4-5-2011

Visual Evoked Potentials: Analysis of the Fovea and Perifovea

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Recommended Citation

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O.D., Doctorate of Optometry, Southern College of Optometry – 1996
B.S., Physical Science, Memphis State University – 1992

A Thesis Submitted to The Graduate School at the University of Missouri-St.
Louis in partial fulfillment of the requirements for the degree
Master of Science in Vision Science

Feb 2011

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20 Feb 2011

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ABSTRACT

Visual evoked potentials (VEP) were used to measure how stimulus properties (pattern VEP check sizes/spatial frequency) and retinal eccentricity (fovea versus perifovea) interact to give rise to the final VEP response. The purposes of this study were to investigate how stimulus check size (spatial frequencies) and retinal eccentricity affect the VEP response, re-examine whether the cortical magnification factor is applicable to VEP measures, and to determine optimal sized VEP checks for foveal and perifoveal stimuli. Earlier studies have shown that check size as well as stimulus location in the visual field does affect the VEP response (Katsumi, Tanino, Hirose, 1986; Harter, 1970; Hughes et al., 1987). Experiments conducted in earlier studies focused more on amplitude than implicit time, and only a few studies investigated if or how the sum of the foveal and perifoveal amplitudes could be used to predict the amplitude of the full field target (Harter, 1970; Rover et al., 1980). Thus, one of the reasons for conducting this research is to add new data to this area of study.

In this study, we used a foveal target that was a two degree circle with a diameter of 3.6 cm; a perifoveal target that was a circular ten degree annulus with an inner diameter of 3.6 cm and an outer diameter of 17.5 cm; and a full field target that was a ten degree circle with a diameter of 17.5 cm. These stimuli sizes were chosen because they stimulate approximately the same amount of cortical area (Horton and Hoyt, 1991; Xing and Heeger, 2000). VEPs were performed on ten healthy adult subjects monocularly through the dominant eye. All test parameters were chosen based on

guidelines from the ISCEV standard for clinical visual evoked potentials--2009 update (Odom et al. 2009).

Measurements of the implicit time (N1 and P1) and amplitude (N1 - P1) were taken using four different pattern VEP check sizes, 0.23, 0.52, 0.83, and 1.78 degrees (spatial frequencies of 0.24, 0.48, 0.97, and 2.18 cycles per degree or cpd respectively). Between subjects, check size (spatial frequency) was found to have a significant effect on implicit time (foveal and perifoveal N1 values, foveal and perifoveal P1 values), and foveal and perifoveal amplitudes. However, within subjects, check size only had significant effects on implicit time (perifoveal N1 and foveal P1 values).

Multiple regression analyses of the VEP amplitudes derived from the foveal and perifoveal (annulus) targets were performed to investigate if the total amplitudes of these stimuli targets could predict the amplitude of the full field stimulus. Results of this analysis showed that when the smallest check size (0.23 degrees) was utilized within the foveal and perifoveal (annulus) targets, the VEP amplitude of the ten degree target (full field stimulus) could be significantly predicted. The strongest predictor of the full field amplitude was the amplitude that was derived from the perifoveal (annulus) stimulus. When the large check size (1.78 degrees) was used within the foveal and perifoveal (annulus) targets, it was not significantly predictive of the amplitude of the ten degree stimulus (full field stimulus).

The findings of this study indicated: (1) stimulus check size (spatial frequencies) and retinal eccentricity did significantly affect the VEP response, (2) cortical magnification factor was only predictive of the full VEP response when the smallest

checks were used and (3) the optimal sized checks for the foveal target was the scaled stimulus for N1 implicit time, scaled for P1 implicit time, and large checks for the amplitude. With the perifoveal stimuli, the optimal sized checks were the large stimulus for N1 implicit time, scaled checks for P1 implicit time, and large checks for the amplitude. Differences exist in sensitivity to specific check sizes (spatial frequencies) depending on the type of VEP measure used (implicit time or amplitude) and area of the retina stimulated. These results are not consistent with a single stimulus being optimal for all measures and that there is a complex interaction between visual targets and responses.

