement on the age at which CS is fully adult like. Some studies concluded that CS reaches adult level during adolescence, while others suggested at a younger age. Table 1-3 summarises the results of subjective studies of the development of CS. Arundale (1978) studied the contrast sensitivity functions in three age groups (8-15, 18-39, and 45-66 yr) using the method of adjustment. His findings indicated that CS of the younger group (8-15 yr) was lower at low and middle spatial frequencies than the middle age group (18-39 yr), although no statistics were provided and only 3 eyes were tested in the 8-15 yr group. A similar result was obtained by Beazley et al. (1980) using a yes-no staircase method. Their study, which spanned the age range between 3 and 29 years, showed that CS increased with age reaching a maximum sensitivity in the 18-29 years age group. However, these researchers admitted that their results may have been affected by criterion difference between the participants. A more recent study (Benedek et al., 2003) concluded that adult-like CS is reached by 11-12 years. The result of this study showed that CS at high spatial frequencies developed earlier than CS at low spatial frequencies. On the other hand, several studies have shown that CS reaches adult-level at an earlier age (between 6 and 9 years). Using the method of adjustment, Derefeldt et al. (1979) found that the CS of their 6-10 year-olds was the same as their 20-40 year old adults. Bradley and Freeman (1982) concluded that contrast sensitivity becomes adult-like around the age of 8 years. Their results demonstrated an increase in CS with age, with their younger subjects (2.5-4 yr) showing a reduction of 0.36 log units in mean sensitivities when compared with adults. Bradley and Freeman (1982) concluded that this reduction could be due to visual factors as well as non-visual factors (such as attention) since they were able to bring the CS of adults down to the level of the younger children by instructing adults to be less attentive during the test. The problem of Bradley and Freeman's (1982) study was that they did not provide any statistics and some of their age groups had only 6 participants. Abramov et al. (1984) found that by 8 years of age the CS is very close to adult level, but also did not provide any statistics. The results of Adams and Courage (2002) showed a fully developed CS at the age of 9 years. Ellemberg et al. (1999) found adult-like CS at the age of 7 years. However, Gwiazda et al. (1997) did not find adult-like CS in their older children tested at the age of 8 years. Atkinson et al. (1981) found that CS and VA of their older (5 years old) preschool children were lower than those of adults. It seems that even when excluding the studies that did not provide statistics (Arundale, 1978; Bradley and Freeman, 1982; Abramov et al., 1984), there is still little agreement on the age at which CS is adult-like. This ranges between 6-15 years.

The next section describes the VEP techniques and reviews the studies of the development of VA and CS using these techniques.

Table 1-3: Subjective studies of the development of contrast sensitivity

Study	Method	Participants age range/group	Results
Arundale (1978)	Method of adjustment	8-15, 18-39, and 45- 66 years (n= 36)	8-15 years had lower CS than the 18-39 years but no statistics provided
Beazley et al. (1980)	Method of limits with yes-no responses	3 – 15 (n = 118) and 18 – 29 years (n= 17)	CS increases with age until 18-29 years
Benedek et al. (2003)	Method of adjustment. Static and dynamic CS at photopic and scotopic conditions	5-6, 7-8, 9-10, 11-12, and 13-14 years. (n= 169)	At photopic conditions: static CS at 5-6 years was lower than that at 9-10 years. Dynamic CS at 9-10 years was lower than that at 11-12 years
Derefeldt et al. (1979)	Method of adjustment	6-10 years (n= 10) and adults (n= 23)	Adult-like at 6-10 years
Bradley and Freeman (1982)	Method of limits with 2AFC	22 months – 16 years (n= 38) and adults (n= 11)	Adult-like at 8 years
Abramov et al. (1984)	Descending method of limits with 2AFC	5 – 8 years (n= 17) and adults (n= 17)	Very close to adults at 8 years but no statistics were provided
Adams and Courage (2002)	CS cards based on TAC test	4.1-, 5-, 5.9-, 7-, 8.1- , 9- year-old (n= 120) and adults (n= 10)	Adult-like at 9 years
Ellemberg et al. (1999)	Method of limits with yes-no responses. Static and temporal CS	4-, 5-,6-, 7-year-old and adults (n= 24/age group)	Static and temporal CS adult-like at 7 years.
Gwiazda et al. (1997)	PL for infants 2AFC staircase for children and adults	Infants: 2-, 4-, 6- and 8- month-old (n= 83) Children: 3-5, 5-7, and 7-8.6 years (n= 84) Adults (n= 15)	Not adult-like at 8 years
Atkinson et al. (1981)	Alley running with 2AFC	3 – 5 years (n= 20) and adults (n= 6)	Not adult-like at 5 years

1.4 Visual evoked potential (VEP)

Visual evoked potentials (VEP) are very small electrical potentials representing the response of the visual cortex to stimuli presented in the middle of the visual field (reviewed in Fahle & Bach, 2006). VEP is considered to be a measure of the integrity of the visual pathway from the optic nerve up to the visual cortex, but can be affected by retinal disorders or the presence of media opacities. For recording VEP responses, at least one electrode is placed on the scalp over the visual cortex (active electrode) and two other electrodes (reference and ground electrodes) on areas that are considered visually inactive. Usually VEPs have small amplitude response (less than 25 μV) compared to the background EEG (up to100 μV) (Lam, 2005). Because the noise-to-signal ratio of the VEP is high, computer averaging of multiple recordings is required to isolate the VEP response from the background noise (EEG). An average of at least 64 recordings is recommended, and at least two averages should be obtained to confirm the reproducibility of the findings (Odom et al, 2010).

The amplitude and/or the latency of the VEP to the visual stimulus can be assessed to determine the normality of the visual system. Because the central visual field is represented more than the peripheral visual field in the visual cortex, the VEP is believed to reflect mainly the activity from the central visual field (Lam, 2005). Unlike the photoreceptors, neurons in the visual cortex do not respond strongly to homogeneous stimuli. Therefore, the stimuli required to elicit strong cortical responses have to be structured in time or in space and time (Heckenlively & Arden, 2006). Temporal modulation in the stimulus is required for recording the VEP response. The rate at which the stimulus is modulated can produce two different types of VEP: transient or steady-state. Transient VEPs are obtained when slow alteration rates (usually not more than 2 Hz) are used. This allows sufficient time for the visual cortex response to return to baseline. Therefore, the transient VEP is considered as representing a complete cycle of the visual system's reaction to a stimulus presentation, which starts and ends with a state of rest (Hartmann, 1995). Transient VEPs are generally described by plots of amplitude versus time. On the other hand, steady-state VEPs are obtained when the stimulus is alternated at higher temporal rates (i.e. high temporal frequencies). In this case, an overlap of responses from the visual system occurs and the brain goes into a continuous state of stimulation until the stimulus ceases. Steady-state VEPs are generally described by plots of amplitude (and phase) versus frequency (Hartmann, 1995).

1.4.1 Standard VEP responses

The International Society for Clinical Electrophysiology of Vision (ISCEV) recommends using one of the three standard transient VEPs in clinical VEP testing (Odom, 2010). These are flash VEP, pattern reversal VEP, and pattern onset/offset VEP.

1.4.1.1 Flash VEP (fVEP)

Flash VEP is obtained by repeatedly presenting short flashes of a spatially wide area of bright light to the eye and measuring the electrical response with scalp electrodes. The flash VEP determines the gross cortical response to illumination of the retina, and usually is used in individuals who cannot fixate for pattern VEP. It can also be performed with the eyes closed or in the presence of media opacities, allowing a measurement of visual function in patients who cannot keep their eyes open (babies or people suffering from coma) or who have media opacities hindering the use of pattern stimuli.

The flash VEP response consists of a series of negative (N) and positive (P) components (Figure 1-5). The most robust component is P2 with a peak which normally has latency between 100-120 ms measured from the stimulus onset (Lam, 2005). The amplitude of P2 is measured from the preceding negative peak (N2) to the peak of P2. A notable drawback of the flash VEP is its high variability (in size, timing, and shape) across subjects compared to the pattern VEP (Lam, 2005).

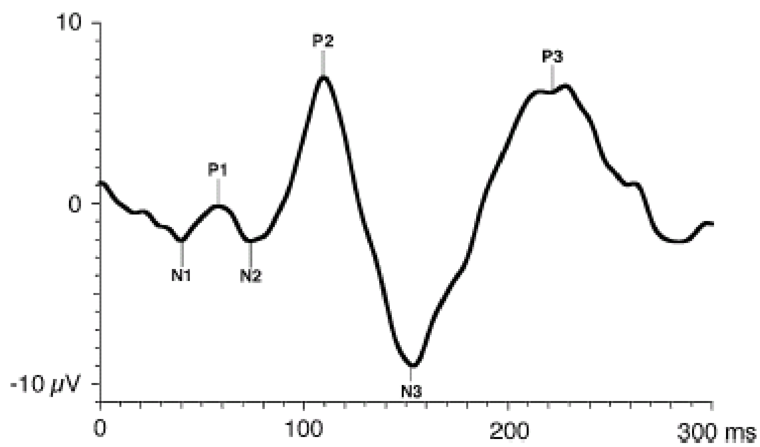

Figure 1-5: A normal adult flash VEP.

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1.4.1.2 Pattern reversal VEP

The pattern reversal VEP is the preferred clinical VEP, owing to its reduced variability of waveform and peak latency across normal subjects (Odom, 2010; Lam, 2005) and high reproducibility within a subject (Lam, 2005). ISCEV's recommended stimulus for pattern reversal VEP is a checkerboard of alternating black and white checks that change phase (i.e. the black changes to white and vice versa). The pattern reversal VEP waveform consists of negative (N) and positive (P) components identified by their mean peak latency in milliseconds (Odom, 2010). The major positive component of the pattern reversal VEP is P100. Other recognizable components are the negative N75 and N135 (Figure 1-6).

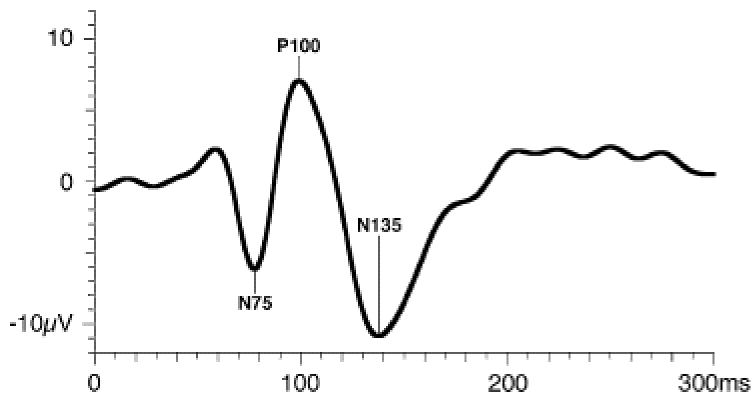

Figure 1-6: A normal adult pattern reversal VEP.

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1.4.1.3 Pattern onset/offset VEP

The pattern onset/offset VEP is triggered by a reversing checkerboard stimulus which is abruptly exchanged with a diffuse blank screen that has the same luminance as the mean luminance of the checkerboard. The waveform of the pattern onset/offset VEP consists of positive and negative peaks designated by order of appearance (Figure 1-7). The main peaks of the pattern onset/offset VEP are C1 (positive with latency around 75 ms), C2 (negative with latency around 125 ms), and C3 (positive with a latency around 150 ms) (Odom, 2010). The pattern onset/offset VEP is particularly useful in patients with nystagmus or poor fixation as the technique is less susceptible than pattern reversal VEP to eye movements or poor fixation.

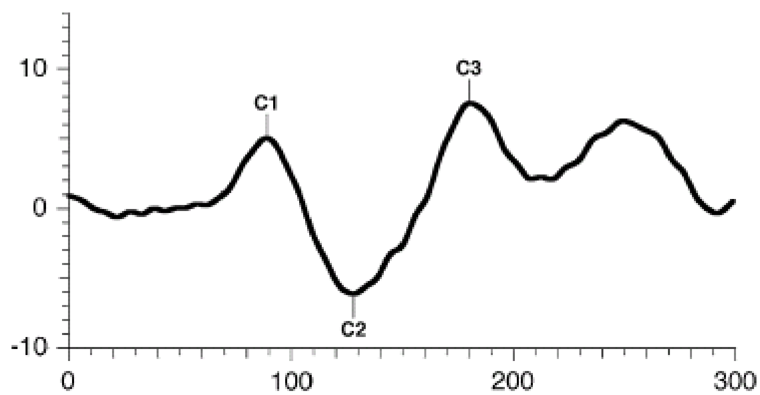

Figure 1-7: A normal adult pattern onset/offset VEP.

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1.4.2 Measuring visual acuity with VEP

Visual acuity can be assessed using steady-state VEP. In this technique, a number of checks that range from large to small or sine-wave gratings that range from low to high spatial frequency are presented. After 50-100 steady-state VEP responses are recorded for each pattern, the average VEP amplitude is plotted against the check size or spatial frequency. The check size or spatial frequency that corresponds to zero amplitude can be extrapolated as an acuity estimate (reviewed in Birch, 2006). This technique takes a long time to obtain an acuity estimate, and is difficult to use in infants or children with a short attention span. On the other hand, the sweep visual evoked potential technique (sVEP) gives an estimate of acuity by sweeping 10 spatial frequencies in about 10 s. The sVEPs are described in more detail in Chapter 2.

1.4.3 Development of visual acuity

Results of electrophysiological studies of visual acuity show that acuity is near adult level at a much younger age than the results of the behavioral studies. Using checkerboard pattern reversal VEP, Sokol and Dobson (1976) found that the amplitude by check-size function for the 6-month-old infants was similar to that of adults with 20/20 acuity (infants of 6 months, like adults, had amplitude check-size functions which peaked at 7.5 or 15 min of arc). That finding was subsequently confirmed by Sokol (1978) and an estimate of acuity was given by extrapolating a regression line from the peak VEP check-size to 0 μV. The acuity improved from 20/150 at 2 months to 20/20 by 6 months. Norcia and Tyler (1985a) studied the development of grating acuity of infants during the first year of life (2 wk – 52 wk age) using sVEP. Their findings indicate that sVEP grating acuity is only 4.5 c/d at 1-month-old and increases to 20 c/d at 8-13 months. The researchers stated that the acuity at the age of 8 months was not “reliably different” from the acuity of the adults (24.3 c/d), but no statistics were provided. Hamer et al. (1989) reported monocular and binocular sVEP acuity norms for infants aged between 2 to 52 weeks, almost the same age range investigated by Norcia and Tyler (1985a). Their acuity estimates for both binocular and monocular acuity (6 c/d at 2-10 weeks of age, and 14 c/d by 20-30 weeks of age) agree with those reported by Norcia and Tyler (1985a).

1.4.4 Development of contrast sensitivity

Several studies have investigated the development of CS in infants by VEP but none have done so for older children. Harris et al. (1976) found that 6-month-olds show CS similar to that in adults for the low and medium spatial frequencies but CS for high spatial frequencies was lower than that in adults. Pirchio et al. (1978) found adult-like VEP CS at all spatial frequencies in 12-month-old infants. Using the sVEP, Norcia et al (1988) found that contrast sensitivity at the age of 10 weeks was close to that of adults at low spatial frequencies (0.5 and 1 c/d) but was significantly lower at higher spatial frequencies (> 1 c/d). The shape of the contrast sensitivity functions (CSF) of infants was similar to that of adults, both of which showed decreasing sensitivity with increasing spatial frequency, but the infants' function drops off 4.5 times faster. Norcia et al. (1990) provided CSF measurements (cross-sectional and longitudinal) in infants between 2-40 weeks of age and a comparison of these measurements with adults' CSF using sVEP. Their results showed, for both longitudinal and cross-sectional data, that contrast sensitivity at low spatial frequencies develops rapidly up to 10 weeks of age reaching an early asymptote of 200 compared to 450 for adults. However, contrast sensitivity at high spatial frequencies continued to develop until at least 30 weeks.

Chapter 2

The technique, validity and clinical use of the sweep VEP

This chapter is published as follows:

Almoqbel F, Leat SJ, Irving E (2008). The technique, validity, and clinical use of the sweep VEP. Ophthalmic Physiol Opt 28:393– 403. Reproduced with permission from Blackwell Publishing LTD.

This article was written by Fahad Almoqbel. Guidance, editing and suggestion were given by Susan Leat and Elizabeth Irving.

2.1 Overview

Vision scientists have concentrated on studying two visual functions when it comes to assessing the sensory visual development in human: visual acuity and contrast sensitivity. The methods used to measure these visual functions can be either behavioral or electrophysiological. A relatively new technique for measuring the visual acuity and contrast sensitivity electrophysiologically is the sweep visual evoked potential (sVEP). This paper is a review of the literature on the sVEP technique: stimulus parameters, threshold determination, validity and reliability of sVEP are discussed. Different studies using the sVEP to study the development of visual acuity, contrast sensitivity, and vernier acuity are presented. Studies have demonstrated that the sVEP is a potentially important tool for assessing visual acuity and contrast sensitivity in non-verbal individuals with disorders affecting their visual system.

Keywords: contrast sensitivity, sweep visual evoked potential, visual acuity, visual development, visually evoked potential

2.2 Introduction

The assessment of vision is an essential part of any ophthalmological or optometric examination with visual acuity being the most commonly measured visual function. Contrast sensitivity is another important visual function that has been studied extensively in terms of its development in infants. A subjective assessment is usually done for verbal and cooperative individuals by using visual acuity and contrast sensitivity charts. In the case of infants and non-verbal or uncooperative patients, an objective (behavioral or electrophysiological) assessment is required. The electrophysiological technique of visual evoked potential (VEP) represents the response of the visual cortex to visual stimuli. This response can be recorded, after being separated from the noise (electroencephalogram (EEG)), from electrodes attached to the scalp. The stimuli used in VEPs can be flash or pattern (checkerboard or grating), transient or alternating, and if it is a pattern stimulus it can be presented as a pattern onset-offset. A more detailed description of the different types of VEP can be found in Leat et al. (1999).

Unlike the conventional pattern VEP, which requires longer recording, the sweep visual evoked potential (sVEP) evaluates visual acuity and contrast sensitivity in a shorter actual recording time. It is essentially a steady-state pattern VEP to a pattern of elements that varies in some aspect over time. Regan introduced this new sVEP technique and demonstrated its use for measuring refractive errors objectively (Regan, 1973). A few years later, the technique was developed for measuring visual acuity (Tyler et al., 1979) and contrast sensitivity (Seiple et al., 1984; Allen et al., 1986; Norcia et al., 1986). Currently, sVEP can measure two types of visual acuity: resolution (grating) acuity and vernier acuity (hyperacuity). Resolution acuity is a measure of a person's ability to detect separation of contours (Duckman, 2006) and the sVEP usually uses a grating pattern, although a checkerboard pattern can be used. Vernier acuity is a measure of the eye's ability to perceive that a misalignment exists between the elements of the stimulus, when compared with a stimulus without such misalignment (Duckman, 2006).

By sweeping spatial frequency from low to high in about 10 s, an estimation of visual acuity is obtained by determining the highest spatial frequency to which the visual system responds. Tyler et al. (1979) concluded that the extrapolated sVEP acuity is comparable to the psychophysical acuity when a fine resolution and high luminance display is used. When measuring contrast sensitivity, contrast is swept with a fixed spatial frequency to determine the lowest contrast to which the visual system responds. Figures 2-1 and 2-2 show examples of the sweep plot for visual acuity and contrast sensitivity, respectively.

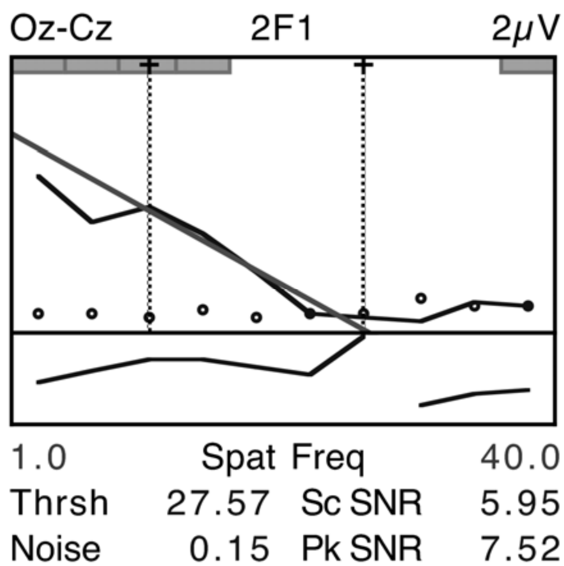

Figure 2-1: Example of visual acuity threshold measurement by sVEP using the PowerDiva system (Norcia, 1999) recording from the Oz electrode giving a visual acuity threshold of 27.57 c/d. The threshold is the average of eight sweeps. Subject aged 8 years. Luminance of screen = 50 cd/m^2. In the top part of the graph, amplitude is plotted against spatial frequency. In the lower part, phase is plotted against spatial frequency. The solid line is the response amplitude at the second harmonic, and the straight line is the regression line. The circles represent the noise. For more detail of these plots see Allen et al. (1986).

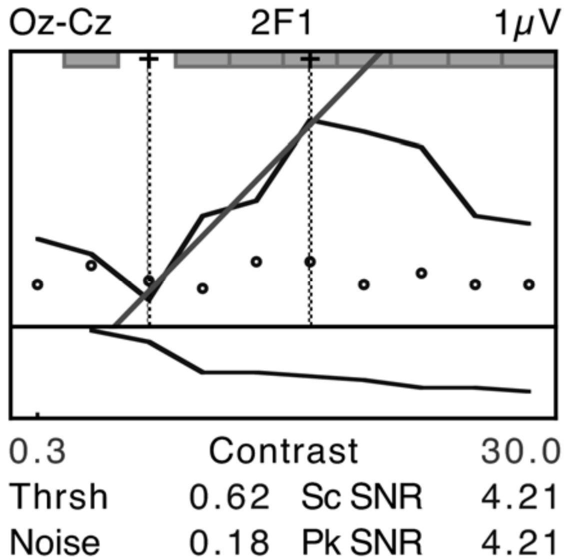

Figure 2-2: Example of contrast threshold measurement by sVEP using the PowerDiva system (Norcia, 1999) recording from the Oz electrode giving a contrast threshold of 0.62. The threshold is the average of eight sweeps. Subject aged 8 years. Luminance of screen = 50 cd/m^2. In the top part of the graph, amplitude is plotted against contrast. In the lower part, phase is plotted against contrast. The solid line is the response amplitude at the second harmonic, and the straight line is the regression line. The circles represent the noise. For more detail of these plots see Allen et al. (1986).

A more recent alternative method (the step VEP) was described by Mackay et al. (2008) who used a brief staircase for quickly determining the acuity threshold using a steady-state VEP.

2.3 Parameters of sweep VEP

Different parameters of sVEP are required to be set by the examiner before starting the test, e.g. sweep type (linear vs logarithmic sweep), sweep range, direction of the sweep (downward vs upward sweeping), luminance of the screen, and temporal frequency. The examiner should also have criteria for accepting the resulting measurement of visual acuity or contrast (e.g. response phase for threshold determination). These parameters and criteria affect the resulting measurement and will be discussed in this section.

Tyler et al. (1979) described many of the parameters of the sVEP technique. For visual acuity measurement, they suggested the use of a linear, rather than a logarithmic, spatial frequency sweep to minimize the delay in the visual response caused by the time constants of both the synchronous filter and the brain response, and also because the logarithmic sweep reduces accuracy at the high spatial frequencies. However, when the range of spatial frequencies that has to be swept linearly to cover the threshold value is uncertain, a logarithmic sweep is preferred (Gottlob et al., 1990). The logarithmic sweep gives an appropriate weight over the whole range of spatial frequencies and is advisable for determining the structure of the spatial frequency tuning function (Tyler et al., 1979). Changing the range of the contrast sweep at a constant rate does not affect the contrast threshold if the range spans the threshold (Norcia et al., 1989). Recently, two studies (Zhou et al., 2007 and Bach et al., 2008) suggested the use of a logarithmic instead of a linear sweep for determining VEP acuity. Zhou et al. (2007) found that plotting the logarithm of the visual angle instead of spatial frequency for estimating visual acuity yielded acuities that were not significantly different from logMAR acuities in children and adults. On the other hand, acuities resulting from plotting spatial frequency linearly were significantly different from logMAR acuity. Bach et al. (2008) used checkerboard stimuli that were swept in logarithmic steps with respect to the check sizes to measured VEP acuity. A stepwise heuristic algorithm was used to determine the optimal range for fitting the regression line. Their VEP acuity estimates for subjects with normal acuity, subjects with normal but artificially reduced acuity, and subjects with reduced acuity due to ocular disease, were highly correlated with the subjective acuity. Interestingly, the relationship between the subjective acuity and the VEP acuity can be found by applying the following formula:

$$\text{Subjective } (VA_{decimal}) = SF_0 / 17.6 \text{ c/d},$$

where SF_0 is the VEP acuity obtained by the stepwise heuristic algorithm. Bach et al. (2008) indicated that this method, giving a constant relationship over a wide range of acuities, overcomes the problem of overestimating sVEP acuity compared to subjective acuity when the latter is low.

The direction of the contrast sweep may affect the measured threshold. Downward sweeps for contrast sensitivity measurement (i.e. starting from high contrast to low contrast) may result in adaptation to the suprathreshold stimulus and ultimately increase the threshold (Brigell et al., 1987; Seiple et al., 1988). Therefore, an upward sweep is used for contrast threshold measurement.

Another parameter to be considered is whether the sweep is continuous or sampled/step-wise (Seiple and Holopigian, 1989). When the sweep is continuous, the contrast or spatial frequency of a grating is changed continuously during recording. On the other hand, the sampled sweep consists of a number of contrast or spatial frequency gratings presented for a fixed period of time during the recording. Most of the newer systems use step sweeps.

Most of the studies of sVEP have used different levels of luminance, ranging from 40 cd/m^2 to 220 cd/m^2. Allen et al. (1992) found that acuity increased in infants and adults when luminance was increased from 0.01 cd/m^2 to 1.0 cd/m^2, and reached an asymptote between 1.0 cd/m^2 and 100 cd/m^2. The acuity function of infants with increasing luminance was shallower than the adult function at the higher luminances. Using two luminance levels (109 cd/m^2 and 20 cd/m^2), Good and Hou (2006) found no difference in sVEP grating acuity (between these luminances) in normal children (ranged between 7 months to 4 years in age), but in children with cortical visual impairment (CVI) the acuity was better at low luminance (i.e. 20 cd/m^2). Although the form of the spatial tuning function depends on the temporal frequency, the extrapolated acuities at two different temporal frequencies (6 & 10 Hz) correlate well (Norcia and Tyler, 1985b).

Another parameter that may affect the sVEP threshold is the electrode placement. Although sVEP is not covered by the ISCEV standard for VEP recordings (Odom et al., 2004) it seems that most of the studies have followed the ISCEV standard for the placement of the active, ground and reference electrodes. However, Allen et al. (1986) found good agreement between two electrode placements (for measuring contrast sensitivity in adults) in which they placed the active electrode 3 cm above the inion, compared with one placed 3 cm laterally, and both were referenced to an electrode 1 cm above the inion. There has been some discussion of Laplacian electrode placements and analysis for steady state VEPs (Srebro, 1992; Mackay et al., 2003a,b) indicating that this may give better signal to noise ratios and therefore reduced recording times, especially for targets close to the acuity threshold (Mackay et al., 2003b). This has not yet been applied to sweep VEPs.

2.3.1 Threshold determination

A linear extrapolation to 0 μV amplitude between the VEP response amplitude and the spatial frequency gives an estimation of sVEP visual acuity threshold (Tyler et al., 1979). A linear extrapolation to 0 μV amplitude between the VEP response amplitude and the log contrast gives an estimation of contrast sensitivity. An advantage of this extrapolation method is that the amplitude variation does not affect the resulting threshold (the intercept), it only affects the slope of the function (Tyler et al., 1979, 1981; Seiple et al., 1988). If multiple spatial frequency peaks are present, the last peak (i.e. with the higher spatial frequency or lower contrast) should be used to extrapolate the threshold (Norcia and Tyler, 1985a, b).

The second harmonic is used for obtaining the threshold for both grating visual acuity (Norcia and Tyler, 1985a) and contrast sensitivity (Norcia et al., 1989), when the stimulus is symmetric because the largest power in the response waveform for a symmetric counter-phase stimulus presentation is present at this frequency. With a stimulus that is asymmetric (e.g. for onset-offset patterns as typically used in vernier acuity measurement) the largest signal is at the first harmonic, and is therefore used for the analysis (Hartmann, 1995; Skoczenski and Norcia, 1999; Zemon and Ratliff, 1982).

By using discrete Fourier analysis (DFT), the amplitude and phase of the second harmonic (for symmetrical stimulation) or first harmonic (for asymmetrical stimulation) are extracted and two criteria have to be met to accept the resulting threshold: the signal to noise ratio (SNR) criterion, and the phase consistency criterion. The SNR is the power present at the response frequency vs that present during the test at the adjacent 'noise' frequency (Norcia and Tyler, 1985a). An SNR of $\geq 3{:}1$ (i.e. the amplitude of the peak response signal has to be at least three times larger than the adjacent noise frequency) has usually been chosen as a criterion to accept a given threshold for grating visual acuity (Norcia and Tyler, 1985a), contrast sensitivity (Norcia et al., 1989) and vernier acuity (Skoczenski and Norcia, 1999). The 3:1 ratio keeps the false signal alarm rate below 0.3% (Norcia and Tyler, 1985a). When measuring visual acuity by sVEP, the phase of the response has to either be constant or gradually lagging the stimulus as spatial frequency increases (because latency increases with increasing spatial frequency). When measuring contrast sensitivity, the phase has to be either constant or gradually leading as contrast increases, since latency decreases with increasing contrast (Norcia et al., 1989). The two criteria for threshold determination (SNR $\geq 3{:}1$ and the phase consistency) result in an unbiased measurement of the VEP actual threshold (Norcia et al., 1989).

2.4 Sweep VEP validity

Validity of any given test can be assessed by comparing the accuracy of its results with another test which has been proven to be valid and accurate. Since young children cannot perform a recognition test of visual acuity (e.g. Snellen acuity), researchers compared sVEP acuity with tests of behavioral visual acuity, which both measure grating acuity. Sokol et al. (1988) compared preferential looking (PL) acuity (for stationary and for phase alternating gratings) with sVEP acuity in a group of infants between the age of 2 and 10 months. They found that the sVEP acuity is 1.5–2.5 octaves higher than the PL acuity for stationary gratings (1 octave difference is a doubling or halving of the number of c/d of visual acuity). The difference in acuity estimates between the two techniques (i.e. PL and sVEP) is less when phase alternating gratings are used for PL, and is dependent on age (2 octaves at 2 months decreasing to 0.5 octave at 12 months). Sokol et al. (1988) suggested that this difference may be due to the different scoring criteria used to estimate acuity in the two techniques: sVEP acuity is estimated by extrapolating from the highest spatial frequency peak to 0 μV, while the PL acuity method estimates a 70–75% correct threshold level. In another study (Sokol et al., 1992), the difference was found to be independent of temporal frequency and more possible reasons for the difference were suggested, such as oculomotor development and attention which can reduce the estimated PL acuity. Riddell et al. (1997) found that the Teller Acuity Cards (TAC) acuity was significantly lower than sVEP acuity in the youngest age group of their 2 weeks to 1 year old subjects. Like the finding of Sokol et al. (1988) regarding the difference between PL acuity for phase alternating gratings and sVEP acuity, the TAC acuity and sVEP difference decreases with age. Riddell et al. (1997) concluded that the systems responsible for processing visual information derived from sVEP and TAC functionally mature at different rates. This conclusion was reached because sVEP involves measuring activity in the primary visual cortex while TAC also requires responses from the higher level of processing including the visual association cortex and non-visual areas of the brain. They supported their conclusion by pathological and MRI data reported by other researchers which indicate that area 17 is myelinated at the age of 3–4 months while myelination of the visual association area takes place during the next 4 months. In the same study, Riddell et al. (1997) did not find a difference in TAC or sVEP acuity between full-term and pre-term infants when compared using conceptual age. The limitation of this study is the difference in sVEP parameters between the two centers where the subjects were tested (e.g. temporal frequency, luminance, method of threshold estimation, and sweep range). Prager et al. (1999) found a low correlation between sVEP acuity and TAC acuity. The correlation between sVEP and transient VEP latency was low as well (r = 0.3). According to Prager et al. (1999), this poor correlation indicates that each of these tests assesses a different aspect of vision. Acuity by sVEP was compared with Snellen acuity in normal adult subjects after defocusing their vision with plus lenses (Katsumi et al., 1996). It should be noted that different types of VA are being compared and that Snellen acuity is not necessarily equal to grating acuity, even when both are measured subjectively. Katsumi et al. (1996) found Snellen acuity to be underestimated by sVEP when it is better than 6/18 and overestimated when it is worse than 6/30. The researchers believed that the underestimation is caused by the limited resolution of the CRT display and the overestimation when the acuity is poor is due to the influence of movement detection and luminosity changes rather than contrast or resolution. Indeed, possible undersampling by the monitor must always be considered in studies of VA, and the test distance may need to be increased to prevent aliasing (Bach et al., 1997).

Like subjective tests of visual acuity (e.g. PL and Snellen acuity), the sVEP can detect developmental trends in visual acuity. The difference of visual acuity estimates of sVEP and these tests indicates the need for establishing normative sVEP data for each age group in order to validate this test.

2.5 Sweep VEP reliability

The test-retest reliability of any given test is estimated by repeating the test on the same subject at two different moments in time. The test-retest reliability of sVEP measurement has been assessed in many studies. Norcia and Tyler (1985b) used two temporal frequencies (6 Hz & 10 Hz) to measure visual acuity in a group of infants. Their results reveal good repeatability based on the highest acuity obtained at each of the two temporal frequencies (standard deviation of 0.19 octaves) with 60–75% of individual sweep records giving a criterion response. In a group of infants (2–52 weeks of age), Hamer et al. (1989) found the absolute magnitude of interocular and test-retest differences to be small (2– 4 times smaller than in behavioral studies), with an average of 0.25 octave in infants older than 10 weeks of age. These researchers concluded that sVEP can detect smaller differences between eyes, and smaller differences between tests, than the behavioral techniques, and can be a sensitive tool to evaluate visual loss in children. Prager et al. (1999) reported an average test-retest difference of 0.68 octaves. This is comparable to a test-retest difference of 0.37–0.56 octaves found in a preferential looking technique (Birch, 1985). Lauritzen et al. (2004) reported that test-retest variability based on the mean of several thresholds of acuity is less than the variability based on the best threshold. They suggested obtaining the mean of at least 10 thresholds for infants. They also concluded that sVEP is more valid for estimating visual acuity and contrast sensitivity in a group of subjects than in individual subjects. Norcia et al. (1990) reported that the between-session variability of the contrast sensitivity function (CSF) is less than 1.0 octave in their study of contrast sensitivity in a group of infants (2–40 weeks).

2.6 Studies of grating visual acuity development by sweep VEP

From the early 80's onward, sVEP has been used to study the development of visual acuity in infants (see Table 2-1 for a summary). Norcia and Tyler (1985a) studied the development of grating acuity of infants during the first year of life (2–52 weeks of age). Their findings indicate that sVEP grating acuity is only 4.5 c/d at 1-month-old and increases to 20 c/d at 8–13 months. Their adult subjects showed a visual acuity of 24.3 c/d, a value which is not clinically or reliably different from that attained by infants at the age of 8 months. Norcia and Tyler (1985a) suggested that the higher acuities in their study compared to previous VEP studies was due to the rapid acquisition of acuity estimates with the sVEP. This rapid acquisition of the acuity estimates is important in the case of infants, who are more likely to be attending to the sVEP 10-s stimulus than the longer stimulus duration of the conventional VEP. Hamer et al. (1989) reported monocular and binocular sVEP acuity norms for infants aged between 2 to 52 weeks, almost the same age range investigated by Norcia and Tyler (1985a). Their acuity estimates for both binocular and monocular acuity (6 c/d at 2–10 weeks of age, and 14 c/d by 20–30 weeks of age) agree with those reported by Norcia and Tyler (1985a). They found only a small difference between the binocular and monocular sVEP acuity, with the binocular acuity being superior by <0.2 octaves only in infants under 6 months of age. Hamer et al. (1989) suggested that the smaller difference between binocular and monocular sVEP acuity when compared to the greater difference found in behavioral studies was due to the different methodology between the techniques. A great deal of cooperation is needed for behavioral testing and that cooperation is likely to be reduced when patching the infant eye to measure monocular acuity, resulting in low acuity estimates. On the contrary, sVEP needs less cooperation than behavioral testing since each sweep requires 10-s of attention. However, lower success rates for monocular testing were observed compared to binocular testing for sVEP. Norcia et al. (1990) studied the development of contrast sensitivity and grating acuity longitudinally in infants between the age of 2 weeks to 40 weeks. Their results confirmed their previous study results, finding that sVEP acuity is about 2.5–9 c/d before the age of 2 months, and ranges between 10 and 20 c/d after 30 weeks of age. The adult acuity in this study was 31.9 c/d. Unlike contrast sensitivity which reached an asymptote at 10 weeks, they observed that acuity develops continuously over this entire age range (up to 30 weeks). They suggested that this dissociation between contrast sensitivity and acuity development after 10 weeks is due to different processes underlying the development of these two visual functions. In the same study, Norcia et al. (1990) obtained predicted acuities from extrapolation of the contrast sensitivity function (CSF). The average difference between the predicted acuity and the measured acuity by sweeping spatial frequency was only 0.4 octaves. The predicted value of visual acuity from extrapolation of CSF in another study (Norcia et al., 1988) was 6.4 c/d vs a measured value of 7.4 c/d, a difference of less than 0.4 octaves. All the studies mentioned so far used a temporal frequency of 6 Hz (i.e. the gratings were alternated at 12 contrast reversals per second). Norcia and Tyler (1985b) measured sVEP acuity in a group of infants (17–25 weeks of age) using temporal frequencies of 6 Hz and 10 Hz. The acuity difference between the two temporal frequencies was only 0.17 octaves, suggesting that changing temporal frequency accounts for only 14% of the variation of the within-subjects acuity. The researchers found no significant difference in acuities between the two temporal frequencies (10.55 c/d at 6 Hz compared to 10.29 c/d at 10 Hz). Prager et al. (1999) reported sVEP acuity lower than the previously mentioned studies for infants at the age of 8 months. Their acuity estimate increased from 9.61 c/d at 4 months to only 10.39 c/d at 8 months. However, the researchers admitted that their 8 months sVEP acuities were 'suspicious', because they did not agree with the published studies reporting acuity of 20 c/d at 8 months (Norcia and Tyler, 1985a). They suggested that the reason for this discrepancy is either an insufficient number of gratings in the stimulus they used or an inappropriate viewing distance.

Table 2-1: Studies of visual acuity development using sVEP

Study	Subjects' Age-range	Temporal frequency	Luminance	Results
Norcia & Tyler (1985a). Spatial frequency sweep VEP: visual acuity during the first year of life.	Infants: 1 – 53 weeks Adults	6 Hz	80 cd/m^2	sVEP acuity increased from 4.5 c/d in the first month to 20 c/d by the age of 12 months. sVEP acuity reached the adult level by 8 months (32 weeks).
Norcia et al. (1990). Development of contrast sensitivity in the human infant.	Infants: 2 – 40 weeks Adults	6 Hz	220 cd/m^2	sVEP acuity in the first two months was 2.5 – 9 c/d and ranged between 10 – 20 c/d after 30 weeks.
Norcia & Tyler (1985b). Infant VEP acuity measurement: analysis of individual differences and measurement error.	Infants: 17– 25 weeks	6 Hz or 10 Hz	80 cd/m^2	Using a temporal frequency of 6 or 10 Hz did not affect the estimated sVEP acuity.
Hamer et al. (1989). The development of monocular and binocular VEP acuity.	Infants: 2 – 52 weeks	6 Hz	80 cd/m^2	For both monocular and binocular viewing, sVEP acuity developed from 6 c/d at 2 -10 weeks of age to 14 c/d by 20 – 30 weeks.
Allen et al. (1992). The effect of luminance on FPL and VEP acuity in human infants.	Infants: 15 – 20 weeks Adults.	6 Hz	0.01cd/m^2, 0.1 cd/m^2, 1.0 cd/m^2, and 100 cd/m^2	VEP acuity was higher than FPL acuity. The improvement in acuity was more in FPL than in VEP when luminance was increased. The acuities of steady-state VEP and sVEP were comparable, with a slightly higher estimate of acuity in sVEP.

Sokol et al. (1988). Infant grating acuity is temporally tuned.	Infants: 2 – 10 months Adults.	0 Hz (stationary gratings), 1.25, 3.75, 7 or 11.5 Hz	31.6 cd/m^2	After the age of 3 months, grating acuity was temporally tuned at 3.75 or 7 Hz. At a temporal frequency of 3.75 and 7 Hz, the acuity was 0.5 to 1.0 octave higher than acuity for stationary, 1.25 or 11.5 Hz gratings. The difference between PL and sVEP acuity for phase alternating gratings was 2.0 octaves at 2 months and decreased to 0.5 octave at12 months.
Sokol et al. (1992). Infant VEP and preferential looking acuity measured with phase alternating gratings.	Infants: 2 – 13 months Children: 1 – 5 years Adults: 22 – 48 years	Infants: 5, 7, and 12 Hz Children: 3.75,7.5, and 12 Hz	31.6 cd/m^2	After 2 years of age, PL grating acuity was no longer tuned. When both are measured with phase alternating gratings, VEP and PL acuity were found to develop at different rates, reaching a similar level at about 12 months. The VEP/PL acuity difference was independent of temporal frequency.
Riddell et al. (1997). Comparison of measures of visual acuity infants: Teller acuity cards and sweep visual evoked potentials.	Preterm infants: 2 – 8 months (corrected age) Full-term infants: 2 weeks – 1 year	Study done in two centers. First Center (CUMC): 6.76 Hz Second center (ISC): 7.5 Hz	CUMC: 150 cd/m^2 ISC: 100 cd/m^2	There was a difference between the rate of development of Teller Acuity Cards (TAC) acuity and sVEP acuity, with TAC a being lower than sVEP acuity but developing at a higher rate. TAC acuity may reach sVEP acuity at about 14 months. No difference in acuity between preterm and full-term infants, both for TAC and sVEP.
Prager et al. (1999). Evaluation of methods for assessing visual function of infants.	Infants: tested at 4 months and 8 months	1.95 Hz	90 lux	The mean value of sVEP acuity increased from 9.61 c/d at the age of 4 months to 10.39 c/d at the age of 8 months. This improvement was statistically significant but not clinically significant. Transient VEP, sVEP, and TAC correlate poorly with one another. Transient VEP's latency was the most sensitive method for detecting visual development.

2.7 Studies of venier acuity development by sweep VEP

The development of vernier acuity has been investigated using sVEP in two studies. Skoczenski and Norcia (1999) found that vernier acuity is poorer than grating acuity during infancy, with the vernier acuity taking more time to develop. They suggested that these two types of acuity are limited by different mechanisms during development. Grating acuity is limited by retinal factors whereas vernier acuity is limited by cortical factors. Since amblyopes show greater losses in vernier acuity than grating acuity (Levi and Carkeet, 1993), the researchers concluded that sVEP vernier acuity provides a rapid and sensitive measurement to detect amblyopia.

In another study, Skoczenski and Norcia (2002) extended the age range studying the development of vernier acuity from infancy to adolescence. Their results showed that sVEP grating acuity becomes adult-like at the age of 6 years while vernier acuity continues to develop after 6 years to reach the adult level between 10 to 14 years. At the age of 6 months, vernier acuity threshold was found to be about eight times greater than that of an adult.

2.8 Studies of contrast sensitivity development by sweep VEP

Norcia et al. (1989) used sVEP to study the contrast response function (CRF) of the infant (the function of the response amplitude against contrast). They found the form of the CRF to be similar to that in adults: the response increases monotonically as a linear function of log contrast near threshold. As in adults, infant's CRF measured by sVEP may consist of a two-lobed function (Norcia et al., 1989). There is an increase in the response amplitude at low contrast followed by stability, or even a decrease, then another increase of the amplitude at high contrast. Norcia et al. (1988) measured the sVEP contrast sensitivity in a group of infants between the ages of 7 and 11 weeks, and another group of adults. They found that contrast sensitivity at the age of 10 weeks was close to that of adults at low spatial frequencies (0.5 and 1 c/d) but was significantly lower at higher spatial frequencies (>1 c/d). The shape of the contrast sensitivity function (CSF) of infants was similar to that of adults, both of which showed decreasing sensitivity with increasing spatial frequency, but the infant's function drops off 4.5 times faster. The maximum peak of the CSF curve attained by infants was 203 compared to 340 attained by adults. The same group of researchers studied the longitudinal and cross-sectional development of sVEP contrast sensitivity in infants between the age of 2 weeks to 40 weeks (Norcia et al., 1990). Their results showed that, for both longitudinal and cross-sectional data, contrast sensitivity at low spatial frequencies develops rapidly up to 10 weeks of age reaching an early asymptote of 200 compared to 450 for adults. However, contrast sensitivity at high spatial frequencies continues to develop until at least 30 weeks. The researchers compared sVEP contrast sensitivity with psychophysical contrast sensitivity in their adult subjects only. Their results showed slightly higher psychophysical contrast sensitivity than the sVEP sensitivity, with the best threshold of sVEP giving a CSF of a similar shape to that obtained psychophysically (sVEP CSF was 0.6 octaves lower than the psychophysical CSF). Norcia et al. (1990) pointed out that the peak sVEP contrast sensitivity of their adult subjects in this study is higher than a previous study (Norcia et al., 1986) due to the higher luminance they used (220 cd/m^2 vs 80 cd/m^2). Oliveira et al. (2004) evaluated the contrast sensitivity in full-term and pre-term infants by sVEP at the age of 3 and 10 months. Their results reveal similar CSF in full-term and pre-term infants. Peterzell and Kelly (1997) studied the spatial frequency tuned channels underlying the CSF using sVEP and suggested that these channels are of a similar shape in VEP and psychophysical CSF.

As shown in Tables 2-1 and 2-2, the published studies of sVEP visual acuity and contrast sensitivity have focused on the development of these visual functions in infants and the comparison of them with adults. The lack of studies of sVEP contrast sensitivity and visual acuity which span the human developmental process from infancy through childhood is an obstacle to introducing this technique to clinical practice.

Table 2-2: Studies of contrast sensitivity development using sVEP

Study	Subjects' age-range	Temporal frequency	Luminance	Results
Norcia et al. (1989). Measurement of spatial contrast sensitivity with the swept contrast VEP.	Infants: 9-23 weeks Adults	6 Hz	220 cd/m^2	The infant sVEP contrast response function (CRF) has a form similar to that in adults. sVEP contrast threshold is independent of the sweep range, as long as it spans the threshold.
Norcia et al. (1990). Development of contrast sensitivity in the human infant.	Infants: 2 – 40 weeks Adults	6 Hz	220 cd/m^2	Contrast threshold at low spatial frequencies developed from 7% at the age of 2-3 weeks to 0.5 % at 9 weeks which is still below the adults threshold of 0.32 – 0.22 %. After 9 weeks of age, contrast threshold remained constant at low spatial frequencies and showed a systematic increase at high spatial frequencies.
Peterzell et al. (1997). Development of spatial frequency tuned "covariance" channels: individual differences in the electrophysiological (VEP) contrast sensitivity function.	Infants: 8, 14, 20, and 32weeks Adults	6 Hz	For 8 and 14 weeks old: 40 cd/m^2 For older subjects: 80 cd/m^2	Multiple spatial channels are present at all ages tested in this study. In infants, the peak spatial frequency of each channel shifted from lower to higher spatial frequencies with age by a factor of 4, becoming adult-like after 8 months of age.
Norcia et al. (1988). High Visual contrast sensitivity in the young human infant.	Infants: 7 – 11 weeks Adults	6 Hz	220 cd/m^2	sVEP contrast sensitivity at low spatial frequencies for infants at the age of 10 weeks was less than a factor of two lower than that of adults. As the spatial frequency increases, the contrast sensitivity decreases for both infants and adults, but infant sensitivity reduces 4.5 times faster.

Lauritzen et al. (2004). Test-retest reliability of sweep visual evoked potential measurement of infant visual acuity and contrast sensitivity.	Infants: 5.7 – 39.4 weeks Adults	6 Hz	47.6 cd/m^2	Contrast threshold decreased from 2.8 % at 15 weeks of age to 1.8 % at 30 weeks of age.
Oliveira et al. (2004). Contrast sensitivity threshold measured by sweep-visual evoked potential in term and preterm infants at 3 and 10 months of age.	Infants: tested at 3 & 10 months. Adults	6 Hz	159.5 cd/m^2	There was no difference in sVEP CS between term and healthy pre-term infants. This showed that the longer visual experience of the pre-term infants does not improve their sVEP CS.