INTRODUCTION

Visual evoked potentials (VEPs) are used clinically, as well as experimentally, to assess the integrity of the retinal-cortical pathway. Electrophysiological research studies have utilized the pattern VEP to provide evidence of parallel visual pathways (McKerral, Lepore, and Lachapelle, 2001; Rudvin, Valberg and Kilavik, 2000; Souza et al., 2008); determine properties of the magnocellular and parvocellular pathways (Zemon and Gordon, 2006; Tobimatsu et al., 1995); investigate fovea versus peripheral retina interactions (Harter, 1970; Xing and Heeger, 2000); examine binocular function and the effects of stimulus size and localization (Katsumi, Tanino, and Hirose, 1986); analyze first order and second order motion mechanisms (Ellemberg et al., 2003); and estimate human cortical magnification (Slotnick et al., 2001).

VEPs are massed electrical signals that are derived from the occipital cortex in response to visual stimulation. VEPs differ from the electroencephalogram (EEG) in that the EEG is generated by ongoing activity of various cortical areas while the VEP is primarily an occipital lobe response triggered by a visual stimulus (Celesia, 1984).

VEPs are recorded by adhering one or more active electrodes over the occipital lobes and reference and ground electrodes at other positions on the scalp/head. Signals from the electrodes are transmitted to a bandpass differential preamplifier to enhance amplitude and signal-to-noise ratio, and then averaged and digitally filtered by the computer. There are two common types of visual stimuli used for eliciting VEPs: light flashes and pattern contrast reversal. When light flashes or contrast reversals are

presented infrequently (less than one per second), the entire waveform occurs; this is termed a transient response. When light flashes or contrast reversals are repeated frequently at regular intervals (greater than ten per sec), a simple periodic waveform can be captured; this is termed a steady-state response (Celesia, 1984).

The pattern reversal VEP typically contains an initial small negative peak, N1, (N70 or N75 will be called N1), followed by a large positive peak, P1 (P100 will be called P1), and a second negative peak, N2 (N135 will be called N2). The origin of the P100 (P1) in the brain is presumed to reflect the activity of the striate cortex. The neurological source of the P1 component is over the ventrolateral prestriate cortex or Brodmann's Area 18 (Mangun et al., 1993; Di Russo et al., 2003). P1 can be modulated by attention and is associated with activation in the dorsal occipital areas and the posterior fusiform gyrus (Woldorff et al., 1998; Mangun et al., 1997). P100 (P1) is the most consistent and least variable peak compared to N75 (N1) and N135 (N2). The most commonly reported amplitude is the N75-P100 (N1 – P1) peak-to-peak amplitude (Barrett et al., 1976). Figure 1 below shows a normal VEP waveform and Figure 2 shows a VEP apparatus.
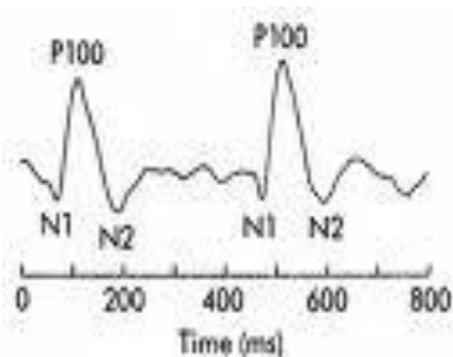
Figure 1 shows a model VEP waveform with N1, P1, and N2 labeled.

Figure 2 shows a VEP apparatus. The monitor with the checkerboard pattern is what the subject views and the monitor with the waveforms is what the tester views.