2.9 Clinical studies of sweep VEP

The sVEP has been recognized as a valuable technique for measuring visual acuity and contrast sensitivity in visually normal persons as well as persons with disorders that may affect vision. It has been suggested that sVEP provides more accurate estimates than behavioral methods for measuring visual acuity in patients with spastic cerebral palsy (SCP). This is because visual acuity, when measured behaviorally, may be underestimated due to the motor impairment, attention or fixation impairment in patients with SCP (da Costa et al., 2004). sVEP is preferable in assessing visual acuity in patients with cortical visual impairment (CVI) because it does not require verbal or motor response (eye movement) to attend the stimulus (Good, 2001). Another advantage is that children with CVI tend to stare at lights (the monitor in sVEP testing). However, sVEP acuity can be difficult to measure in patients with CVI since such patients may have brain malformation, wandering eye movements, seizure activity, or depressed cortical activity due to anticonvulsants. These difficulties can be minimized by monitoring fixation and averaging the VEP signal across many trials (Good, 2001). Although Teller acuity cards underestimate sVEP acuity in some patients with CVI, the two techniques correlate significantly (Good, 2001). Good and Hou (2006) studied the effect of luminance in children with CVI by using gratings with normal luminance (109 cd/m^2) and low luminance (20 cd/m^2). Their results showed that visual acuity is better under low luminance conditions than under normal luminance conditions, unlike children with normal vision whose sVEP grating acuity is similar under the two luminance conditions.

John et al. (2004) found that both sVEP visual acuity and contrast sensitivity, and behavioral visual acuity and contrast sensitivity, are reduced in children with Down syndrome compared to normal children. In this study, behavioral acuity in older children (> 2 years) was 1 octave higher than sVEP acuity for both the children with Down syndrome and the normal children. Higher values of sVEP acuity were found only in the youngest age group (< 2 years). The researchers concluded that their findings agreed with the study of Katsumi et al. (1996) who found that behavioral acuity is between 0.5 and 1 octave higher than sVEP acuity in adults, and also agreed with the study of Allen et al. (1992) who found that behavioral acuity is lower than sVEP acuity in infants, suggesting that there is a transitional period where behavioral acuity becomes superior to sVEP acuity after infancy. This period was found to be between 1–2 years of age (John et al., 2004). John et al. (2004) also suggested that ophthalmic anomalies per se cannot account for the reduction in vision in Down syndrome since they found reduced vision even in children without such anomalies. The researchers also concluded that both congenital abnormalities and age-related neuropathology (such as Alzheimer's which has been reported in persons with Down syndrome as young as 8 years of age) within the visual pathways in Down syndrome may account for the reduced vision.

In a recent retrospective study, Bradfield et al. (2007) found that sVEP acuity can be used to predict the future recognition acuity in children with albinism. They defined a positive predictability of sVEP acuity as final recognition acuity in either eye within one Snellen line of initial sVEP acuity. In another recent retrospective study, Ridder and Rouse (2007) found that sVEP acuity prior to amblyopia therapy can be a good predictor of Snellen acuity after amblyopia therapy with an interclass correlation coefficient (r) of 0.73. In agreement with the study of Katsumi et al. (1996), the researchers found that when the final Snellen acuity (after amblyopia therapy) was poor, the sVEP acuity prior to amblyopia therapy was better than the prior therapy Snellen acuity. When after therapy Snellen acuity was good (6/6 or 0 logMAR), the sVEP was slightly lower than 6/6. When the Snellen acuity is moderately decreased (6/12 or 0.3 logMAR), the sVEP acuity was similar. Gottlob et al. (1990) measured sVEP acuity and recognition acuity (by either Snellen, Allen or tumbling E chart) in children with various visual disorders. The researchers found high correlation coefficient between sVEP acuity and recognition acuity (RA), using best single sweep or vector averaging of many sweeps (r = 0.6–0.89). High correlation was also found among best single sweep acuities using different temporal frequencies (r = 0.79–0.97). It must be noted that high correlation does not imply good agreement, which is better expressed as the coefficient of agreement (Bland and Altman, 1986). Gottlob et al. (1990) used logarithmic sweeps to estimate visual acuity, instead of linear sweeps which are used for acuity estimate in normal children. This is because the range of spatial frequencies which have to be swept is difficult to determine in patients with visual disorders, due to their reduced visual acuity. In a later study, Gottlob et al. (1993) compared sVEP acuity and recognition acuity (RA) in children with organic diseases, nystagmus, strabismus (without amblyopia), and congenital ptosis (without amblyopia). The sVEP acuity result before the child begins to cooperate for RA (Allen picture cards) was compared with the first measure of RA. A significant correlation was found between the sVEP acuity and the RA acuity in children with organic diseases (r = 0.97), and in children with strabismus and alternating fixation (r = 0.92), but the correlation was not significant in children with strabismus (r = 0.61, $p > 0.05$). Gottlob et al. (1993) concluded that predicting the RA acuity by sVEP acuity depends on the patient's disease. The researchers also concluded that the sVEP is a better predictor than PL of later RA in patients with foveal disease, since the VEP assesses the central retinal function. Arai et al. (1997) compared Snellen acuity and sVEP acuity in patients with various ocular disorders. They found high correlation between these two measures of acuity with the lowest correlation in patients with optic nerve disease.

Patients with long-term type 1 diabetes mellitus (DM) but without retinopathy showed significantly lowered correlation between Snellen acuity and sVEP acuity, and lowered sVEP response amplitude (both acuity and contrast) when compared to normal subjects, which could indicate an optic nerve dysfunction in these patients (de Faria et al., 2001). A good correlation (r = 0.85) between PL acuity and sVEP acuity in children with various ocular disorders was demonstrated by Katsumi et al. (1997). They noticed that sVEP acuity is lower than PL acuity when PL acuity is better than 6/38, and is higher than PL acuity when the PL acuity is worse than 6/38. Crow et al. (2003) reported results of sVEP contrast sensitivity in patients with Alzheimer's dementia (AD). Their findings, like previous psychophysical and flash VEP studies, revealed a reduction in contrast sensitivity (especially at lower spatial frequencies) in patients with AD compared to a control age-matched group. They ascribed this reduction in contrast sensitivity to disease within the primary afferent visual pathway rather than to an overall cognitive deficit. Crow et al. (2003) suggested that sVEP is superior to other behavioral or VEP techniques for assessing contrast sensitivity in patients with AD because it does not require prolonged fixation and attention, which could be affected in these patients.

2.10 Conclusion

The sVEP technique has been shown to be valuable in assessing visual acuity, contrast sensitivity, and vernier acuity in infants and individuals with short attention span. The advantage of the rapid recording of the thresholds of these functions makes it possible to add a new and reliable (repeatable) dimension to study the development of vision. The fact that the visual acuity measured by sVEP gives different values from other tests of visual acuity raises a question that it may measure responses of the brain that are different from those measured by the other tests, and urges for normative age-related sVEP data. Coupling sVEP with behavioral techniques can give a better understanding of the limits of visual acuity and contrast sensitivity in nonverbal children.

Chapter 3
Research objectives

3.1 Purpose

The main aim of this thesis was to determine whether VA and CS are adult-like at the age of 6-8 or 9-12 years by using objective and subjective methods. The objective method was the sVEP and it became apparent from the literature review of this technique (Chapter 2) that it has many parameters that may affect VA or contrast thresholds. Therefore, the purpose of Chapters 4 and 5 of this thesis was to study the effects of these parameters on VA and contrast thresholds and determine the parameters that give the most valid and repeatable estimates of VA and contrast thresholds.

The literature review in Chapter 1 revealed that there is little agreement on when VA and CS reach adult levels (ranging from 3 – 6 years for VA and 6-18 years for CS). This discrepancy between the studies could be a result of using different methods in measuring these functions. For example, those studies which used classical psychophysical methods (e.g. constant stimuli, method of adjustment, or method of limits) without a forced-choice paradigm usually produced thresholds that may be affected by changes in the participant's response criterion. The studies that have used forced-choice paradigms are likely to be less affected by the participant's response criterion (Kelly & Savoie, 1973). In addition, there were no studies comparing objectively measured VA or CS between older children and adults. Therefore, in Chapter 6 objective (sVEP) and subjective (psychophysical) procedures were employed to study the development of VA and CS in older children and determine whether these functions are adult-like by 6-8 or by 9-12 years. By using a 2AFC procedure and a SDT procedure in Chapter 6, measures of VA and CS can be obtained without being influenced by the participant's response criterion. Furthermore, the criterion employed by the participants can be measured and compared across different age groups in the SDT procedure. Although SDT can help to control the criterion, only one previous study has applied this in children (Mayer, 1977).

3.2 Hypotheses

● The main hypothesis in this thesis is that adults have better VA and CS compared to children aged 6-8 years, but not compared to children aged 9-12 years.

Other secondary hypotheses are:

● The criterion used to fit the regression line for the determination of the sVEP VA and contrast threshold and the stimulus luminance have an effect on the threshold value and the number of the viable sVEP plots in children between 6-8 years old.

● The electrode placement, temporal frequency, sweep direction, presence of a fixation target, stimulus area, and sweep duration have an effect on the sVEP VA and contrast threshold and the number of the viable sVEP plots in children between 6-8 years old and/or adults.

● The criterion used by children aged 6-8 years old is different from the criterion used by the 9-12 years old or adults in the SDT procedure.

Chapter 4
Effects of the criterion for threshold determination and luminance on the sweep VEP threshold

4.1 Introduction

Sweep visually evoked potential (sVEP) is an electrophysiological technique for measuring visual acuity (VA), contrast sensitivity (CS) and vernier acuity. This technique has been mainly used to study the development of VA or CS in visually normal infants or to measure VA or CS in persons with visual disorders or communication difficulties that hinder subjective testing (see Almoqbel et al. (2008) for a review of the sVEP).

There are many parameters involved in the measurement of sVEP (Almoqbel et al., 2008) and differences in each of these may introduce significant variability between the results of the studies that use this technique. Some systematic investigation to arrive at parameters that give repeatable and valid measurements is needed as there are no ISCEV standards for the sVEP technique (Odom et al., 2010). It has been recommended that the sVEP plot should meet two criteria to be accepted and used to determine the threshold: the signal to noise ratio (SNR) criterion and the phase consistency criterion (Norcia and Tyler, 1985a; Norcia et al., 1989). First, the amplitude of the peak response signal should be at least three times larger than the noise at an adjacent frequency (SNR of $\geq$3:1) (Norcia and Tyler, 1985a; Norcia et al., 1989). Secondly, for the phase consistency criterion, the phase should be constant or gradually lagging as the sweep moves from supra-threshold to threshold (e.g. as the spatial frequency increases) when measuring VA or gradually leading as the sweep moves from threshold to supra-threshold (e.g. as the contrast increases) when measuring CS (Parker and

Salzen, 1977; Vassilev and Strashimirov, 1979; Norcia et al.; 1989; Seiple and Holopigian, 1989). Campbell and Maffei (1970) were the first to find that there is a linear relationship between VEP amplitude and the log of contrast and to propose that the threshold be determined by the extrapolation of a regression line between the amplitude of the peak VEP (μV) and log contrast to 0 μV amplitude. This technique has been generally accepted for determining the threshold value in the sVEP studies. An extrapolation to 0 μV amplitude between the VEP peak amplitude and spatial frequency plotted linearly gives an estimation of the sVEP VA and an extrapolation to 0 μV amplitude between the VEP peak amplitude and the log contrast gives an estimation of contrast threshold (Tyler et al., 1979; Norcia and Tyler, 1985; Norcia et al., 1985; Norcia et al., 1986; Allen et al., 1986; Norcia et al., 1990; Lauritzen et al., 2004 and de Faria et al., 1998). However, Zemon et al. (1997) used the intercept with an SNR of 1 to determine the threshold.

An important parameter in determining the threshold is the range over which the extrapolation technique is performed (i.e. the data points that are included to fit the regression line). Norcia et al. (1989) suggested criteria for choosing this range. Starting from the end of the sVEP plot below threshold (last data point), each data point and its neighbor are checked on phase and local artifact criteria. The range is then defined as ending at the data point where the amplitude function rises and stays above an SNR of 1.5. The regression line is then fitted between the peak of the amplitude response and the last data point with an SNR > 1.5, given that at least three points are included in the fit and one of them has an SNR of > 3, or at least two points if both have an SNR of > 3. Gottlob et al. (1990) used the first point at which the SNR dropped below 1.5 as the last point to be included in the regression line fit. Bach et al. (2008), recording steady-state VEP (ssVEP), used an algorithm that selects the range of responses that were significantly above the noise level at the 0.05 level for the regression line fitting. This resulted in a constant relationship between the ssVEP acuity and subjective Landolt C acuity for adults with normal and reduced VA. This relationship can be found by applying the following formula:

$$\text{Subjective } (VA_{decimal}) = SF_0 / 17.6 \text{ c/d},$$

where SF_0 is the VEP acuity obtained by the algorithm.

Ridder et al. (1997) fitted the regression line starting from the peak of the amplitude response to the last point that is above noise. If there were no data points between the peak of the amplitude response and the noise level, the threshold was taken as the value at the peak. They defined any data point to be noise if either the 95% confidence intervals for the amplitude at the point overlapped with zero, or the 95% confidence intervals for the phase at the point were greater than 90˚. In another study, Ridder (2004) compared Ridder et al.'s (1997) method with a second method in which any data point was defined as noise if its SNR was < 2 and the regression line was fitted between the peak of the amplitude response and the first data point that was defined as noise. The two methods gave results that were not significantly different from each other. He also obtained estimates of the threshold extrapolating to 0, 1 and 2 μV and found that the acuity estimates at 0 μV agreed best with Bailey-Lovie logMAR acuity. The study of Ridder (2004) is the only study that compared different criteria for determining the range of points to use for the regression line fitting (in particular, for determining the end near threshold). Most studies picked the criteria for choosing the range of the regression line fit based on theoretical reasons and have not studied them per se.

Another parameter that may affect the sVEP threshold is the mean luminance of the screen and few studies have investigated that effect. Allen et al. (1992) found that sVEP VA increased in infants and adults when luminance was increased from 0.01 to 1.0 cd/m^2, and reached an asymptote between 1.0 and 100 cd/m^2. Using two luminance levels (109 cd/m^2 and 20 cd/ m^2), Good and Hou (2006) found no difference in sVEP VA (between these luminances) in normal children (ranging between 7 months to 4 years in age), but in children with cortical visual impairment (CVI) the acuity was better at low luminance (i.e. 20 cd/m^2).

The purpose of this study is to investigate the effects of different criteria for choosing the end point for the regression line fitting and the luminance on the sVEP VA and contrast thresholds in children. Additionally, the effects of these parameters on the number of viable readings (according to the criteria described below) obtained from the five active electrodes that were used in this study was investigated. We hypothesize that parameters may be chosen such that they will give better repeatability and more viable readings.

4.2 Methods

4.2.1 Stimuli

The stimuli were horizontal sinewave pattern-reversal gratings. The display screen was a Phillips FIMI MGD403 black and white CRT monitor, with a resolution of 1600 × 1200 (8 bits) and a refresh rate of 60 Hz. Three luminance levels were used: 25, 50 and 100 cd/m^2. The following parameters were used: the gratings alternated at 7.5 Hz, the duration of the sweep was 10 seconds, ten analysis bins were used, linear sweeps were used for VA measurement and logarithmic sweeps for contrast threshold measurement and the stimulus area was approximately 15° × 15° square for contrast threshold measurement and 6° × 6° square for VA measurement. For VA, the contrast was 90% and the spatial frequency of the reversing stimulus was increased in a linear sweep from 1 to 40 cpd. For contrast thresholds, the stimuli were 1 or 8 cycle per degree (cpd) gratings. These were chosen to represent low and high spatial frequencies, as the visual system is known to respond differently for different spatial frequencies. The sweep range depended on the luminance and the responses of the subject. In general, a sweep with a lower range of contrast was attempted first, and, if a viable plot (according to the criteria described below) was not obtained with this range after six sweeps, the range was increased to a higher range of contrast. The range was either 0.40–40% or 2.20–90% for 25 cd/m^2, while for 50 cd/m^2 it was 0.3–30% or 1.6–50% and for 100 cd/m^2 it was 0.23–23% or 1.12–90%. To maintain fixation, a small fixation target was placed in the center of the stimulus. The size of the fixation target was 0.23– 0.69° for VA and 0.57–1.72° for contrast threshold. For children who were not attending the small fixation target, a small toy on a stick was held at the center of the screen and jiggled. The size of the toy was 0.69° for VA and 1.72° for contrast threshold. If fixation was lost during any of the sweep trials, the trial was stopped and discarded. A total of eight trials for each condition was obtained, and the trials were averaged together for that particular condition.

4.2.2 Recording

Binocular sVEPs were recorded by PowerDiva software (version 1.9) developed by Norcia (Smith–Kettlewell Eye Research Institute, San Francisco). VEP responses were acquired with a Grass Telefactor Neurodata Acquisition (DAQ) system Model 12, with an amplification of 20 K. For recording the sVEP, seven electrodes (five active channel electrodes, one reference electrode and one ground electrode) were connected to a Grass Bio-Potential Amplifier Model CP511, followed by the DAQ system. The artifact detector was set to 200 μV. The DAQ rate used to capture the EEG signals was 601.08 Hz. A low pass filter of 100 Hz and a high pass filter of 0.1 Hz were used. Amplitude and phase of the VEP response were determined at the second harmonic (2F) frequency using the recursive least square (RLS) method (Tang and Norcia, 1995). Recording was executed in a dark room except for the light of the display screen.

The sVEPs were recorded from the occipital cortex using five Grass 1 cm cup diameter gold active channel electrodes, one reference and one ground electrode. The electrode placement varied from the International 10/20 system (Odom et al., 2010) in that the active electrodes were separated by 2.5 cm and the reference electrode was placed at 50% distance between the inion and nasion (PowerDiva electrode placement, Figure 4-1, Vladimir Y. Vildavski, personal communication). The position of Oz (the central electrode) was 1.5 cm above the inion. The other four electrodes were placed laterally on either side of Oz, separated from each other by 2.5 cm. The ground electrode was placed on the forehead.

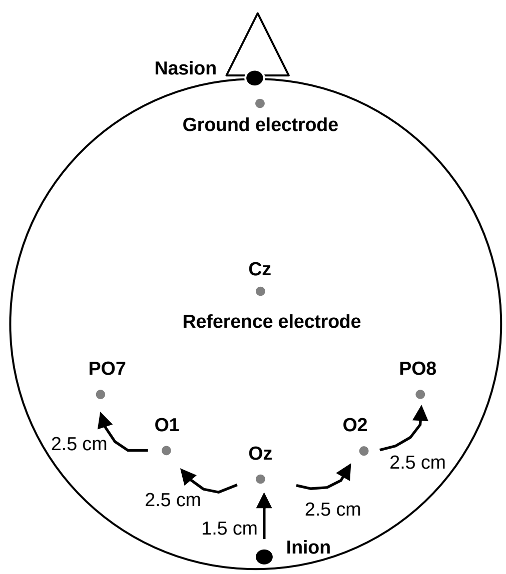

Figure 4-1: The PowerDiva electrode placement.

4.2.3 Subjects

Six children aged 6-8 years took part in experiment 1 and 11 children of the same age range took part in experiment 2 (repeatability). The participants were recruited from the Optometry Clinic at the School of Optometry, University of Waterloo. Inclusion criteria were monocular VA of 6/7.5 or better as measured on a Bailey–Lovie logMAR chart, and no ocular disease as indicated in the files of the participants. Exclusion criteria were presence of amblyopia, strabismus, heterophoria more than 6^{Δ}, spherical refractive error of more than −2.00 or +1.00 D, astigmatism of more than 1.50 D, or anisometropia of more than 1 D. The study was approved by the Office of Research Ethics at the University of Waterloo.

4.2.4 Determination of the sVEP threshold

Figure 4-2 shows typical plots produced by the PowerDiva system, previously described by Norcia (Norcia, PowerDiva Manual). Threshold was determined by extrapolation of the regression line from the signal peak to zero amplitude against spatial frequency for VA and against percentage contrast for contrast threshold. The best-fit regression line was fitted between the two vertical dashed lines, which can be moved by the experimenter.

Three general criteria for accepting a plot as viable were applied:

(1) The peak SNR should be ≥ 3. The noise was determined by the mean amplitude at the two frequencies about 1 Hz on either side of the stimulus frequency.

(2) Phase should be constant or gradually changing within the range used for the regression line.

(3) The PowerDiva software also applies one more criterion which is that the extrapolated threshold should be close to the last data point used to calculate threshold.

For data analysis, five other criteria were then also applied. These determined the end point (range of data points) for the regression line fitting and were applied in turn. A threshold value was determined from each one. Different criteria were chosen because, although previous studies are in agreement that a regression line should be fitted to determine threshold, few studies have specified how to determine the range of data points to be included. For all of the criteria, the signal peak was defined as the peak closest to the threshold, with an SNR ≥ 3, i.e. if there were multiple peaks, the peak that was used was the one closest to the highest spatial frequency (for VA plots) or the lowest contrast (for CS plots) with an SNR ≥ 3. The vertical line that defined the start of the regression line (Figure 4-2) was placed at this peak. The other vertical line was moved and determined the end of the range of data points that were used for the regression line fit. The software automatically adjusts and fits the regression line to the data points between the vertical lines.

The five criteria for fitting the regression line to determine the threshold were as follows:

- Criterion 0 (C0): this was derived from the PowerDiva output, i.e. the threshold originally given by the software (Figure 4-2a).
- Criterion 1 (C1): the range over which the regression line was fitted was determined by eye, to give the best apparent regression line fit from the peak to the point where the amplitude was close to zero (Figure 4-2b).
- Criterion 2 (C2): the range for the regression line fit was defined as the data between the signal peak and the last data point (furthest from the peak) with an SNR ≥ 1 (Figure 4-2c). On occasions, when the last data point with an SNR ≥ 1 was selected for the end of the regression range, the plot turned grey. This indicated that it was not an acceptable plot according to the software criterion, because the determined threshold was too far removed from the range used

for the regression fitting. In that case, the vertical line which defined the end of the regression line was moved to the previous data point having SNR ≥ 1 which gave an acceptable plot.

- Criterion 3 (C3): criterion 3 was developed because Criterion 2 sometimes resulted in a threshold beyond the sweep range, as shown in Figure 4-2d. Criterion 3 was similar to Criterion 2, but was defined so that the threshold should be within the sweep range of the stimuli actually used.
- Criterion 4 (C4): this criterion was similar to Criterion 2 except that the SNR should not fall below one at any point within the range used for regression line fitting, as shown in Figure 4-2e. Thus, the vertical line denoting the end of the range was moved to the last data point with an SNR ≥ 1 and with no data points falling below 1 in the range.

There were occasions when some of these criteria resulted in no movement of the end of the regression line and therefore produced identical results.

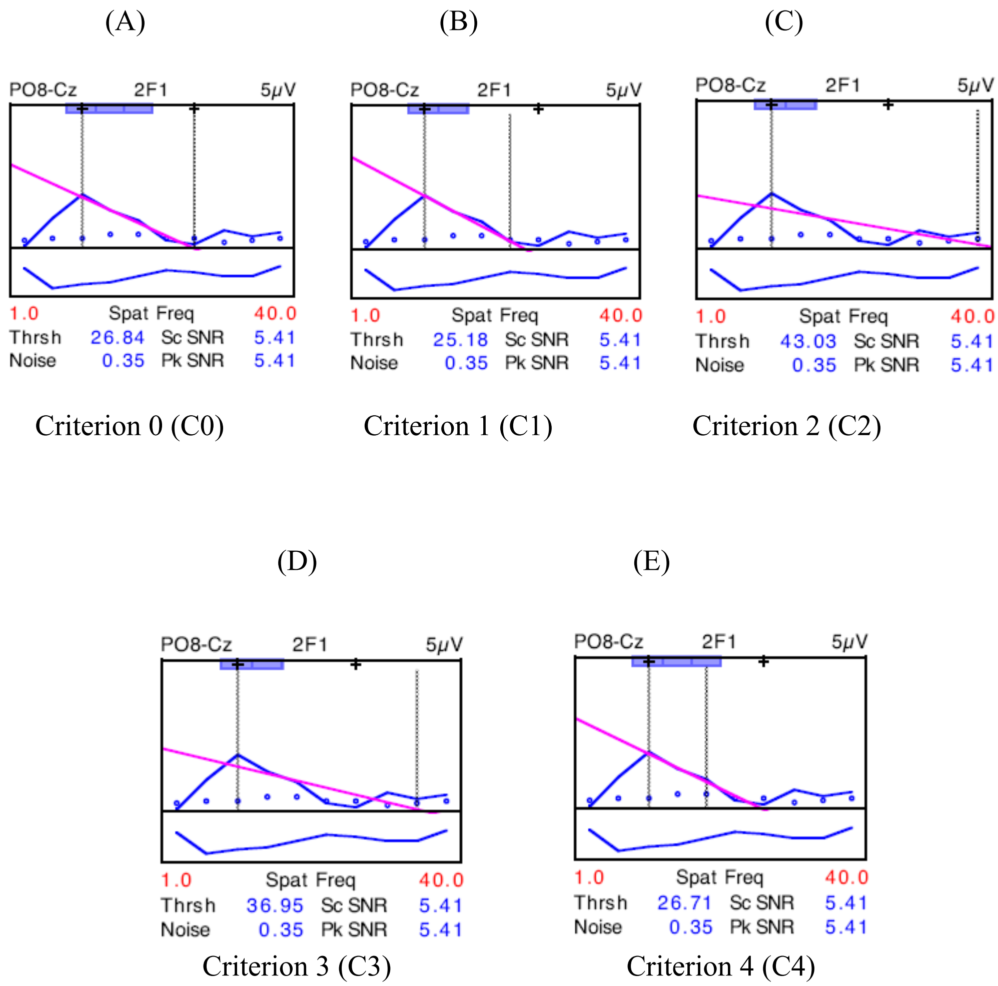

Figure 4-2: Example showing VA threshold determined by different criteria: (a) Criterion 0, (b) Criterion 1, (c) Criterion 2, (d) Criterion 3, (e) Criterion 4 for the PO8-C_Z electrode, at the second harmonic. In the *top section* of each plot, amplitude (between 0 and 5µV) is plotted against spatial frequency. In the *lower section*, phase is plotted against spatial frequency. The *solid blue line* in the upper plots is the response amplitude at the second harmonic, and the *straight pink line* is the regression line. Thresh gives the threshold from the current regression line. Sc SNR is the peak SNR within the range selected for the regression line and Pk SNR is the peak SNR of all the data. The *dots* represent the noise. For more details of these plots see Allen et al. (1986).

4.2.5 Experiment 1: Effect of luminance on sVEP visual acuity and contrast thresholds

SVEP VA and contrast thresholds were measured at three different levels of luminance: 25, 50 and 100 cd/m^2. The order of the luminance levels was randomized. Six children (three males and three females) took part in this experiment (mean age 6.33 years, SD ± 0.81).

4.2.6 Experiment 2: Repeatability

Test-retest repeatability was performed for sVEP VA and contrast threshold on 11 children on two different visits. Only children who gave viable plots of VA or contrast threshold measurements with all the five criteria and in both visits were included. This resulted in the inclusion of eleven children for VA and nine children for contrast threshold. For VA repeatability, there were six male and five female participants (mean age = 6.81 years, SD ± 0.75). For contrast threshold repeatability, there were four male and five female participants (mean age = 7 years, SD ± 0.71). The stimulus parameters for VA and contrast threshold measurement were as above, but only a luminance of 50 cd/m^2 was used (chosen based on the results of Experiment 1) and contrast threshold was measured at a spatial frequency of 1 cpd.

4.2.7 Data analysis

For each subject, thresholds obtained from each acceptable plot of the active electrodes were log-transformed. The VA or contrast threshold for an individual participant was calculated as the arithmetic mean of all the log-transformed thresholds obtained from the acceptable plots of the five active electrodes. The number of viable readings (out of five electrodes) was also used as an outcome variable. The results were analyzed using repeated measure ANOVA with the Statistical Analysis System (SAS) software. The smaller number of subjects required the use of the method of Winer (Winer, 1971 and Winer, 1971) which assumes sphericity and makes use of all the data in the analysis of variance. The co-efficient of repeatability was determined for the test–retest repeatability (Bland and Altman, 1986).

4.3 Results

4.3.1 Experiment 1: Effect of luminance on sVEP visual acuity and contrast thresholds

ANOVA showed that there was a main effect of criterion on VA (p = 0.029) with no main effect of luminance (p = 0.72) and no interactions (p = 0.53). Post hoc t-test (LSD) showed that C1 was significantly different from C2, C3, and C4, giving poorer VA (Figure 4-3). C0 was not significantly different from any of the other criteria.

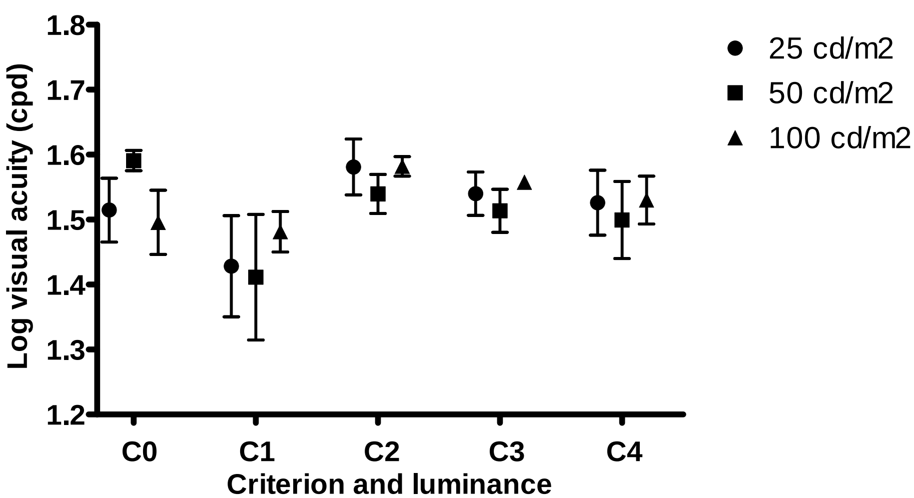

Figure 4-3: Mean sVEP visual acuity at three luminance levels: 25, 50 and 100 cd/m^2. Thresholds were determined with criteria C0-C4. Error bars are SEM.

For contrast threshold at 1 cpd, there were main effects of criterion ($p < 0.001$) and luminance ($p = 0.036$) with no interaction ($p = 0.76$). Post hoc t-test (LSD) showed that C2 and C3 were significantly different from C0, C1, and C4, giving lower contrast thresholds. C1 was also significantly different from C4, giving higher contrast threshold. The luminance of 25 cd/m^2 gave higher contrast thresholds than 50 or 100 cd/m^2 (Figure 4-4).

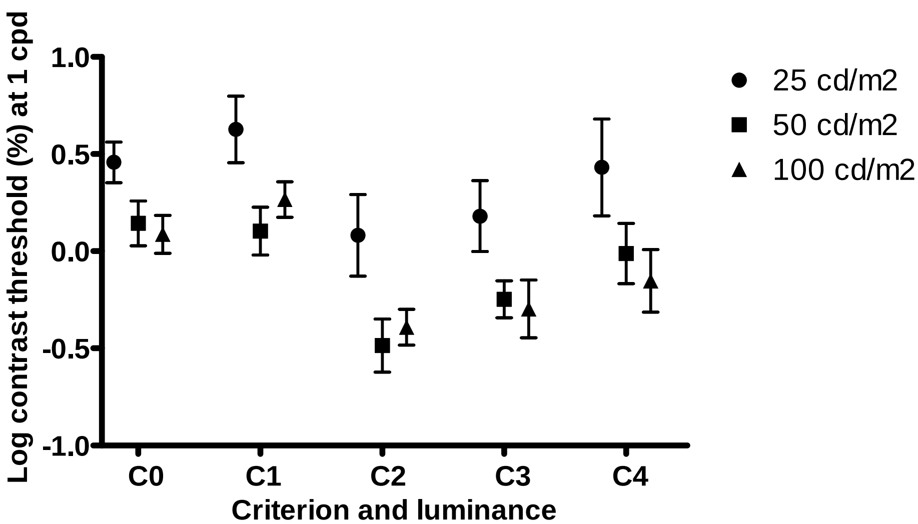

Figure 4-4: Mean sVEP contrast thresholds at 1 cpd at three luminance levels: 25, 50 and 100 cd/m^2. Thresholds were determined with criteria C0-C4. Error bars are SEM.

For contrast threshold at 8 cpd, there was a main effect of criterion ($p < 0.001$) with no main effect of luminance ($p = 0.2$) and no interactions ($p = 0.53$). Post hoc t-test (LSD) showed that C2 and C3 were significantly different from C0 and C1, giving lower contrast thresholds. A significant difference was also found between C4 on the one hand, and C0 and C2 on the other hand. C4 gave lower contrast thresholds than C0 and higher contrast thresholds than C2 (Figure 4-5).

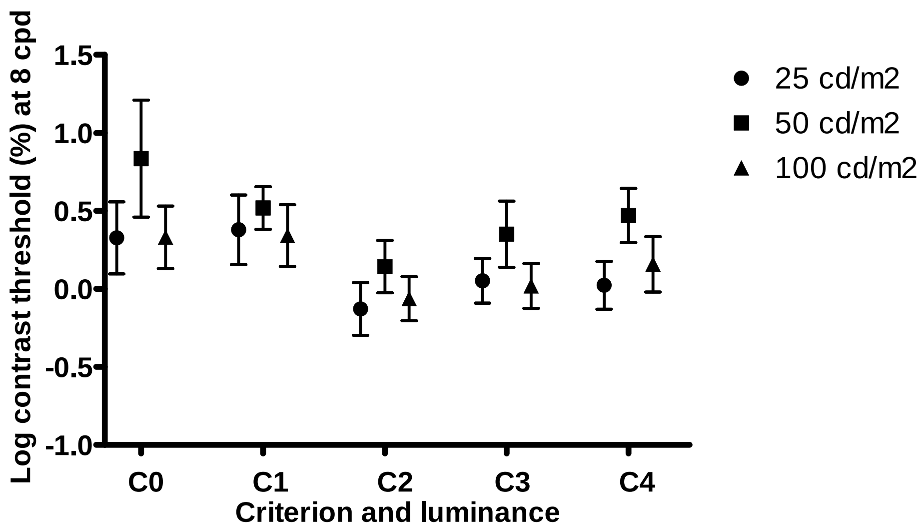

Figure 4-5: Mean sVEP contrast thresholds at 8 cpd at three luminance levels: 25, 50 and 100 cd/m^2. Thresholds were determined with criteria C0-C4. Error bars are SEM.

With regard to the number of viable readings, there was a main effect of criterion on the number of viable readings for VA (p = 0.0014) with no main effect of luminance (p = 0.73) and no interaction (p = 0.92). Post hoc t-test showed that C0 was significantly different from C1, C2, C3, and C4, giving fewer viable readings (Figure 4-6).

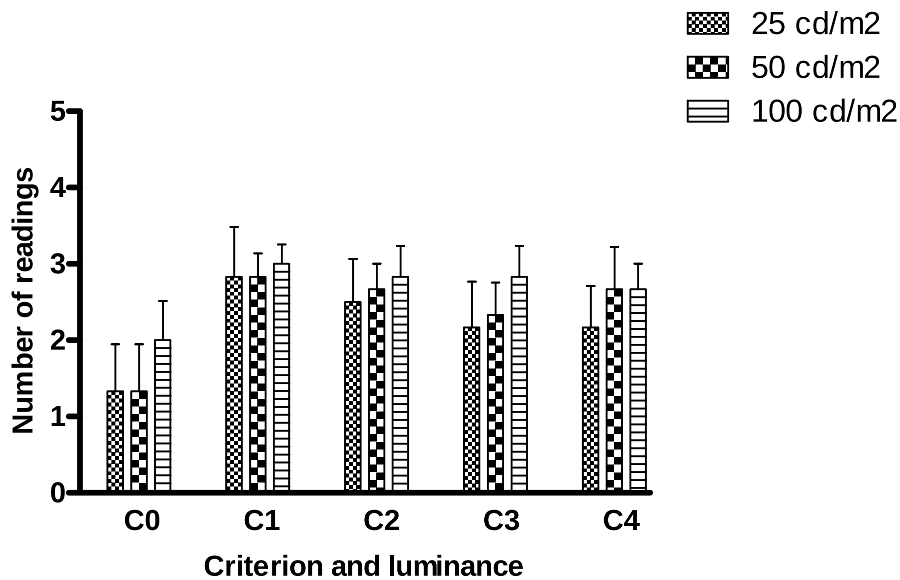

Figure 4-6: Mean number of readings for visual acuity at three luminance levels: 25, 50 and 100 cd/m^2. Number of readings were determined with criteria C0-C4. Error bars are SEM.

For contrast threshold at 1 cpd, there was a main effect of criterion ($p = 0.015$) on the number of viable readings with no main effect of luminance ($p = 0.32$) and no interaction ($p = 0.57$). Post hoc t-test (LSD) showed that C0 was significantly different from C1, C2, C3, and C4, giving fewer viable readings (Figure 4-7).

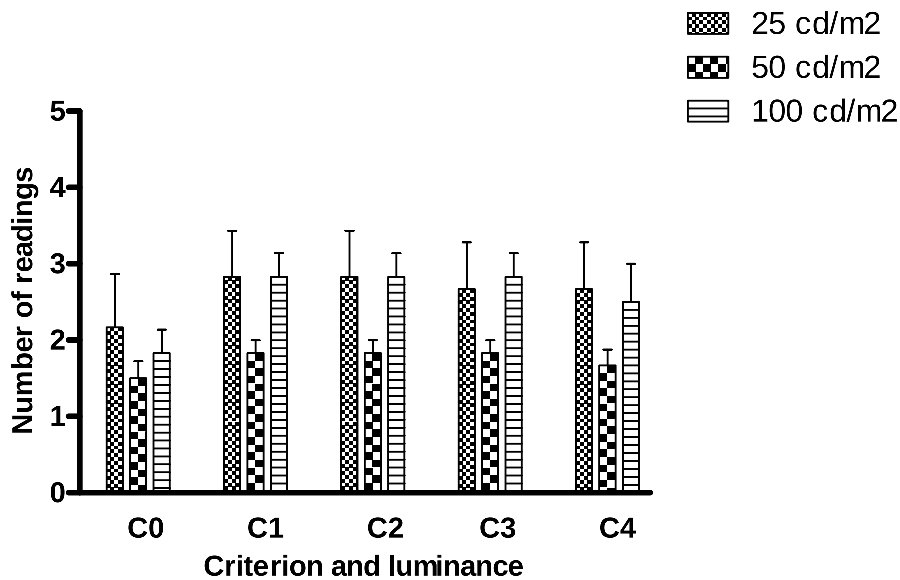

Figure 4-7: Mean number of readings for contrast threshold at 1 cpd with three luminance levels: 25, 50 and 100 cd/m^2. Number of readings were determined with criteria C0-C4. Error bars are SEM.

For contrast at 8 cpd, there was a main effect of criterion (p = 0.0081) on the number of readings with no main effect of luminance (p = 0.55) and no interaction (p = 0.91). Post hoc t-test (LSD) showed that C0 was significantly different from C1, C2, and C3, giving fewer viable readings (Figure 4-8).

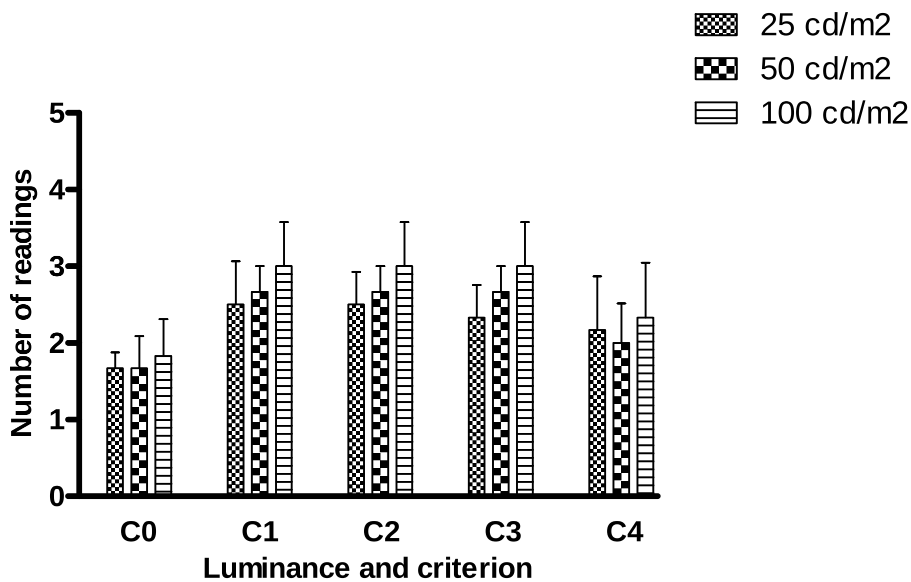

Figure 4-8: Mean number of readings for contrast threshold at 8 cpd with three luminance levels: 25, 50 and 100 cd/m^2. Number of readings were determined with criteria C0-C4. Error bars are SEM.

4.3.2 Experiment 2: repeatability

Table 4-1 shows the coefficient of test-retest repeatability (COR) for the different criteria.

Table 4-1: Coefficients of test-retest repeatability.

	C0	C1	C2	C3	C4
Visual acuity					
Mean difference	-0.05	-0.04	-0.02	-0.03	-0.06
COR	0.25	0.27	0.17	0.21	0.21
Contrast threshold					
Mean difference	-0.23	-0.11	0.07	-0.05	-0.22
COR	0.85	0.84	0.51	0.21	0.70

For both VA and contrast threshold, C2 and C3 tend to give lower COR compared to the other criteria. For VA C2 gave lower COR than C3, while for contrast threshold C3 gave lower COR than C2.

4.4 Discussion

In this study, the effects of different criteria for choosing the end point for the regression line fitting and the level of luminance on the sVEP VA and contrast thresholds were investigated. Additionally, the effect of these parameters on the number of viable threshold readings obtained from five active electrodes was investigated. The results indicate that C2 and C3 tended to be similar to each other and different from the other criteria. C2 and C3 tended to give lower (better) contrast thresholds and higher (better) VA than the other criteria. C2 and C3 also tended to give better repeatability than the other criteria. The similarity between C2 and C3 in the results is not surprising, since C3 is the same as C2 except that the threshold has to be within the sweep range for C3. In most of the cases, the threshold determined by C2 was within the sweep range; hence, the C3 threshold was the same as C2.

It is generally recommended that the sweep range cover the expected threshold values of the participants (Norcia and Tyler, 1985a and Ridder, 2004). Although, for both VA and contrast threshold measurements, we chose sweep ranges that would be expected to cover the threshold values, this may not always be the case. Therefore, it may be acceptable to use a threshold that is outside the sweep range (e.g., C2). C0, C1 and C4 tended to be similar to each other. They ignore the data points which are close to the noise level and hence, give more conservative estimates of threshold (i.e. poorer VA and contrast thresholds). C2 has a less conservative SNR criterion than used by Norcia et al. (1989) which was an SNR of > 1.5 or Ridder (2004) who used an SNR of > 2. Ridder (2004) found no difference in VA thresholds with the two methods that he compared. All these SNR criteria are empirical. Therefore, the choice of the range of the data points to be included in the regression line fit may be made based on the criterion that gives the best repeatability and the best validity against psychophysical thresholds. As mentioned above, C2 and C3 gave the best repeatability in children. Yadav et al. (2009) studied the effect of these criteria in adults and found that C2 and C3 also gave the best repeatability in adults. However, C3 resulted in some missing data for VA in adult subjects (there were no viable readings for any of the five electrodes).

In addition to test-retest repeatability, Yadav et al. (2009) investigated the validity of all the criteria (C0-C4) in adult participants by comparing their thresholds for VA and contrast at 1 and 8 cpd against psychophysically determined thresholds at the same luminance levels that were used for children in this study. C2 and C3 gave the best agreement with the psychophysical thresholds in adults as indicated by their low coefficients of agreement compared to the other criteria. Yadav et al. (2009) also found that, for both VA and contrast thresholds, the only criterion that was not significantly different from the psychophysical thresholds at all the luminance levels was C2. Validity was not investigated in children since they behave differently in psychophysical testing situations compared with adults (Atkinson et al., 1981; Bradley and Freeman, 1982 and Abramov et al., 1984).

For VA and contrast thresholds at 1 and 8 cpd, C1, C2 and C3 consistently gave more viable readings than C0 (Fig. 4-6, 4-7, and 4-8). Obtaining a greater number of viable sVEP plots presumably would yield more reliable threshold measurements.

With regard to the effects of luminance, the results of sVEP VA measurements agree with Allen et al. (1992) who did not find a significant increase in VA over the range of 1 to 100 cd/m^2 and Good and Hou (2006) when comparing VA with luminance of 20 and 109 cd/m^2. The only effect of luminance in this study was on the contrast thresholds at 1 cpd where the luminance at 25 cd/m^2 produced higher contrast thresholds than the luminance at 50 or 100 cd/m^2.

The final threshold that we considered was obtained by averaging all the thresholds from the acceptable plots of the five active electrodes. It is true that the active electrodes PO7, O1, O2 and PO8 tend to give lower amplitudes at the peak signal than the central electrode (Oz), but this should not affect their thresholds since the extrapolation to 0 μV is insensitive to variations in VEP amplitude (Tyler et al., 1979).

In summary, this study considered different criteria for the range of regression line fitting to determine sVEP VA and contrast thresholds. The results showed that C2 and C3 gave better VA and contrast threshold than the other criteria. C2 and C3 also gave better repeatability than the other criteria. C1, C2 and C3 consistently gave more viable readings than C0. Considering all these results and the validity results in Yadav et al. (2009), C2 and C3 gave the best repeatability and validity among all the criteria. Because C3 resulted in some missing data in the repeatability for adults (Yadav et al., 2009), C2 seems to perform the best and is recommended for the determination of the sVEP VA or contrast thresholds. Therefore, C2 will be used to determine the sVEP thresholds in the following studies presented in this thesis. The luminance results indicated that a luminance of at least 50 cd/m^2 should be used.

Chapter 5

Effects of sweep VEP parameters on visual acuity and contrast thresholds in children and adults

This chapter is published as follows:

Almoqbel FM, Yadav NK, Leat SJ, Head LM and Irving EL (2011). Effects of sweep VEP parameters on visual acuity and contrast thresholds in children and adults. *Graefes Arch Clin Exp Ophthalmol* 249: 613-623. Reproduced with permission from Springer.

	Concept/design	Recruitment	Acquisition of data	Analysis	Write-up/ publication
Almoqbel	Developed	Child participants	Child participants	Child and adult data	Write-up
Yadav	Developed	Adult participants	Adult participants	Adult data	Editing and suggestions
Leat	Initiated and directed			Guidance	Editing and suggestions
Head		Child participants			Editing
Irving	Initiated and directed			Guidance	Editing and suggestions

Table of the role of each author in this publication

5.1 Overview

Background: There are many parameters that may impact the thresholds obtained with sweep visually evoked potentials (sVEP), yet a number of these parameters have not been systematically studied, and there is no recognised standard for sVEP recording. In this study, the effects of electrode placement, temporal frequency, sweep direction, presence of a fixation target, stimulus area, and sweep duration on visual acuity (VA) and contrast thresholds of the sVEP were investigated. Additionally, the effect of these parameters on the number of viable threshold readings obtained from five active electrodes was investigated.

Methods: Participants were six children (aged 6-8 years) and six adults (aged 17-30 years) with normal vision. Binocular sVEP VA and contrast thresholds were measured for two electrode placements (ISCEV and PowerDiva) of five active electrodes, three temporal frequencies (6, 7.5, and 10 Hz), two sweep directions (low to high and high to low), presence or absence of a fixation target, three stimulus areas, and three sweep durations.

Results: There were differences between adults and children with respect to visual acuity, the adults having better VA than the children ($p = 0.033$ in experiment 2). Overall, there were more viable readings at 7.5 Hz than at either 10 or 6Hz ($p = 0.0014$ for VA and 0.001 for contrast thresholds). The adults performed better (in terms of viable readings) with the fixation target than without it ($p = 0.04$). The smallest stimulus size used gave rise to fewer viable readings in both adults and children ($p = 0.022$ for VA and 0.0001 for contrast thresholds). The other parameters (electrode placement, sweep direction and sweep duration) did not give rise to significant differences.