ASSESSMENTS WITH VEPs

In humans, the assessment of the retino-cortical pathways is mainly based on the amplitude and implicit time (latency) of the scalp-recorded pattern-reversal visual evoked potential (Chiappa, 1990; Regan, 1989) whose components are derived from prestriate and striate cortical areas (Ducati, Fava and Motti, 1988; Maier et al., 1987). Gratings and checks are most effective in exploring the function of V1 because it is presumed that V1 is comprised of local spatial frequency analyzers (De Valois et al., 1979). By choosing an appropriate stimulus size, specific areas of the retina can be predominantly stimulated. Approximately 80 percent of the pattern VEP response arises from the central eight degrees of the stimulus field (Chiappa, 1997).

VEPs are valuable in assessing ocular and systemic disorders and its response is affected by manipulation of stimulus parameters such as type of pattern, check size or spatial frequency, field size, contrast, mean luminance of the stimulus field and

background luminance, method and rate of presentation (Tobimatsu and Celesia, 2006; Klistorner et al., 1998)). P100 latency (implicit time) increases as luminance of the pattern decreases due to the reduction of retinal illuminance (Tobimatsu et al., 1988). The P100 implicit times typically show an increase of 10-15 ms per log unit of decreased retinal illuminance (Tobimatsu et al., 1988). Low contrast causes reduced amplitudes and longer implicit times (Chiappa, 1997; Tobimatsu et al., 1993). Small size patterns ranging between 0.17 and 0.25 degrees preferentially stimulate the fovea, while patterns subtending greater than 0.50 to 0.67 degrees stimulate both the foveal and perifoveal areas. Celesia (1984) conducted a study in which 74 patients with Multiple Sclerosis were tested monocularly and VEPs were recorded to both checkerboard-pattern-reversal and flashes of increasing frequency. Seventy-four percent of the patients had delayed or absent VEPs to the pattern-reversal, but only 44 percent of patients had abnormal responses to the flash test. These results show that the type of stimuli used for testing is paramount in detecting systemic and ocular pathologies (Celesia, 1984).

Position of the pattern element is also important when trying to preferentially stimulate the fovea or perifovea. When eccentrically positioned stimuli are scaled (increased in linear size in order to stimulate the same amount of cortex as if viewed with the fovea), it is expected that a signal of a similar order of amplitude from each stimulating element will be produced (Baseler et al., 1994; Levi et al., 1985; Meredith and Celesia, 1982; Strasburger et al., 1994).

Meredith and Celesia (1982) conducted experiments on a total of 16 subjects to investigate the effects that retinal eccentricity had on the pattern reversal VEP and conditions that would preferentially stimulate the fovea and peripheral retina. Experiments were performed in a partially darkened room with a background luminance of 0.06 foot lamberts. Each subject was seated in a chair with his/her head resting on a chin-rest that was located at the center of a 60 cm translucent hemisphere. Pattern reversals were produced by a fast lateral displacement of a black-and-white checkerboard through one square. The checkerboard pattern was back-projected to the hemisphere. The projection system was placed on a movable holder that could be rotated in vertical and horizontal directions so that various regions of the visual field could be stimulated with equal quantum energy. Subjects were directed to fixate on a small red dot at the center of the screen and all experiments were conducted monocularly.

Three experimental paradigms were used. The first experimental paradigm consisted of a 2 degree 18' (2.3 degrees) full field containing 16 checks of 34'30" of arc (0.57 degrees). The visual stimulus was moved in a stepwise manner from the point of fixation to the 18 degree isopter in the horizontal, vertical and oblique meridians. Fourteen normal subjects were tested with this paradigm. Results showed that stimulation at the fixation point evoked a reproducible potential characterized by three negative-positive deflections. The first negative wave, N1, had a peak mean latency of 75.6 +/- 11.6 msec and amplitude of 0.6 +/- 0.4 μV. In four subjects, this wave was absent. The second deflection, P1, was positive and had a mean latency of 102.3 +/- 9.7

msec and amplitude of 3.1 +/- 1.27 µV. A negative wave, N2, followed P1 and this wave

had a mean latency of 144.5 +/- 15.3 msec and amplitude of 5.4 +/- 2.7 µV. Similar

evoked potentials were produced when the visual stimulus was located within the two

degree isopter. When the stimulus was moved from the fixation point along the

horizontal, vertical, and oblique meridians, the amplitude of responses declined

drastically, and no responses were usually detected beyond the four degree isopter