Conclusions: A temporal frequency of 7.5 Hz, a stimulus area of 4° or larger for VA and 10° or larger for contrast thresholds, and the use of a fixation target gave more viable readings, and may be indicated for future application. Consideration of the number of viable readings showed more differences between parameters than the actual thresholds, and it is suggested that more readings presumably would yield more reliable threshold measurements.

Keywords: sVEP, visual evoked potential, visual acuity, contrast sensitivity

5.2 Introduction

The sweep visual evoked potential (sVEP) is an objective test for assessing visual acuity (VA) and contrast sensitivity (CS) (for a review, see Almoqbel et al., 2008). With many parameters involved in the measurement of the sVEP and the lack of standard recording technique under ISCEV (Odom et al., 2010), one may wonder if these parameters have any effect on the sVEP's measured threshold. One important parameter is the electrode placement. Although many studies (Good and Hou, 2006; Arai et al., 1997; John et al., 2004; Peterzell and Kelly, 1997; Prager et al., 1999 and Riddell et al., 1997) have followed the ISCEV standards (Odom et al., 2010) for the placement of the active, ground and reference electrodes, others (Norcia and Tyler, 1985a; Norcia and Tyler, 1985b; Norcia et al., 1988; Norcia et al., 1989; Norcia et al., 1990; Hamer et al., 1989; Back et al., 2008; da Costa et al., 2004; Oliveira et al., 2004; Crow et al., 2003; Gottlob et al., 1990; Gottlob et al., 1993; Lauritzen et al., 2004; Ridder et al., 2007; Seiple et al., 1989; Tyler et al., 1979; Zemon et al., 1997 and Zhou et al., 2008) used different electrode placements, and only Allen et al. (1986) compared between two electrode placements.

Other parameters are related to the stimulus characteristics. These include the temporal frequency, sweep direction, stimulus area and sweep duration of the stimulus. Norcia and Tyler (1985b) found no significant difference in acuities obtained from infants at temporal frequencies of 6 or 10 Hz. The same conclusion was reached by Sokol et al. (1992) for temporal frequencies of 5, 7, or 12 Hz in infants (2-13 mo) and adults. Allen et al. (1996) also found no significant difference in acuities in adult subjects for a range of temporal frequencies between 2 and 20 Hz. Gottlob et al. (1990) used four temporal frequencies (4, 6, 7.5, or 12 Hz) to measure sVEP VA in children with various ocular disorders. They concluded that using 4 Hz gave higher (decimal) acuity estimates than 12 Hz for patients with good optotype acuity.

A handful of studies (Nelson et al., 1984; Brigell et al., 1987 and Seiple et al., 1988) have investigated the effect of sweep direction (low-to-high vs high-to-low contrast) on contrast threshold in adults. These studies agreed that sweeping from high contrast to low contrast resulted in poorer contrast thresholds compared to those obtained when sweeping in the other direction, as a result of contrast adaptation. Nelson et al. (1984) found that the VA of their adult subjects were poorer when sweeping from low to high spatial frequency compared to those obtained when sweeping from high to low spatial frequency. They related this finding to adaptation to the low spatial frequency gratings at the beginning of the sweep.

Studies on the pattern VEP have shown that the stimulus field size affects the VEP amplitude when using low spatial frequencies but not high spatial frequencies. The amplitude decreases as the stimulus area is decreased (Spinelli et al., 1983; Katsumi et al., 1988 and Sakaue et al., 1990). One study (Tyler et al., 1979) looked at the effect of stimulus area on the sVEP in adults. Its findings showed that the estimated VA did not change when changing the stimulus area, despite the decrease in the sVEP amplitude at lower spatial frequencies as the stimulus area decreases. To our knowledge, no studies have been conducted to investigate the effect of stimulus area on the sVEP contrast threshold or on the number of viable readings of the active electrodes of VA or contrast thresholds.

The main advantage of the sVEP over the conventional steady-state pattern VEP, where each spatial frequency or contrast level is recorded in a separate trial, is its short recording time. The recording duration could be as short as 10 seconds. However, little is known of the effects of sweep duration on the VA or contrast threshold, which ranged from 10 to 20 seconds in most of the studies reporting sVEP threshold measurements (Arai et al., 1997; Norcia et al., 1989; Norcia et al., 1986; Sokol et al., 1988 and Katsumi et al., 1997). There is only one study (Ridder et al., 1998) that has actually investigated the effect of sweep duration, and this used the sVEP VA as the outcome.

In a previous study (Yadav et al., 2009) we investigated the effects of luminance and different criteria for the range of data points used for regression line fitting on the sVEP VA and contrast thresholds in children and adults. The results showed that luminance of 25 cd/m^2 gave poorer contrast thresholds at 1 cpd than 50 or 100 cd/m^2 and that fitting the regression line from the signal peak that has an SNR≥3 to the last data point with an SNR ≥ 1 (criterion 2) gave better repeatability and validity, and more viable readings. The purpose of this study was to investigate the effects of electrode placement, temporal frequency, sweep direction, the presence of a fixation target, stimulus area, and sweep duration on the sVEP VA and contrast thresholds and on the number of viable readings obtained from the five active electrodes that were used in all the experiments, and to determine if these were different for children versus adults. We expect that a large stimulus area coupled with using five active electrodes will yield more viable readings than a smaller stimulus area, due to the stimulation of a larger population of retinal and cortical cells. This, in turn, will provide more accurate estimates of the VA and contrast threshold. Additionally, using a fixation target to maintain stable fixation will probably produce more readings, higher VA or lower contrast thresholds.

5.3 Methods

Six adults (17 to 30 years) and six children (6 to 8 years) participated in each experiment (except the first experiment, which had seven children). Inclusion criteria were VA of 6/7.5 or better as measured on a Bailey–Lovie logMAR chart, and no ocular disease. Exclusion criteria were presence of amblyopia, strabismus, heterophoria more than 6^{Δ}, spherical refractive error of more than −2.00 or +1.00 D, astigmatism of more than 1.50 D, or anisometropia of more than 1 D. The study was approved by the Office of Research Ethics at the University of Waterloo, and followed the tenets of the Declaration of Helsinki.

5.3.1 Stimuli

Horizontally-oriented sinewave pattern-reversal gratings were used in all the experiments. The display screen was a Phillips FIMI MGD403 black and white CRT monitor, with a resolution of 1600 × 1200 (8 bits) and a refresh rate of 60 Hz. The average luminance of the screen was 50 cd/m^2. Except where indicated, the following parameters were used: the gratings alternated at 7.5 Hz, the duration of the sweep was 10 seconds, ten analysis bins were used, linear sweeps were used for VA measurement and logarithmic sweeps for contrast threshold measurement, and the stimulus area was approximately 15° × 15° square for contrast threshold measurement and 6° × 6° square for VA measurement. To maintain fixation, a small fixation target was placed in the center of the stimulus. The size of the fixation target was 0.23– 0.69° for VA and 0.57–1.72° for contrast threshold. For children who were not attending the small fixation target, a small toy on a stick was held at the center of the screen and jiggled. The size of the toy was 0.69° for VA and 1.72° for contrast threshold. If fixation was lost during any of the sweep trials, the trial was stopped and discarded. A total of eight trials for children and ten trials for adults were recorded for each threshold measurement. For VA measurement, a linear sweep from 1 to 40 cpd was used, with the contrast of the gratings set at 90%. For contrast threshold measurement, a logarithmic sweep between 0.31 and 30% or 1.60 and 90% was used, with the spatial frequency of the grating being 1, 4, or 8 cpd.

5.3.2 Recording

Binocular sVEPs were recorded by PowerDiva software (version 1.9) developed by Norcia (Smith–Kettlewell Eye Research Institute, San Francisco). VEP responses were acquired with a Grass Telefactor Neurodata Acquisition (DAQ) system Model 12, with an amplification of 50 K for adults and 20 K for children. For recording the sVEP, seven electrodes (five active channel electrodes, one reference electrode, and one ground electrode) were connected to a Grass Bio-Potential Amplifier Model CP511, followed by the DAQ system. The artifact detector was set to 100 µV for adults and 200 µV for children. The DAQ rate used to capture the EEG signals was 601.08 Hz. A low pass filter of 100 Hz and a high pass filter of 0.1 Hz were used. Amplitude and phase of the VEP response were determined at the second harmonic (2F) frequency using the recursive least square (RLS) method (Tang and Norcia, 1995). Recording was executed in a darkened room. In experiment 1, electrodes were placed in two different ways (ISCEV vs PowerDiva placement, explained later). The PowerDiva electrode placement was used for the remainder of the experiments.

5.3.3 Experiment 1: Electrode placement and temporal frequency

Two electrode placements were compared in this experiment, and three temporal frequencies were used. The first electrode placement (ISCEV placement) was according to the international 10–20 system (Odom et al., 2010), and the other was that recommended by the PowerDiva software developer (personal communication, V. Vildavski). We refer to it as “PowerDiva placement”. In the ISCEV placement, the active electrodes were placed at PO7, O1, Oz, O2 and PO8. The distance between the inion and the nasion over the vertex was measured. Oz was placed above the inion at 10% of the measured distance. The reference electrode was placed 30% from the nasion. The ground electrode was placed 10% from the nasion, on the forehead. The distance from Oz to the nasion around the skull was measured (circumferentially). The other four active electrodes (PO7, O1, O2 and

PO8) were placed laterally on either side of Oz, separated from each other by 10% of the measured distance. The PowerDiva electrode placement, labeled as PO7, O1, Oz, O2 and PO8 by the PowerDiva software, are not the same as ISCEV PO7, O1, Oz, O2 and PO8. However, we have maintained the nomenclature for the purpose of comparison. The position of Oz (the central electrode) was 1.5 cm above the inion. The other four electrodes were placed laterally on either side of Oz, separated from each other by 2.5 cm. The reference electrode was placed 50% between the nasion and Oz. The ground electrode was placed on the forehead. Three temporal frequencies (6, 7.5, or 10 Hz) were used with each electrode placement. The spatial frequency for the contrast threshold measurement was 4 cpd.

5.3.4 Experiment 2: Sweep direction and the presence of a fixation target

The parameter to be varied (spatial frequency or contrast percentage) was swept from well below threshold to well above threshold and vice versa. For VA, the spatial frequency of the grating stimulus was swept from 1 to 40 cpd or from 40 to 1 cpd, with or without the presence of a fixation target. For contrast threshold measurement, the contrast percentage was swept from 0.31 to 30% or from 30 to 0.31%, with or without the presence of a fixation target. In some cases, where a viable plot was not obtained after six sweeps, a higher contrast range was used (1.60 to 90%). Contrast threshold was measured for spatial frequencies of 1 and 8 cpd.

5.3.5 Experiment 3: Stimulus area

The effect of stimulus area on VA and contrast thresholds was investigated in this experiment. A spatial frequency of 1 cpd was used for the contrast threshold measurement. The original size of the grating stimulus was 28 cm H X 26.5 cm V. Because the software does not allow the size of the stimulus to be manipulated, two white cardboard surrounds were used to mask the screen. The central area of the two cardboards measured 17.7 cm H × 16.7 cm V and 11.1 cm H × 10.5 cm V respectively. The cardboard masks were placed on the monitor screen when performing the test for smaller stimulus areas. Hence, the stimulus areas for the VA measurement at 250 cm from the screen were approximately 6, 4, and 2° squares. The stimulus areas for the contrast threshold measurement at 100 cm from the screen were approximately 15, 10, and 6° squares.

5.3.6 Experiment 4: Sweep duration

In this experiment, the effect of the sweep duration on the VA and contrast threshold was investigated. The sweep durations were 10.7, 14.7, or 20 seconds. Ten analysis bins were used in each of the three sweep durations. The spatial frequency for the contrast threshold measurement was 1 cpd.

5.3.7 Determination of the sVEP threshold:

Viable (acceptable) plots: Any of the five sVEP VA or contrast threshold plots, obtained from the five active electrodes, at the second harmonic was deemed to be viable if it met the following criteria:

1) Its peak signal to noise ratio (SNR) was ≥ 3.

2) The phase of the response was constant or lagging as the sweep moved from supra-threshold to threshold.

If the sVEP acuity or contrast plot met these criteria, threshold was determined by extrapolation of a regression line from the signal peak to zero microvolt amplitude against spatial frequency for VA measurement and against percentage contrast for contrast threshold measurement. The regression line was fitted between two vertical dashed lines. The first dashed line was placed at the peak of the amplitude response that was closest to the threshold and had an SNR ≥ 3 and the second dashed line was placed at the last data point with an SNR ≥ 1 (Figure 5-1). We have shown that fitting the regression line this way has better repeatability and validity, and gave more viable plots than other methods (Yadav et al., 2009). The PowerDiva software imposed an additional criterion, in which the extrapolated threshold should be close to the last data point included in the regression line fit (not more than 1 bin away from the second dashed line). Thresholds obtained from each acceptable plot of the active electrodes were log-transformed. The VA or contrast threshold for an individual participant was calculated as the arithmetic mean of all the log-transformed thresholds obtained from the acceptable plots of the five active electrodes, and the number of acceptable plots was also used as an outcome variable.

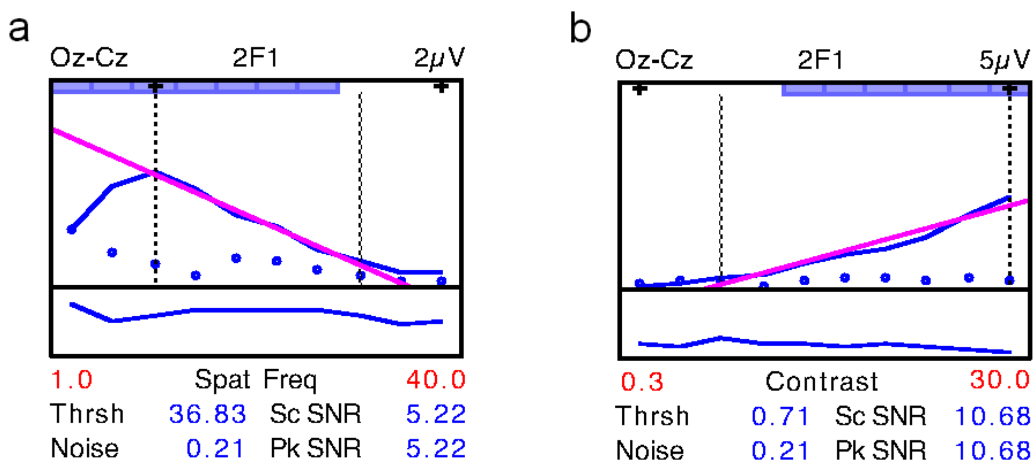

Figure 5-1: Example showing visual acuity (a) and contrast (b) sVEP plots from the Oz electrode. In the *top section* of each plot, amplitude is plotted against spatial frequency (a) or contrast percentage (b). In the *lower section*, phase is plotted against spatial frequency (a) or contrast percentage (b). The *solid line* is the response amplitude at the second harmonic, and the *straight line* is the regression line. *Thrsh* gives the threshold from the current regression line. *Sc SNR* is the peak signal to noise ratio within the range selected for regression line and *Pk SNR* is the peak SNR of all the data. The *dots* represent noise. See text for how the regression line was fitted.

5.3.8 Statistical analysis

A mixed ANOVA was used for each experiment, plus post-hoc analysis with LSD or t-tests. The analysis was undertaken with Statistica, Statistical Analysis Software (SAS) or Excel (t-tests). In experiment 1, for the threshold analysis, where there was some missing data, we assumed sphericity and performed the ANOVA according to Winer (Winer, 1971 and Winer 1971), which uses all the data in the analysis of variance.

For the number of readings, the repeated measures were done on the ranked data. Normal probability plots of the residuals of the number of readings data show straight lines, indicating that the assumption of the normality of the residuals is met.

5.4 Results

5.4.1 Experiment 1: Electrode placement and temporal frequency

Because all adults did not give viable VA measurements with the ISCEV placement at 10 Hz, a mixed ANOVA was performed only for 6Hz and 7.5 Hz (two age groups × two temporal frequencies × two electrode placements). This revealed a borderline effect of age group ($p = 0.054$), with no significant effects of electrode placement or temporal frequency, and no interactions ($p > 0.05$). Adults gave higher VA (in log cpd) than children (Figure 5-2a). For the contrast threshold data, since only one adult subject gave a contrast threshold measurement with the ISCEV and PowerDiva placements at 6 and 10 Hz respectively, we performed an ANOVA only for the children's data at all three temporal frequencies (three temporal frequencies × two electrode placements). This indicated that there were no main effects of electrode placements or temporal frequency, and no interactions ($p > 0.05$). A repeated measures ANOVA for the temporal frequency in which both adults and children gave contrast threshold data (i.e., 7.5 Hz) was also done (two age groups × two electrode placements). This revealed no significant effect of age group or electrode placement, and no interactions ($p > 0.05$) (Figure 5-2b).

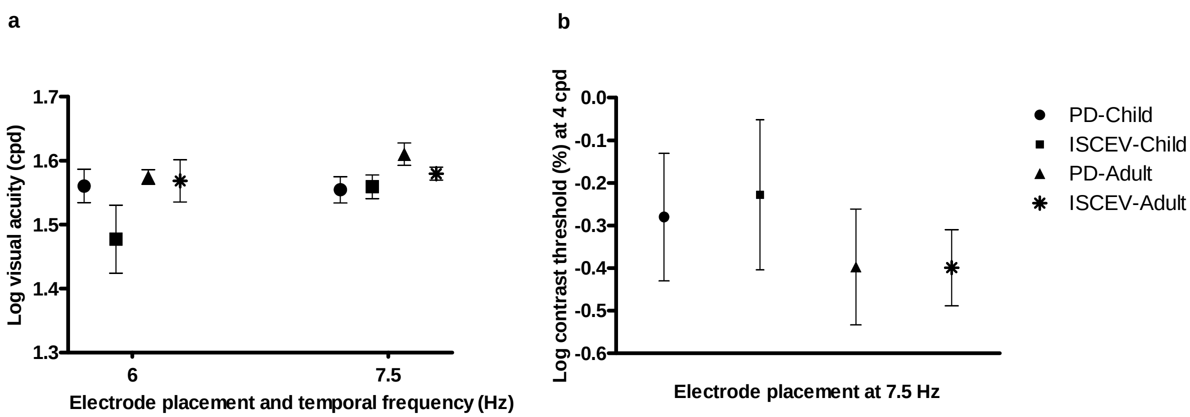

Figure 5-2: sVEP mean log visual acuity (a) at temporal frequencies of 6 and 7.5 Hz, and contrast thresholds for 4 cpd (b) at temporal frequency of 7.5 for six adults and seven children with PowerDiva (PD) and ISCEV electrode placements. Error bars represent SEMs.

With regard to the number of readings for VA (Figure 5-3a), there was no main effect of electrode placement ($p = 0.17$). There was a main effect of temporal frequency ($p < 0.0001$) and an interaction between age group and temporal frequency ($p = 0.0014$) for VA. Overall, both children and adults produced more viable readings at 7.5Hz compared to 6 or 10Hz. Since there was no main effect of electrode placement, we pooled the data for the two electrode placements in order to explore the interaction. This showed that there was no significant difference in the number of readings between children and adults at 6Hz (t-test, $p = 0.57$), but there were significant differences at 7.5 Hz ($p = 0.03$) and 10Hz ($p = 0.00002$). Adults gave more viable readings at 7.5 Hz than children, whereas children gave more viable readings than adults at 10 Hz. For contrast threshold at 4 cpd (Figure 5-3b), there was no main effect of electrode placement ($p = 0.38$), but there were main effects of age group ($p = 0.0082$) and temporal frequency ($p = 0.0001$) with no interactions. Children gave more viable readings than adults. Post hoc t-tests (LSD) showed that 7.5 Hz was significantly different from 6 and 10 Hz ($p < 0.05$), giving more viable readings overall.

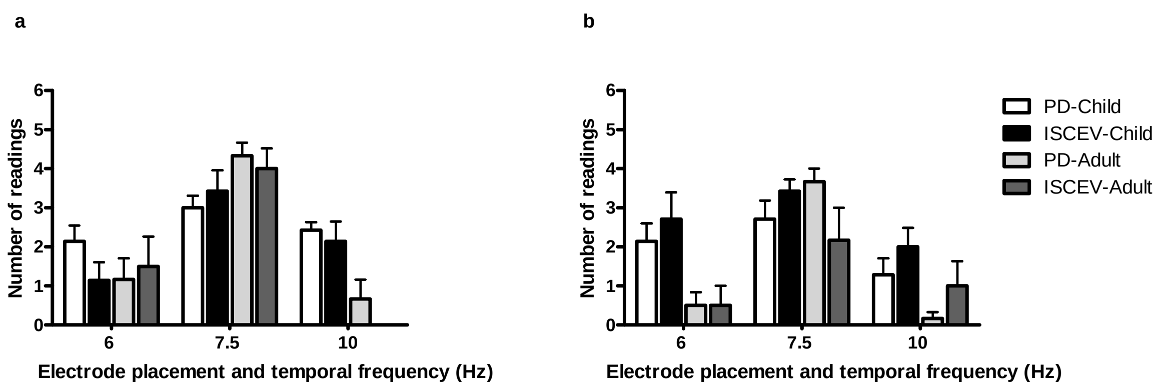

Figure 5-3: Mean number of readings for six adults and seven children with PowerDiva (PD) and ISCEV electrode placements and for three temporal frequencies. Error bars represent SEMs. Visual acuity (a) and contrast thresholds for 4 cpd gratings (b).

5.4.2 Experiment 2: Sweep direction and the presence of a fixation target

Figure 5-4a shows sVEP VA in children and adults against the presence (FT) or absence (WFT) of a fixation target and the direction of sweep. A mixed ANOVA showed a main effect of age group ($p = 0.033$), but no main effects of the presence of the fixation target or the sweep direction ($p > 0.05$) and no interactions of age group with the presence of fixation target or the sweep direction ($p > 0.05$). Adults produced superior VA compared to children. Figure 5-4b,c shows sVEP contrast thresholds at 1 or 8 cpd in children and adults against the presence (FT) or absence (WFT) of fixation target and the direction of the sweep. For contrast threshold at 1 and 8 cpd, mixed ANOVAs showed no main effects of fixation target, sweep direction, or age group ($p > 0.05$) and no interactions.

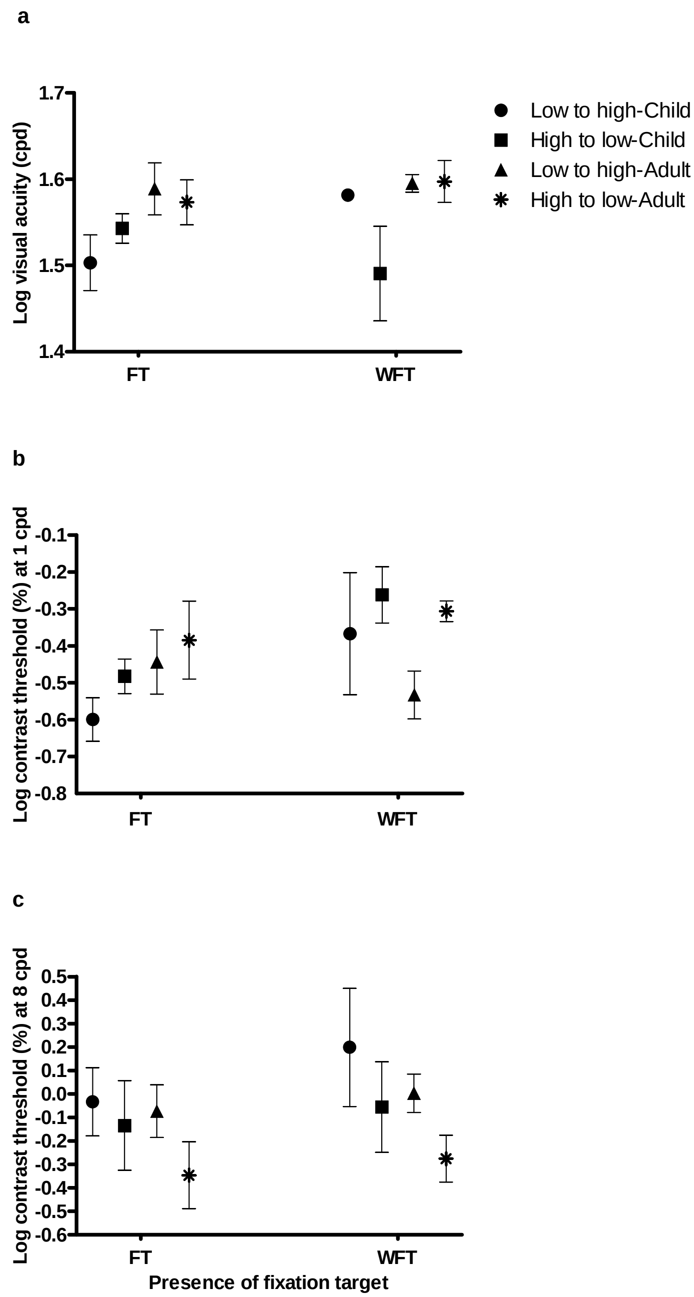

Figure 5-4: sVEP mean log visual acuity (a), contrast thresholds for 1 cpd (b), and contrast thresholds for 8 cpd (c) for six adults and six children determined when sweeping from low to high or from high to low in spatial frequency (for visual acuity) or in contrast (for contrast threshold). ***FT*** **= with fixation target.** ***WFT*** **= without fixation target. Error bars represent SEMs.**

With regard to the number of readings, there were no main effects of sweep direction, age group or the presence/absence of the fixation target for VA, or contrast thresholds at 1 or 8 cpd (Figure 5-5). However, there was an interaction between age group and fixation target ($p = 0.014$) for the number of readings for contrast threshold at 1 cpd. Since there was no main effect of sweep direction, we pooled the data for the two sweep directions, and performed a t-test to see if there was a significant difference in the number of readings between children and adults when the fixation target was present (FT) and when it was absent (WFT). This showed that there was no significant difference between children and adults when the fixation target was present (FT). However, children gave more viable readings than adults when the fixation target was absent (WFT) ($p = 0.02$). Adults gave more viable readings when the fixation target was present (FT) than when it was absent (WFT) (paired t-test, $p = 0.04$).

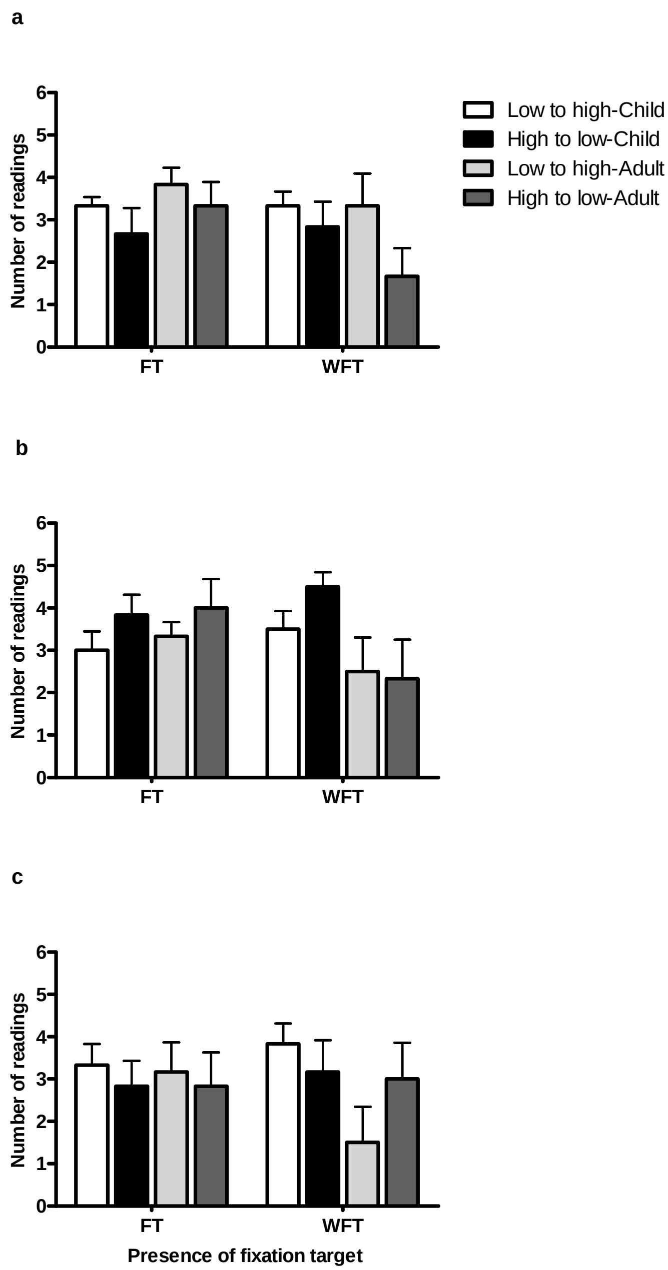

Figure 5-5: Mean number of readings for six adults and six children when sweeping from low to high or from high to low in spatial frequency (for visual acuity threshold) or in contrast percentage (for contrast threshold). Visual acuity (a), contrast thresholds for 1 cpd gratings (b), and contrast thresholds for 8 cpd gratings (c). *FT* = with fixation target. *WFT* = without fixation target. Error bars represent SEMs.

5.4.3 Experiment 3: Stimulus area

Figure 5-6a,b shows the VA and contrast threshold at 1 cpd in children and adults against the stimulus area. Mixed ANOVAs showed that there were no main effects of age group or stimulus area, and no interactions (all $p > 0.05$).

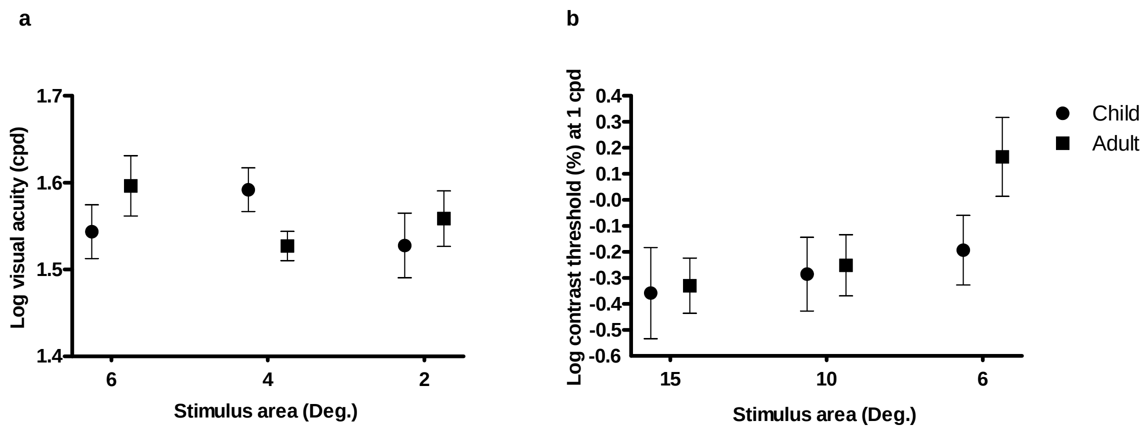

Figure 5-6: sVEP mean log visual acuity (a) and contrast thresholds for 1 cpd (b) for six adults and six children determined with three stimulus areas. Error bars represent SEMs.

Figure 5-7a,b shows the number of readings obtained from VA and contrast threshold measurement in children and adults against the stimulus area. There were main effects of stimulus area on the number of readings for VA ($p = 0.022$) and contrast threshold at 1 cpd ($p = 0.0001$). Post hoc t-tests (LSD) showed that the smallest stimulus area (2°) for VA measurement gave significantly fewer readings than the larger stimulus areas. As can be seen from Figure 5-7b, there was an interaction between age group and stimulus area for the number of readings of contrast threshold at 1 cpd ($p < 0.001$). There was little difference between the areas for children, but the adults gave fewer viable readings with the smallest stimulus area.

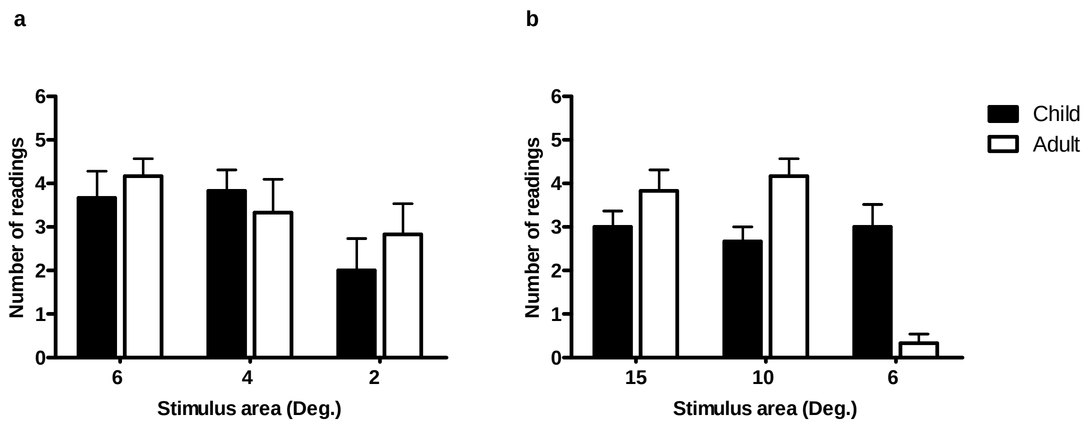

Figure 5-7: Mean number of readings for six adults and six children for the three stimulus areas. Error bars represent SEMs. Visual acuity (a) and contrast thresholds for 1 cpd gratings (b).

5.4.4 Experiment 4: Sweep duration

VA and contrast threshold at 1 cpd are plotted against the sweep duration in Figure 5-8a,b. There were no main effects of duration or age group on VA ($p = 0.72$ and 0.13 respectively) or contrast threshold ($p = 0.61$ and 0.52 respectively). There were also no main effects of duration on the number of readings obtained when measuring VA or contrast thresholds (Figure 5-9a,b, $p = 0.58$ and $p = 0.43$ respectively) and no effects of age group ($p = 0.29$ and $p = 0.14$ respectively). There was no interaction for any of the measures.

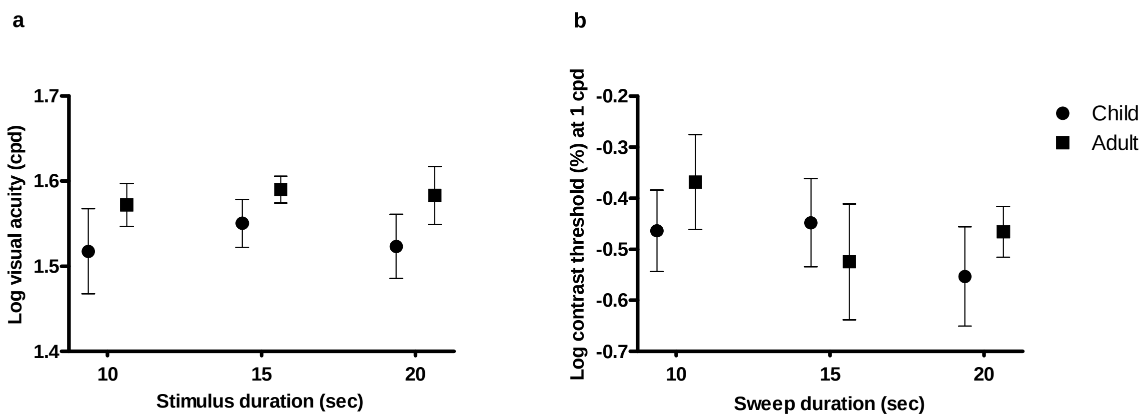

Figure 5-8: sVEP mean log visual acuity (a) and contrast thresholds for 1 cpd (b) for six adults and six children determined with three sweep durations. Error bars represent SEMs.

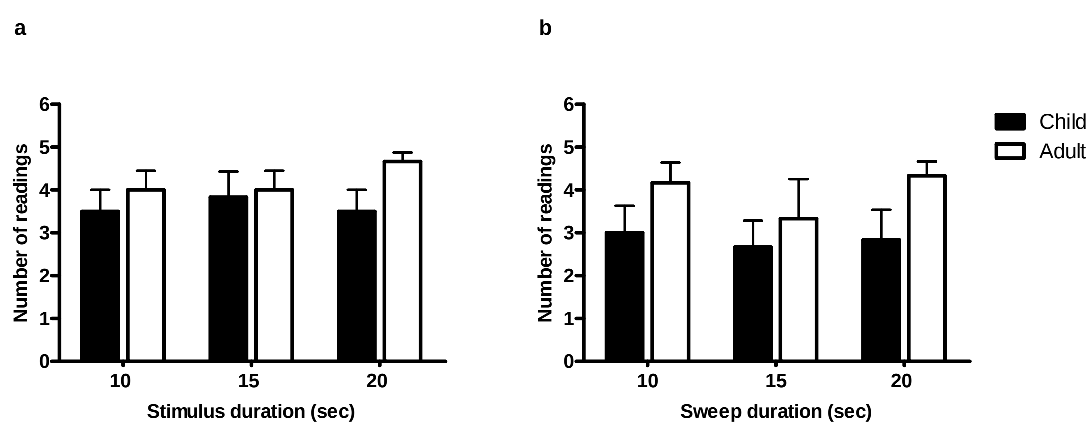

Figure 5-9: Mean number of readings for six adults and six children for three sweep durations. Error bars represent SEMs. Visual acuity (a) and contrast thresholds for 1 cpd gratings (b).

5.5 Discussion

Since the sVEP test for measuring VA or contrast thresholds has many parameters that may vary between one study and another, it is difficult to generalize the results of a particular study or compare the results from two studies if the manipulation of these parameters affects the outcome measure.

With regard to the electrode placement, our results for the contrast threshold agree with those of Allen et al. (1986) who did not find a significant difference between two bipolar electrode placements in five adults. In that study, the researchers placed the active electrode 3 cm above the inion in one placement and 3 cm lateral to the inion in another placement, and both were referenced to an electrode 1 cm above the inion with the ground electrode on the ear (see Figure 2; Allen et al., 1986). In this study, we used five active electrodes for each electrode placement. The major difference between the PowerDiva placement and the ISCEV placement is in the distance between the inion and the midline electrode (Oz). This distance is 1.5 cm with the PowerDiva placement, and on average about 3.2 cm in children and 3.5 cm in adults with ISCEV placement. The distance between the active electrodes in both placements is about 2.5-3.0 cm. It seems that the difference between the two electrode placements was not large enough to produce any effect on the contrast threshold. We also did not find a significant difference in VA between the two electrode placements. Furthermore, no significant effect of electrode placement on the number of viable readings for either VA or contrast thresholds was found. This insensitivity to the exact electrode positions probably reflects the fact that the VEP measures dipoles which exert their electrical field over a distance, and thus can be detected at a range of distances. In practical terms, therefore, these electrode placements can be considered interchangeable. The lack of sensitivity to electrode placement is reassuring, as it is likely that there is some variability in exact electrode placement between sessions, technicians and patients. For example, in some people the inion is less clearly defined than in others.

Our data agree with the previous studies using similar temporal frequencies, which show no effect of temporal frequency on sVEP thresholds in normal subjects. Norcia and Tyler (1985b) and Sokol et al. (1992) measured sVEP VA in infants using 6 or 10 Hz, and 5, 7, or 12 Hz respectively. Neither study found an effect of temporal frequency on VA. Allen et al. (1996) did not find an effect of temporal frequency (ranging from 2 to 20 Hz) on VA in infant and adult subjects, for either the central or peripheral field. Gottlob et al. (1990) found good correlation between acuities obtained under temporal frequencies of 4, 6, 7.5, or 12 Hz in patients with various ocular disorders, and in normal subjects between 3 weeks and 11 years of age. However, they found that children with good optotype acuity have better sVEP acuity when using lower temporal frequencies, while those with poor optotype acuity produced better sVEP acuity when using higher temporal frequencies. Nelson et al. (1984b) did find that VA was poorer when using gratings with temporal frequency of 21.5 Hz than with gratings reversing at 1.5 Hz. They found the opposite when measuring contrast sensitivity at 4 cpd (contrast threshold was better with 21.5 Hz). In contrast, Seiple et al. (1984) measured sVEP and psychophysical contrast thresholds in adults at three temporal frequencies (1.5, 3.5, and 21.5 Hz), and concluded that the thresholds were better when using 1.5 Hz. We cannot compare our results with the results of Nelson et al. (1984b) or Seiple et al. (1984), since we used temporal frequencies that were between 6 and 10 Hz. The current study is the only one that has considered the number of viable readings. None of our adult subjects gave a criterion response for visual acuity measurement at 10 Hz, and we found that 7.5 Hz tends to yield more viable readings than 6 or 10 Hz for both VA and contrast threshold measurements. Hence, we carried out the subsequent experiments (experiment 2, 3 and 4) with a temporal frequency of 7.5 Hz.

Our results for the effect of sweep direction on sVEP VA do not agree with those of Nelson et al. (1984a), who found poorer acuities when sweeping from low to high spatial frequency compared to sweeping in the other direction. This study used sweep duration of 20 seconds while ours was 10 seconds, which might explain why we did not find an adaptation effect in our study. Also, our results for the effects of sweep direction on sVEP contrast threshold do not agree with those of Nelson et al. (1984a), Brigell et al. (1987), and Seiple et al. (1988), in which an increase of the threshold was found when sweeping from high contrast to low contrast. All the researchers agreed that the increase is due to adaptation to the high contrast at the beginning of the sweep. Again, they used a 20-second sweep, while ours was 10 seconds. Although we did use 20 seconds sweep time when investigating the effect of sweep duration (see experiment 4), the contrast was only swept from low to high in that experiment, and no adaptation effects would be expected. We also did not find a significant effect of sweep direction overall on the number of viable readings for VA or contrast thresholds.

We did not find a main effect of the presence of a fixation target on either VA or contrast thresholds, or on the number of readings for VA or contrast thresholds. This could be as a result of monitoring the fixation of children and excluding any trial where fixation was lost, and the fact that adults maintain their fixation at the center of the stimulus regardless of the presence of a fixation target. However, adults gave more viable readings with the fixation target than without it for one stimulus condition (CS for 1 cpd).

Tyler et al. (1979) used different stimulus areas (15, 12, 10, 8, 6, 4, and 2˚) to measure sVEP VA in adults. Their findings agree with ours, in which there was no effect of stimulus area on the sVEP threshold, in children or in adults. Tyler and his colleagues did find that the amplitude at the lower spatial frequencies increased as the stimulus area was increased, but this change in amplitude did not affect the threshold, since the extrapolation to 0 μV involves the high spatial frequency. We have not looked at the amplitude as an outcome measure in our study. Our study is the first to investigate the effect of stimulus area on the sVEP contrast threshold, and it showed that the stimulus area does not affect the contrast threshold when measured for a 1 cpd gratings. Although the stimulus area did not affect the threshold, it did have an effect on the number of viable readings for both VA and contrast thresholds. Fewer readings were obtained for VA when the smallest area (2°) was used, and for contrast threshold in adults with the smallest area of 6°. This could be a result of stimulating fewer neurons in the peripheral visual field (Spinelli et al., 1983), which might be responsible for detecting this relatively low spatial frequency. We suggest that a larger stimulus area gives a larger or more widespread cortical response, resulting in more electrodes giving a peak amplitude reading that reached our criterion, but that this did not affect the mean threshold, since according to Tyler et al. (1979) a lower amplitude still gives rise to the same cut-off threshold when the extrapolation is performed.

Ridder et al. (1998) used three ranges of spatial frequency sweeps (low, medium, and high) with six spatial frequencies in each range. They swept each spatial frequency for duration of 8 seconds (a total of 48 seconds for each sweep). When they calculated the sVEP acuity for each second for each range of spatial frequency, they did not find a significant difference in sVEP acuity across the different seconds, indicating that the sweep duration did not affect the estimated acuity. In this study, we used the same range of spatial frequencies (1–40 cpd), with spatial frequencies at all the ten analysis bins being 1, 5.33, 9.67, 14, 18.33, 22.67, 27, 31.33, 35.67, and 40 cpd for all the sweep durations used. Thus, each spatial frequency was presented for 1, 1.5 or 2 seconds for the sweep durations of 10, 15, or 20 seconds, respectively. For both VA and contrast threshold, sweep durations between 10–20 seconds did not have an effect on the extrapolated threshold or the number of viable readings for the active electrodes. Furthermore, we did not allow our subjects to adapt to the stimulus before the beginning of trials by asking them to close their eyes between trials. Thus, no adaptation effect would be expected.

In summary, we considered the effect of various parameters on visual acuity and contrast thresholds, as well as a new outcome measure, the number of viable readings from five active electrodes. This study showed that electrode placement, temporal frequency, sweep direction, the presence of a fixation target, stimulus area, and sweep duration did not affect the sVEP thresholds for either VA or contrast. However, some of these parameters do affect the number of viable readings when using more than one active electrode. More viable readings were obtained with a temporal frequency of 7.5 Hz for both VA and contrast thresholds, and with a stimulus area of 4° or larger for VA and 10° or larger for contrast thresholds. Since more viable readings presumably results in more confidence in the measurement of VA or contrast threshold, we would recommend using those parameters which give more viable readings in future studies. Finally, it should be mentioned that these results were obtained with individuals with VA of 6/7.5 or better, and may not necessarily apply to individuals with poorer VA.

Chapter 6

Development of visual acuity and contrast sensitivity in children: comparison of sweep VEP and psychophysics

6.1 Introduction

It is known that different visual functions mature at different ages (Lewis & Maurer, 2005). While the development of visual acuity (VA) and contrast sensitivity (CS) has been extensively studied in infants, there are fewer studies that have followed the development of VA (Mayer & Dobson, 1982; Birch et al., 1983; Ellemberg et al., 1999) and CS (Arundale, 1978; Derefeldt et al., 1979; Beazley et al., 1980; Bradley & Freeman, 1982; Ellemberg et al., 1999; Adams and Courage, 2002) until they become adult-like. Additionally, the studies that do exist do not agree on the timescale for the maturation of these functions. These studies used traditional psychophysical measures of VA or CS in children which can be affected by non-visual factors such as attention or response criterion (Ellemberg et al., 1999; Bradley & Freeman, 1982; Abramov et al., 1984). The influence of the response criterion makes it difficult to conclude whether any improvement in the measured VA or CS with age is a result of developmental or criterion change. To overcome the problem of response criterion, one ideally would either use an objective technique such as visually evoked potential (VEP), a psychophysical technique that is criterion-free such as alternative forced choice (Kelly & Savoie, 1973), or a signal detection theory (SDT) paradigm which produces a detectability measure that is independent from criterion (Macmillan & Creelman, 2005).

The VEP studies of the development of VA (Norcia & Tyler, 1985a; Norcia et al., 1990 and Sokol et al., 1992) and CS (Norcia et al., 1988; Norcia et al., 1990; Norcia & Tyler, 1986 and Oliveira et al.,

2004) compared infants with adults to describe the rapid developmental phase of these functions at the beginning of life without an attempt to track this development until it reaches adult levels. Regarding subjective methods, a few studies have used the criterion-free forced-choice method to study the development of VA or CS. Stiers et al. (2003) used a two alternative forced-choice (2AFC) procedure to measure grating acuity and a 4 alternative forced-choice procedure (4AFC) to measure Landolt C optotype acuity. Their results indicated that both grating acuity and optotype acuity were not adult-like at the age of 6 years. Other studies used behavioral methods such as the operant preferential looking (OPL) technique and found adult-like acuity by the age of 3-5 years (Mayer & Dobson, 1982) or 5 years (Birch et al., 1983). Although the OPL is a modification of the forced-choice preferential looking (FPL) which rewards the child's correct responses, Mayer and Dobson (1982) did not rule out the possibility of the effect of the response criterion on their results. They pointed out that this effect can be investigated using a SDT procedure. Ellemberg et al. (1999) found adult-like grating VA by the age of 6 years. However, they used the method of limits with a yes-no response and thresholds measured with this method are usually affected by the participant's criterion. It should be noted that grating acuity and optotype acuity are thought to follow different developmental courses. Grating acuity may reach adult levels earlier than optotype acuity (Lewis & Maurer, 2005).

Many of the studies that have followed the development of CS until it becomes adult-like have used psychophysical methods that are subject to criterion differences between children and adults. For example, Arundale (1978), Derefeldt et al. (1979) and Benedeck et al. (2003) all used the method of adjustment, while Beazley et al. (1980) used a yes-no staircase technique. We are aware of only one study that had used a SDT paradigm to investigate visual development in children (Mayer, 1977). In that study, Mayer investigated the development of anisotropy in children by measuring CS for horizontal and vertical gratings and compared it to CS for diagonal gratings. Her results indicated that children at the age of 5 years did not show anisotropy (i.e. there was no difference between CS for horizontal or vertical grating and diagonal gratings). However, children at the age of 11 years showed anisotropy as a result of the increase in CS to horizontal and vertical gratings, but not oblique gratings, from 5 years to 11 years.

The purpose of this study was to determine whether VA and CS are adult-like by 6-8 or by 9-12 years and to compare objective and subjective methods. The objective method was the sweep visual evoked potential (sVEP), and the subjective methods included a 2AFC and a SDT procedure. The 2AFC and SDT procedures were used so that differences in criterion, if any, between children and adults would not confound threshold measurements.

6.2 Methods

6.2.1 Participants

There were three age groups (16 participants/group) in this study: 6-8 year olds (mean age = 7.5 years, SD ± 0.80), 9-12 year olds (mean age = 10.7 years, SD ± 0.95) and adults (21-33 year olds; mean age = 28.1, SD ± 3.52). Adults were defined as individuals aged 18 years or older. Each group had 8 males and 8 females. Exclusion criteria were a history of ocular disease or amblyopia, presence of strabismus, heterophoria more than 6^{Δ}, spherical refractive error of more than -2.00 or +1.00 D, astigmatism of more than 1.5 D, or anisometropia of more than 1 D. Participants wore their best spectacle correction for all testing. Most of the child participants were recruited from the Optometry Clinic at the School of Optometry, University of Waterloo. The files of potential child participants were screened and children who show attention problems or learning disabilities (as indicated by the clinician) were not included in the study. Adult participants were students at the University of Waterloo. Most of the children were tested after the school time (3-5 pm), while adults were examined at different times of the day. Three children did not complete testing (two withdrew from the study before doing their last session and one did not understand the psychophysical procedure).

6.2.2 Sweep VEP procedure

The experimental set up for the sVEP procedure and the criteria for fitting the regression line were described in Almoqbel et al. (2011) (Chapter 5). The ISCEV electrode placement (Almoqbel et al., 2011) was used in this experiment along with stimulus parameters shown in Table 6-1.

Table 6-1: Stimulus parameters for the sVEP procedure

Parameter	Contrast threshold	Visual acuity
Distance	100 cm	250 cm
Luminance	50 cd/ m^2	50 cd/ m^2
Fixation target	Present	Present
Stimulus area	17.7 H X 16.7 V (10^o)	17.7 H X 16.7 V (4^o)
Contrast	Swept	90%
Spatial frequency	1 or 8 cpd	Swept
Temporal frequency	7.5 Hz	7.5 Hz
Range of sweep	0.33 to 30% or 1.77-90%	1 to 40 cpd
Direction of sweep	Low to high contrast	Low to high spatial frequency
Duration of sweep	10 sec	10 sec
Number of steps	10	10

6.2.3 Psychophysical procedure

6.2.3.1 Visual acuity

VA was measured in two ways, logMAR (the logarithm of the minimum angle of resolution) letter VA and grating VA. LogMAR VA (crowded and uncrowded) with the Bailey-Lovie chart was measured using by-letter scoring (Hazel and Elliott, 2002). The test distance was 3 meters and the chart had a luminance of 104 cd/ m^2. Participants were forced to guess until they got to the last line on the chart which had logMAR acuity of -0.2 at the 3 meter testing distance. Uncrowded VA was measured by covering all surrounding letters with a white paper mask and showing only one letter at a time.

Grating VA was measured with the PowerDiva psychophysical software (Norcia, PowerDiva Manual) using a temporal two alternative forced-choice (2AFC) staircase procedure. Table 6-2 shows the parameters used for grating VA measurement. The stimuli, which were chosen to be equivalent to the sVEP stimuli, were horizontal sine-wave gratings. In each trial, a test stimulus (grating) was randomly presented in one interval and a null stimulus was presented in the other. The null stimulus was a luminance matched blank screen. After each trial, the participant had to verbally indicate which interval contained the test stimulus. The software changed spatial frequency depending on the participant's response after each trial. The range of spatial frequency was 25-60 cpd. The staircase was a 2 down, one up staircase such that the stimulus intensity went down to a less visible stimulus (i.e. higher spatial frequency) after the participant made two consecutive correct responses, and the stimulus decreased in spatial frequency after the participant made one incorrect response. This resulted in a 77% correct threshold (Norcia, PowerDiva Manual). The step size was 1/10th of the total range selected. The staircase used the last ten measurements to calculate the threshold and stopped when the standard error of these was less than two step sizes and when the slope was close to zero.

Table 6-2: Stimulus parameters for grating visual acuity measurement

Distance	400 cm
Luminance	50 cd/ m^2
Fixation target	Present
Stimulus area	28 H X 26.5 V (4^o)
Contrast	90%
Spatial frequency	25-60 cpd
Temporal frequency	7.5 Hz

6.2.3.2 Contrast sensitivity

For each participant, the contrast threshold was measured with the Morphonome™ Image Psychophysics software (Tyler & McBride, 1997) using two procedures: a temporal 2AFC staircase procedure and a yes-no signal detection theory procedure. The parameters of the stimulus were chosen to match as closely as possible those of the sVEP procedure. The stimulus was a horizontal sine-wave grating with temporal frequency of 6.3 Hz and spatial frequency of either 1 cpd or 8 cpd. Michelson contrast was used and the luminance of the screen was 50 cd/m^2. The participant responded verbally and the experimenter entered the participant's response into the computer. Participants were given breaks between blocks of trials. Children were allowed to watch a cartoon movie during the breaks, if they preferred to.

Two-alternative forced choice procedure:

For each spatial frequency (1 or 8 cpd) an initial temporal 2AFC staircase, starting with contrast that was expected to be well above threshold (2% for 1 cpd and 7% for 8 cpd), was initially run to determine the appropriate starting contrast level for the 2AFC staircase that would be used to find the threshold. The duration of the stimulus was 957 ms and the inter-trial interval was 533 ms. The step size was 0.15 log unit. A beep accompanied each stimulus interval. A feedback sound was used to indicate when the participant made the first error in responding to a trial. When the participant made the first error the staircase was terminated. The contrast level that was 5 step sizes above the level of this first error was used as the starting contrast for the 2AFC staircase that determined the threshold. This 2AFC staircase had a step size of 0.15 log units and a maximum number of 30 trials, with no feedback. The minimum number of trials was 14. For every correct response, the staircase decreased the contrast by one step and for every incorrect response, the contrast increased by three steps. There were two stopping rules: a) the number of trials reached 30, or b) the slope of the regression line of the last 14 trials was less than 1/14 and the standard deviation was less than 1 staircase step. The threshold was calculated as the moving average of the last 14 trials. Two 2AFC staircases were run and the average of these thresholds was taken as the final threshold.

Signal detection theory procedure:

A yes-no procedure which incorporated catch trials (noise) along with stimulus trials (signal) was used. In any given block of trials, three levels of contrast were presented in the stimulus trials with each contrast level presented 20 times. The contrast threshold obtained by the 2AFC procedure was chosen as the middle contrast level in the SDT. The step size was 0.11-0.16 log units and determined the separation between the middle contrast level (i.e. second contrast level) and the first (lower) and the third (higher) contrast levels. The step size was determined by a pilot study so that the lower and higher contrast levels yield d' values that span a range below and above d' of 1. The percentage of catch trials was 30% of the total of stimulus trials. The presentation of stimulus/catch trials was randomized by the software. The participant was required to say “yes” when s/he saw the grating and “no” when s/he did not. For each stimulus presentation there were four possible outcomes: hit, miss, false alarm, or correct rejection. For each contrast level the software gives the number of signal trials in which the participant reported seeing the stimulus (hits) and those in which the participant reported not seeing the stimulus (miss). Also for the catch trials the software gives the number of catch trials in which the participant reported not seeing the stimulus (correct rejection) and those in which the participant reported seeing the stimulus (false alarm). After the participant finished each block of trials, the hit rate (H) for each contrast level and the false alarm rate (F) were calculated as follows:

H = number of stimulus trials seen/ number of stimulus trials presented

F = number of catch trials seen/ number of catch trials presented

The detectability (d') was then calculated for each contrast level as follows:

$d' = z(H) - z(F)$ (Macmillan & Creelman, 2005)

where, z is the z score

The d' values should span a range below and above d' of 1. If they did not, a larger step size was used. The three d' values were then plotted against contrast and linear regression was used to interpolate the contrast that corresponded to a d' of 1. This contrast was taken as the contrast threshold determined by the SDT procedure and is a common definition of threshold (Klein, 2001).

The criterion (c) was calculated for each contrast level as follows:

$c = -0.5\,(z(H) + z(F))$ (Macmillan & Creelman, 2005)

The criterion values were plotted against d' and linear regression again was used to determine the criterion that corresponds to a d' of 1 and this was taken as the participant's criterion at threshold. A positive value of c indicates a tendency to say "no", whereas a negative value indicates a tendency to say "yes" (Macmillan & Creelman, 2005).

It should be noted that, in all the psychophysical tests, trials in which the child shows sign of reduced attention (e.g. by looking away from the screen) were repeated and the child was asked to keep looking at the screen.

6.2.4 Statistical analysis

One-way ANOVA was used to compare the means of all age groups for the crowded and uncrowded logMAR VA followed by Tukey's multiple comparison post hoc test. A mixed ANOVA was used for the grating VA (3 age groups X 2 procedures), contrast thresholds at 1 cpd (3 age groups X 3 procedures) and contrast thresholds at 8 cpd (3 age groups X 3 procedures) followed by Fisher's LSD post-hoc test. One-way ANOVA was used to compare the means of all age groups for each procedure separately for grating VA, contrast thresholds at 1 cpd and contrast thresholds at 8 cpd followed by Tukey's multiple comparison post hoc test. A separate analysis for each procedure was performed because the higher variability of the sVEP data could have masked age differences in the other procedures. One-way ANOVA was also used to compare the means of all age groups for the criterion (*c*) followed by Tukey's multiple comparison post hoc test. One-way ANOVAs were performed with the GraphPad Prism software (GraphPad Software Inc., San Diego, CA) and Mixed ANOVAs were performed with Statistica (StatSoft Inc., Tulsa, OK).

6.3 Results

6.3.1 Visual acuity

Figure 6-1 shows crowded and uncrowded logMAR VA for all age groups. One-way ANOVA for the logMAR VA revealed a significant effect of age on crowded ($p = 0.0001$) and uncrowded ($p < 0.0001$) VA. Tukey's multiple comparison test showed that the 6-8 year olds gave poorer VA than the

9-12 or adults for both crowded and uncrowded VA but there was no significant difference between the 9-12 year olds and the adults.

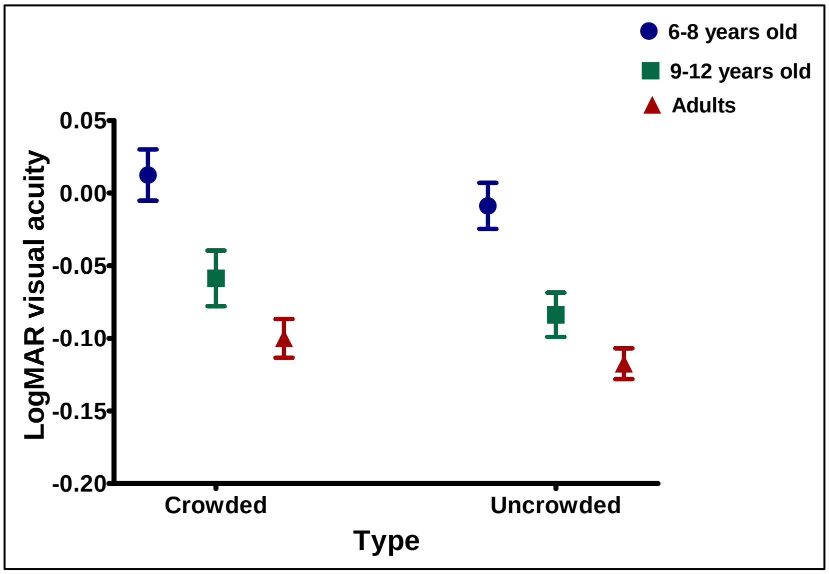

Figure 6-1: logMAR visual acuity. Error bars are SEM.

Figure 6-2 shows the grating VA (sVEP and the staircase) for all age groups. Mixed ANOVA revealed a significant effect of age ($p = 0.002$). Fisher's LSD test showed that the 6-8 year olds had poorer VA than the 9-12 year olds or adults, but no other differences were significant. There was also a significant effect of procedure ($p = 0.003$) for grating VA. The sVEP gave poorer VA than the staircase. There was no interaction between age and procedure ($p = 0.34$).

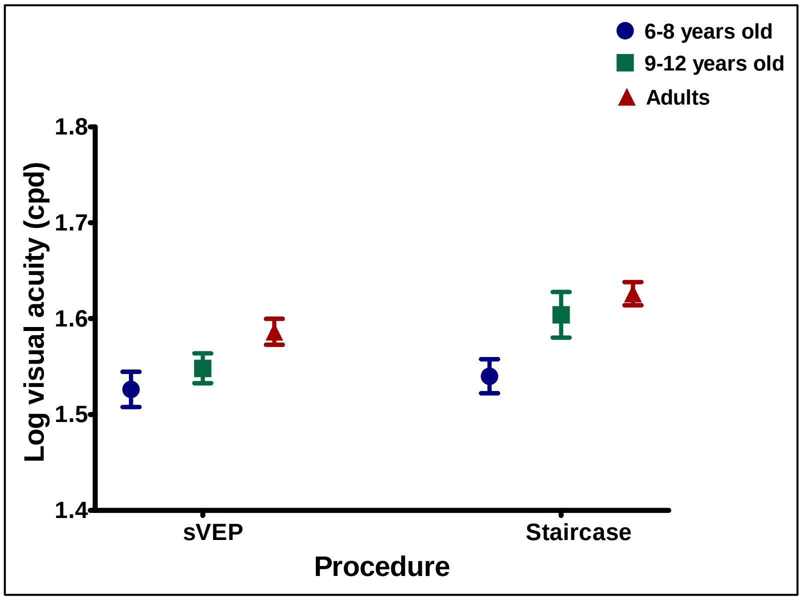

Figure 6-2: Log grating visual acuity. Error bars are SEM.

When considering each procedure separately, one-way ANOVA showed that there was a significant effect of age on the sVEP VA ($p = 0.03$) and the staircase VA ($p = 0.006$). Tukey's multiple comparison test showed that the 6-8 year olds had poorer VA than adults with the sVEP and than both adults and the 9-12 year olds with the staircase procedure, but there were no other significant differences.

The presence of a significant difference between the 6-8 year olds and both the 9-12 year olds and adults in the grating VA measured with the staircase procedure made it possible to plot the individual grating VAs for all the participants against their ages and find when the grating VA becomes adult-like (Figure 6-3) (this was not possible when the difference was only found between the 6-8 year olds and adults, because of the age gap between the 9-12 year olds and adults). Iterative linear regression to find the point when there was a significant difference between the regression line of the 6-8 year olds and the 9-12 year olds children's staircase VA indicates that the grating VA becomes adult-like between the age of 9 and 10 years.

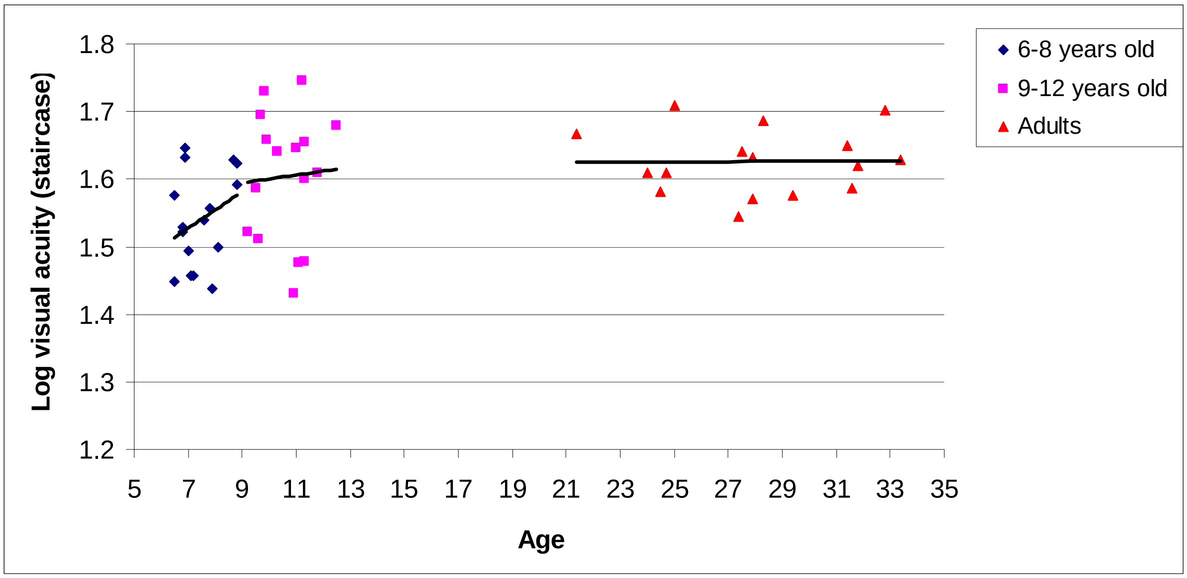

Figure 6-3: Log grating acuity obtained with the staircase procedure for each participant plotted against age.

6.3.2 Contrast sensitivity

6.3.2.1 Contrast threshold at 1 cpd

Figure 6-4 shows sVEP, staircase, and SDT log contrast thresholds at 1 cpd for all age groups. Mixed ANOVA revealed that there was a significant effect of procedure ($p < 0.0001$). Fisher's LSD test showed that the sVEP gave the poorest (i.e. highest) contrast thresholds followed by the staircase and the SDT procedure (all $p < 0.05$). Overall there was no significant effect of age ($p = 0.14$).

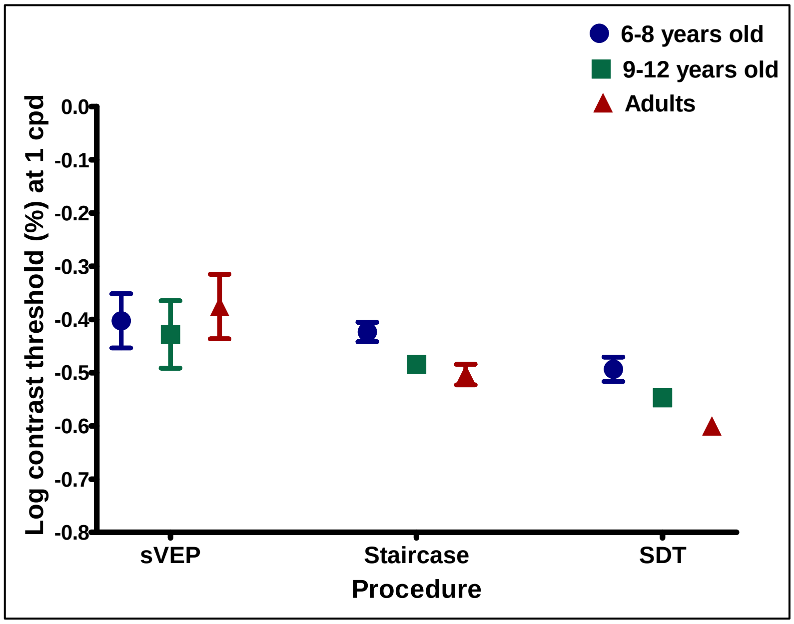

Figure 6-4: Log contrast threshold at 1 cpd. Error bars are SEM.

When considering each procedure separately, one-way ANOVA revealed a significant effect of age for the staircase ($p = 0.008$) and SDT ($p = 0.0003$). Tukey's multiple comparison test showed that the 6-8 year olds gave poorer contrast thresholds than adults with each procedure, but there were no other significant differences. There was no significant effect of age for the sVEP ($p = 0.82$).

6.3.2.2 Contrast threshold at 8 cpd

Figure 6-5 shows sVEP, staircase, and SDT log contrast thresholds at 8 cpd for all age groups. Overall, mixed ANOVA showed that there was no significant effect of age or procedure ($p = 0.16$ and 0.34, respectively).

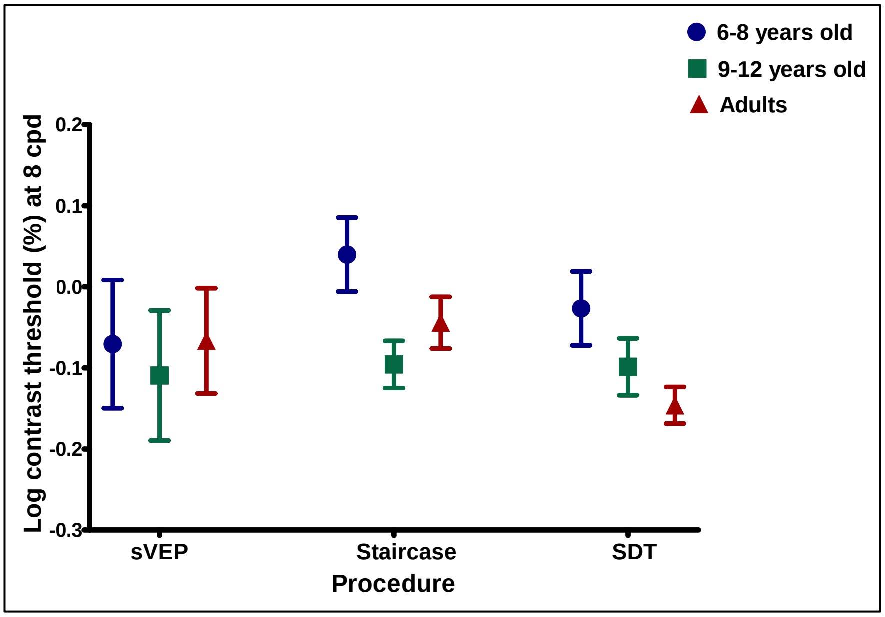

Figure 6-5: Log contrast threshold at 8 cpd. Error bars are SEM.

When each procedure was considered separately, one-way ANOVA showed that there was a significant effect of age for the staircase (p = 0.036). Tukey's multiple comparison test showed that the 6-8 year olds gave poorer contrast thresholds than the 9-12 year olds, but there were no other significant differences. There were no significant effects of age for the sVEP or the SDT (p = 0.91 and 0.07, respectively).

6.3.2.3 Criterion

Figure 6-6 shows the criterion (*c*) adopted by each age group when measuring contrast thresholds at 1 cpd. One-way ANOVA revealed that there was a significant effect of age on the criterion (p = 0.009). Tukey's multiple comparison test showed that the adults were more likely to say "no" in the yes-no SDT procedure than both child groups, but there was no difference between the two groups of children.

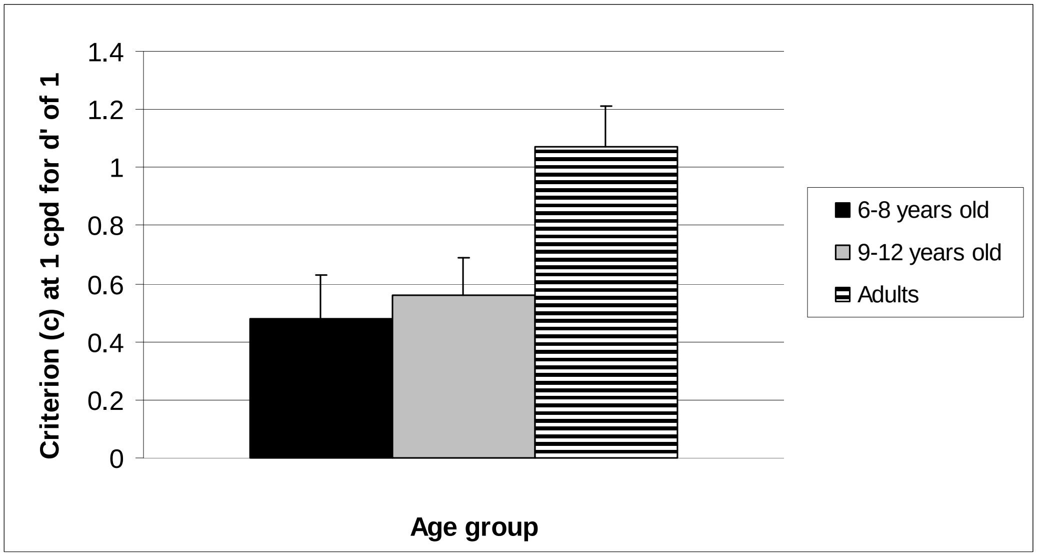

Figure 6-6: Criterion (c) at *d'* of 1 for contrast threshold at 1 cpd. Error bars are SEM.

Figure 6-7 shows the criterion (*c*) adopted by each age group when measuring contrast thresholds at 8 cpd. One-way ANOVA revealed that there was a significant effect of age on the criterion ($p = 0.01$). Tukey's multiple comparison test showed that the adults were more likely to say "no" in the yes-no SDT procedure than the 9-12 year olds, but there were no other significant differences.

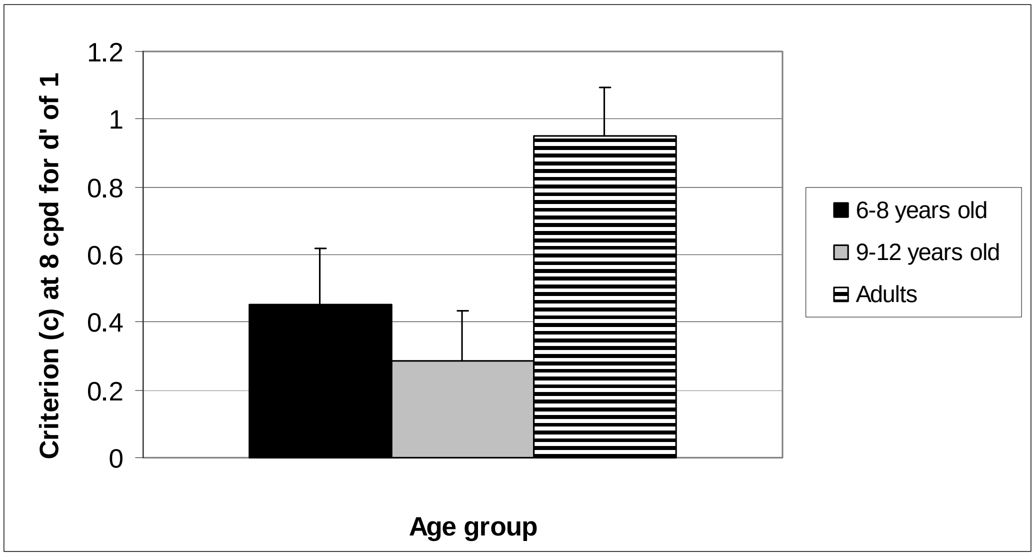

Figure 6-7: Criterion (c) at *d'* of 1 for contrast threshold at 8 cpd. Error bars are SEM.

6.4 Discussion

6.4.1 Visual acuity

According to Simons, crowded optotype tests show the maturation of VA with age better than uncrowded optotype tests in children who are able to be tested with optotypes (Simons, 1983). Our results showed a significant increase of crowded logMAR VA from 0.012 at the age 6-8 years to -0.1 in adults. The uncrowded logMAR VA also showed the same trend; VA increased from -0.01 at the age of 6-8 years to -0.12 in adults. A few studies have investigated the development of letter VA in children until it becomes adult-like. Our results for uncrowded (single-letter) do not agree with those of Jeon et al. (2010) who found that single-letter acuity is adult-like at the age of 8 years. They used a 2AFC procedure to measure single-letter acuity for the letter E, and required that their participants have VA of at least 20/25 (for the 5 year-olds) or 20/20 (for the 8 year olds, 11 year olds, and adults) as an inclusion criterion. Using the outcome variable (VA) as an inclusion criterion may influence the results: a lot of children with normal vision may be excluded, and as a result the difference between the adults and children will be underestimated. In our study, we measured single-letter acuity with the Bailey-Lovie logMAR chart using by-letter scoring and did not use VA as an inclusion criterion. These differences between our study and Jeon et al.'s (2010) could explain the differences in the results. Drover et al. (2008) used crowded optotypes and concluded that there was a difference between 7 year olds and 8-10 year olds. Although they had adult participants in their study, Drover et al. (2008) did not comment on whether the 8-10 year olds had adult-like VA. Stiers et al. (2003) used a 4AFC procedure to measure the development of VA using uncrowded Landolt C's in children between 2.5 - 6 years of age and compared the results to adults. Although they did not include older children as in the current study, our results agree with their results in that adult-like VA is not yet found in the 6 year olds. Using by-letter scoring, Dobson et al. (2009) provided normative monocular VA for Early Treatment Diabetic Retinopathy Study charts (EDTRS) in emmetropic children between the age of 5 and 12. Although they did not include adult participants, the investigators concluded that their older child group (12-<13 years) were at least 1 line worse than adults' VA in other studies. We cannot compare our data to Dobson et al.'s since they did not make a direct comparison between children and adults. It may be concluded, therefore, that optotype VA is not adult-like by 6-8 years.

Stiers et al. (2003) concluded that grating VA is still not adult-like at the end of the 5th year. They used a 2AFC procedure (the same procedure that we used in this study) and found that the VA at the age of 5 years 9 months was 36 c/d and that of the adults was 50.41 c/d. Although they did not include children older than 6 years of age, our results agree with their findings in that grating VA is not adult-like by the age of 6 years. Our 6-8 year olds had VA of 35.01 c/d which is almost the same as the VA of their 5 years 9 months old (36 c/d). Mayer and Dobson (1982) found somewhat different results using OPL with 2AFC for children and OPL with two psychophysical procedures (yes-no and 2AFC) for adults. They found adult-like grating acuity in children between the ages of 3-4 years. They found adult-like VA by the age of 3 years when comparing the children OPL thresholds with the adults' yes-no thresholds, and adult-like VA by the age of 4 when comparing the children OPL thresholds with the adults' 2AFC thresholds. In the current study, we used the same procedure (2AFC) to measure grating VA in children and adults, and our findings indicate that grating VA becomes adult-like between 9-10 years. Birch et al. (1983) also used OPL to measure VA in children and adults and found adult-like acuity at the age of 5 years (VA was 30 c/d in the 5 year olds compared to 31.6 c/d in adults). A possible reason for the adult-like VA at the age of 5 in Birch et al.'s (1983) study is the presence of a ceiling effect. They used gratings with eight spatial frequencies and the two highest spatial frequencies were 24 and 36 c/d. This may have lowered their adults' group mean VA if some of their adult participants had a VA better than 36 c/d. In our study, the range of spatial frequency that we used in the 2AFC staircase was from 25-60 c/d. Birch and Hale (1988) studied the development of monocular and binocular grating acuity, from birth to 5 years old, with an OPL procedure and found the binocular acuity of the 4-5 year old to be 32 c/d (close to that of Birch et al. (1983)). This value is slightly lower than in our younger age group (35.1 c/d in the 6-8 year old). When the grating VA of the 4-5 year olds in Birch and Hale's (1988) study and the grating VA for the 6-8 year olds obtained with the 2AFC staircase in our study are considered together, there is evidence of the developmental process in grating VA. Heersema and van Hof-van Duin (1990) found that, at the age of 4 years, grating VA as measured by the acuity card procedure is still not adult-like. Their adult participants had a binocular acuity of 0.65 min arc (46.2 c/d), which is close to the adult's acuity in this study (42.53 c/d or 0.71 min arc). However, their 4 year olds had binocular acuity of 0.9 min arc (33.33 c/d) which is very close to (but again still lower than) our 6-8 year olds (35.1 c/d or 0.85 min arc). Our results do not agree with those of Ellemberg et al. (1999) who found adult-like grating

VA in the 6th year of life. The researchers used the method of limits which does not exclude criterion differences between children and adults. Ellemberg et al. (1999) argued that non-visual factors such as criterion differences or attention differences did not likely affect their results since, in their study, children 4-6 years old had reduced spatial CS at all spatial frequencies but their sensitivities were reduced only at lower temporal frequencies for the temporal CS.

The sVEP technique has been used to study the development of VA mainly in infants (Norcia & Tyler, 1985a; Norcia et al., 1990 and Sokol et al., 1992) and the results indicate that VA develops from about 5 c/d at the first month of life to about 16-20 c/d at 7-13 months. In the study of Norcia and Tyler (1985a) VA was found to be 20 cpd at the age of 8-13 months compared to 24.3 c/d in adults. The researchers stated that the VA between the 8-13 months and the adults was not “reliably different”, but did not support this conclusion statistically. Skoczenski and Norcia (1999) found that sVEP grating VA at the age of one year is within about a factor of two of the adult value. In the present study, we found that adult-like VA with the sVEP is reached later, between the ages of 9-12 years old. Several other electrophysiological studies indicate that the visual system continues to mature beyond early childhood. Brecelj et al. (2002) found that there is a decrease in PERG (pattern electroretinograms) amplitude and the PVEP latency until the age of 18 years. Results from multifocal VEP show that the latency of the dominant negative peak in the superior field and the positive peak in inferior field decreases with age until 13 years of age (Balachandran et al, 2004).

In summary, our sVEP and psychophysical (logMAR and 2AFC staircase) VA results agree with these previous studies, in that the 6-8 year olds did not have adult-like VA. Also our results show the same developmental trend for the sVEP and the psychophysical measures, where the VAs of the 6-8 years were consistently lagging behind the VAs of the adults.

6.4.2 Contrast sensitivity

Although our results did not indicate that there was an overall significant effect of age for the contrast threshold at 1 cpd, the 6-8 year olds did not show adult-like contrast threshold with the staircase or SDT procedures. The higher variability of the sVEP thresholds compared to the staircase or the SDT thresholds, as can be seen from figure 6-4, might be the reason that an overall effect of age was not found. An overall significant effect of age was also not found for the contrast threshold at 8 cpd. However, an effect of age was found with the staircase procedure, in which the 6-8 year olds gave significantly poorer contrast thresholds than the 9-12 year olds. When comparing the error bars in figure 6-4 to those in figure 6-5, it can be seen that measuring contrast thresholds at 8 cpd results in threshold measurements that are more variable than those at 1 cpd. This is true for all the procedures (sVEP, staircase, and SDT) and all age groups. Therefore, it is difficult to draw a firm conclusion about the development of contrast sensitivity after the age of 6-8 years at higher spatial frequencies from this study. We used psychophysical procedures (2AFC and SDT) that are not affected by changes in the participant's criterion. Hence, the differences in thresholds that we did find between children and adults are reliable, but the variability in the data where no differences were found could have masked any differences.

Our finding for psychophysical contrast threshold agrees with the studies that have found that adult-like CS is not reached until somewhere between ages 9 and 14 years (Mayer, 1977; Adams and Courage, 2002; Benedek et al., 2003 and Nielsen et al., 2007), and the studies that have not found adult-like CS in children aged 6-8 years (Abramov et al., 1984; Scharre et al., 1990; Gwiazda et al., 1997 and Leat and Wegmann, 2004). Mayer (1977) was the only study that used an SDT technique in children. Mayer found that anisotropy becomes adult-like at the age of 11 years as a result of an increase in CS to the horizontal and vertical gratings that started at the age of 5 years. In our study contrast thresholds were not adult-like until the age of 9-12 years (with both SDT and 2AFC tests). We cannot compare our criterion (*c*) results to the criterion index in Mayer (1977) since criterion was not considered in her study.

Our results for psychophysical contrast threshold do not agree with the findings of Arundale (1978), Beazley et al. (1980), Bradley and Freeman (1982) and Ellemberg et al. (1999). Arundale (1978) found that CS is not yet adult-like at low and medium spatial frequencies at the age of 8-15 years. However, Arundale did not provide any statistics and tested only 3 children in a wide age range (8-15 years old) while we tested 16 children in each of our child groups (6-8 and 9-12 years old). Beazley et al. (1980) found that CS reaches adult levels between 18-29 years old. The researchers used a yes-no staircase, and admitted that this method may have been affected by criterion differences between the participants in any of the age groups that they included or between the age groups themselves. The researchers recommended using a forced-choice procedure to overcome the criterion effects, but argued that it could be difficult to perform in children. Bradley and Freeman (1982) used a 2AFC procedure and concluded that CS reaches adult levels around the age of 8 years. However, the researchers had 38 children (with only 26 who completed testing) ranging in age from 2.5 – 16 years and they decided to put the participants in groups after they obtained the data, which resulted in groups with only 6 participants. They also did not give any statistics and their conclusion was likely to be based on observations drawn from the figures of CS for each age group. Bradley and Freeman (1982) ascribed the differences in CS between children and adults to visual as well as non-visual (attention) factors, since they were able to bring the CS of adults down to the level in the younger children by instructing the adults to be less attentive during the test. This indicates that even when procedures that control for change in criterion are used, differences in attention may still influence the results. In our study, however, we used psychophysical procedures that are unaffected by an important non-visual factor which is the change in criterion, and children were being watched during testing. Trials in which a child showed signs of reduced attention (e.g. by looking away from the screen while giving an answer) were repeated and the child was asked to keep looking at the screen. We also asked the children if they needed a break after each block of trials to make sure that they did not get bored and less attentive. However, this does not guarantee that the children's attention was as good as the adults and that they were not making decisions quicker than adults. Bradley and Freeman (1982) also tested some children with a yes-no staircase procedure and noticed that younger children tended to say "yes" regardless of whether the stimulus was present or not (i.e. children used a less conservative criterion than adult). This is in agreement with our finding that younger children were less likely to say "no" than adults. Ellemberg et al. (1999) used the method of limits to study the development of CS in children and concluded that CS becomes adult-like at the age of 7 years. Although Ellemberg et al. (1999) dismissed the possibility of criterion change with the method that they used (method of limits) by arguing that the between participant variability in mean thresholds for each age group was small, it is possible that most of the participants in each age group adopted a criterion that is different than the criterion adopted by the participants in other age groups. This is exactly what we found in our study when we investigated the criterion adopted by each age group in the yes-no SDT procedure. Although the between participant variability was small for contrast thresholds at 1 cpd with the SDT procedure (as indicated by the error bars in figure 6-4), the criterion adopted by the youngest group (6-8 years) was significantly different from the criterion of the adult group (children were less likely to say "no" than adults, indicating a more liberal criterion). It may be concluded, therefore from all these studies and the present one, that there is more evidence that CS is not adult-like by 6-8 years.

One limitation of this study is that most of the children were examined after school time (between 3-5 pm) while most of the adults were examined at different times of the day. Clearly, a fatigue effect cannot be entirely ruled out. However, we watched the children during the test sessions and they were given regular breaks and additional breaks if they felt tired or sleepy. Additionally, the sVEP testing and the psychophysical testing were performed in two different days, with the order of contrast threshold (and also spatial frequency for the contrast threshold measurement) or VA testing being randomized.

6.4.3 Anatomical development of the visual system

The results from the methods that we used to measure VA and CS (sVEP, 2AFC and SDT procedures) showed the same trend (i.e. VA and CS are not fully developed at 6-8 years). The thresholds obtained with these methods should not be affected by the most commonly confounding factor in visual development studies which is the participant's criterion toward saying "yes, the stimulus is present". Therefore, the difference in thresholds between the youngest age group and the older children group or adults can be explained based on differences between these groups in the development of the visual system. As discussed in Ellemberg et al. (1999), three main anatomical differences have been found between the visual system of children and adults: the length of the outer segment of the foveal cones, the cone packing density in the fovea and the synaptic density in the visual cortex. Yuodelis and Hendrickson (1986) reported that at the age of 45 months the length of the foveal cone outer segment is still 30-50% shorter than that in adults, and cone packing density in the fovea is only half that in the adults. Huttenlocher et al. (1982) and Garey and de Courten (1983) reported that the synaptic density in the visual cortex increases between the age of 2 months to the age of 8 months, then starts decreasing until it reaches adult-level at the age of 11 years. The effects of the reduced outer segment length and cone packing density in infants were modeled along with other retinal and optical factors that were found to be not adult-like in infants (Banks & Bennet, 1988; Wilson, 1988; reviewed by Banks and Crowell, 1993). The reduced packing density of the foveal cones causes the Nyquist frequency of cone mosaic to be less than the adult's , which is 59.7 c/d, and in turn leads to reduced visual acuity (Banks and Bennet, 1988; Wilson, 1988). The reduced outer segment length leads to reduced photon catch by the cones and consequently to reduced CS (Banks and Bennet, 1988; Wilson, 1988). Banks and Bennet (1988) concluded that there are still major postreceptoral differences which contribute to the poor VA and CS in infants, while Wilson (1988) concluded that the differences in photoreceptors are sufficient to explain the poor VA and CS. As there are no available anatomical data for children above the age of 4 years, we cannot confirm that the observed non-adult-like VA and contrast thresholds in our 6-8 years old were due to an immature fovea.

6.5 Conclusion

The present study showed that even when methods (VEP, 2AFC, and SDT) are used that are not affected by the most commonly confounding factor, which is criterion differences, there are still differences between older children and adults. The study showed that VA and CS are not adult-like until the age of 9-12 years. The reasons for the reductions in these functions in the 6-8 year olds are more likely anatomical or physiological than behavioral.

Chapter 7
General discussion and conclusions

There were two aims of this thesis. The main aim was to determine whether VA and CS are adult-like by the age of 6-8 or 9-12 years. The majority of the studies of the development of VA and CS have used subjective methods. The use of subjective (psychophysical) and objective (electrophysiological) methods together can provide a more comprehensive idea about the maturation of these visual functions. Furthermore, employing psychophysical techniques that give threshold measurements that are not affected by the subject's response criterion overcomes the problem of criterion changes encountered in other developmental studies. Having decided to use sweep VEP for the objective measure, it became apparent that there are many parameters which may influence the final threshold. Therefore, the subsidiary aim was to find a criterion for the determination of the sVEP threshold that is repeatable [it should be noted that testing the validity of the criterion in adults was not part of this thesis, but was based on the results of Yadav et al. (2009)] and to study the effect of many of the sVEP parameters on the threshold.

In Chapter 4, different criteria for the range of regression line fitting to determine sVEP VA and contrast thresholds in 6-8 years old children were studied to find the best criterion in terms of repeatability and the number of viable threshold readings obtained from five active electrodes. Also in this chapter, the results of the effects of luminance on the sVEP VA and contrast thresholds and the number of viable threshold readings were reported. The results showed that criterion C2 (in which the range for the regression line fit was defined as the data between the signal peak and the last data point (furthest from the peak) with an SNR $\geq$ 1) and criterion C3 (which was similar to C2, but was defined so that the threshold should be within the sweep range of the stimuli actually used), were the best criteria in terms of repeatability and validity in visually normal individuals [validity testing was done on adults by Yadav et al. (2009)]. Also C2 and C3 were consistently the criteria that gave more viable readings and better thresholds (i.e. higher VA and lower contrast thresholds). Yet, C2 is preferable over C3 since C3 resulted in some missing data in the repeatability for adults, according to Yadav et al. (2009). Further research, however, is required to confirm that C2 performs best for patients with poor VA. The results also indicated that a luminance of at least 50 cd/m^2 should be used for sVEP.

Chapter 5 investigated the effects of electrode placement, temporal frequency, sweep direction, presence of a fixation target, stimulus area and sweep duration on the sVEP VA and contrast threshold and the number of viable threshold readings in 6-8 years old children and adults. The results showed that these parameters did not affect the sVEP VA or contrast thresholds. However, a temporal frequency of 7.5 Hz, for both VA and contrast thresholds, and a stimulus area of 4˚ or larger for VA and 10˚ or larger for contrast threshold, gave more viable readings.

In Chapter 6 the objective sVEP method and psychophysical methods [two-alternative forced choice (2AFC) and signal detection theory (SDT)] were employed to determine whether VA and CS become adult-like at the age of 6-8 years or 9-12 years. The results indicated age-related changes in threshold values and that these visual functions do not become adult-like until the age of 9-12 years. LogMAR VA (both crowded and uncrowded) also indicated that recognition acuity is not adult-like until the age of 9-12 years. The fact that there is maturation still occurring at the high frequencies (VA) of the objective sVEP measure between the 6-8 year olds and the adults, but not at lower frequencies (CS at 1 and 8 cpd) is in agreement with other studies (Norcia et al., 1986; Norcia et al., 1990) that have found earlier development of sensitivity for low versus high spatial frequencies. In that Chapter it was also reported, based on the SDT results, that children do show differences in criterion compared with adults in psychophysical testing and this warrants the use of SDT or forced-choice procedures to overcome this problem in any developmental study.

7.1 Conclusions

Several conclusions are drawn in this thesis and are as follows:

1. The criterion for the regression line fitting affects the threshold value more than the other parameters in sVEP. C2 and C3 gave better VA and contrast thresholds and also gave better repeatability and validity than the other criteria. However, C2 is preferable over C3 since C3 resulted in some missing data in the repeatability for adults according to Yadav et al. (2009).

2. A luminance of at least 50 cd/m^2, a temporal frequency of 7.5 Hz, a stimulus area of 4˚ or larger for VA and 10˚ or larger for contrast threshold measurement should be used for sVEP.

3. VA and CS do not become fully adult-like until the age of 9-12 years.

4. Children do have different criterion than adults as shown by the SDT procedure.

5. The SDT procedure can be applied in children as young as 6 years old.

7.2 Limitations

The studies conducted in this thesis have a number of limitations that need to be addressed. First, the results of Chapters 4 and 5 were obtained for individuals with VA of 6/7.5 or better. Hence, the generalization of the results to people with poorer VA still needs to be investigated before the criterion can be applied clinically. The use of the C2 for the study is justified, however, as all participants in the study had normal development of VA.

Secondly, in all of the studies in Chapters 4, 5 and 6, the majority of the child participants were seen after school time (between 3-5 pm) while most of the adult participants were seen at different times of the day. This was an unavoidable arrangement since testing was conducted during week days. Obviously, some of the children may have been fatigued after a long day at school and, as a consequence, may have not been as alert as the non-fatigued adults. As a result, the thresholds of the possibly fatigued children may be poorer than the non-fatigued participants, especially in the psychophysical testing. Fatigue can be a factor for some of the adult participants as well. However, all participants were being watched for alertness and were given regular breaks between sessions of testing.

Thirdly, the studies reported in Chapters 4 and 5 had a sample size of six participants (except in the repeatability study in which there were ten participants). Although this small sample size was enough to detect differences in the outcome measures (thresholds and number of viable readings) between the criteria for fitting the sVEP regression line in Chapter 4, it might not give enough power for some of the other parameters investigated.

Fourthly, in Chapter 6, where the development of VA and CS were studied across different age groups, there was an age gap between the 9-12 year olds and adults. In cases where the differences in thresholds were found only between the 6-8 year olds and the adults, it was not possible to plot the data as in figure 6-3 and determine exactly when the thresholds became adult-like because of that age gap. The age groups in this study were chosen because the age at which VA or CS become adult-like was between 6 and 12 years in most of the studies reported in the previous literature. This selection of age groups left a gap between the 9-12 year olds and adults (21- 33 years old). The ideal design for developmental studies would be either a cross-sectional design with the participants divided into age groups of 1 year or a longitudinal design. However, both designs are not feasible since a large number of participants would be required for the former and a long period of time is needed for the latter. Furthermore, longitudinal studies are associated with problems of high cost and participant drop out.

7.3 Future research

Future research in the areas covered in this thesis may include the following:

1. The application of the different criteria for fitting the regression line in sVEP on patients with poor vision to confirm whether C2 is also the best criterion in this case by using repeatability and validity studies. In addition, the effects of the different sVEP parameters on VA and contrast threshold in patients with poor vision should be investigated.

2. Larger sample size in future sVEP studies should be used as this thesis indicated large variability (which may hide some real differences) between the subjects especially for contrast threshold measurement.

3. SDT could be applied in developmental studies that concern other aspects of vision (such as VA and vernier acuity) in children as young as 6 years of age.

In summary, the best techniques available to measure VA and CS have been employed in this thesis and it was found that these functions do not become adult-like until the age of 9-12, but these techniques do not guarantee that the differences between children and adults are genuine. For example, it has been noticed that children in psychophysical testing start to guess when they approach threshold even when a forced-choice method was used (Abramov et al., 1984) which would have the effect of raising the threshold. Moreover, the objective measure used in this thesis, the sVEPs, might be subject to inter-individual differences in the position of the visual cortex with respect to the skull (Suttle, 2001) or inter-individual variations of the cortical gyri and sulci formation (Lam, 2005), which may also vary between adults and children. Other differences which exist between children and adults such as skull thickness and size should not affect the sVEP threshold, as the skull thickness affects the amplitude of the VEP but not the extrapolated threshold (Tyler et al, 1979) and the ISCEV electrode placement takes into account the differences in skull size. Finally, it is perhaps significant that the maturity timing that we find here is similar to known cortical changes in synaptic density. The synaptic density in the visual cortex increases between 2-8 months of age and then starts decreasing until it reaches adult levels at the age of 11 years (Garey and de Courten, 1983 and Huttenlocher et al., 1982).

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Date:	Sep 01, 2008
ISSN:	0275-5408
Publication Type:	Journal
Volume:	28
Issue:	5
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