(small amplitude responses were detected on only two subjects when the stimulus was

outside the four degree isopter). The validity of the differences in amplitude of the

evoked potentials that were elicited at fixation (zero to two degrees) and four to six

degrees eccentricity was evaluated with the paired t test. These amplitude differences

were statistically significant for each eccentricity with a P < 0.001.

Paradigm II was conducted to determine the smallest size of total field required

to evoke a reproducible response at the fixation point and to compare it with visual

acuity. Six participants were tested with paradigm II. Variable size fields were studied

at three positions: fixation, nasal eccentricity outside the eight degree isopter, and

nasal eccentricity outside the fourteen degree isopter. The overall size of the field and

the size of each individual check were varied until no response could be obtained or the

limitation of the experimental apparatus had been reached. The size of the fields

ranged from 6'42" to 20'42" (0.11 to 0.34 degrees) and contained four individual checks

of 3'27" and 10'21" (0.057 and 0.175 degrees) respectively. Results showed that there

was no consistent relationship between field size, check size, and visual acuity. Most of

the subjects could detect the four checks at sizes smaller than the one necessary to elicit

an evoked potential. Responses to the small stimuli consisted of a small potential

characterized by a broadened positive wave, occasionally followed by a prominent

negative wave. No responses were obtained outside the central four degree isopter

with stimuli that was 2 degree 18' (2.3 degrees). However, evoked potentials could be

elicited outside the foveal region by using larger stimuli. Increasingly larger fields and

larger checks were needed to elicit an evoked potential as the stimulus was moved from

the fixation point to the eight degree and fourteen degree eccentricity. Calculations of

the square millimeters of striate cortex activated by the smallest stimulus at the three

positions were performed based on the magnification factor of Cowey and Rolls (1974),

Rovamo and Virsu (1979) and Virsu and Rovamo (1979). Table 1 below shows the

smallest size of stimuli required to produce an evoked response at three retinal

eccentricities and the estimated size of striate cortex activated.

Table 1

Retinal Eccentricity	N	Field Size (Range)	Mean +/- SD (Field)	Check size (Range)	Mean +/- SD (Check size)	Striate Cortex mm^2 (Rovamo-Virsu	Striate Cortex mm^2 (Cowey and Rolls)
Fixation	6	6'54"-20'42" (0.11^o-0.34^o)	13'17"$\pm$ 5'4" ($0.21^o \pm 0.08^o$)	3'27"- 10'21" (0.05^o-0.16^o)	6'35" $\pm$ 2'5" ($0.11^o \pm 0.03^o$)	1.78-5.34 mm^2	3.48-10.41 mm^2
Outside 8 deg nasal	6	3°-3^o27' (3°-3.45^o)	3^o18'$\pm$34' ($3.3^o \pm 0.01^o$)	34'30"-51'45" (0.57^o-0.86^o)	44'39" $\pm$ 10' ($0.80^o \pm 0.16^o$)	6.93-7.96 mm^2	6.30-7.24 mm^2
Outside 14 deg nasal	6	4^o36'-6^o54' (4.6^o-6.9^o)	5'45' $\pm$56' ($5.75^o \pm 0.93^o$)	1^o9'-2^o7' (1.15^o-2.12^o)	1^o43' $\pm$14' ($1.71^o \pm 0.23^o$)	5.71-8.56 mm^2	5.37-8.01 mm^2

Paradigm III encompassed calculating three field sizes to activate the same amount of striate cortex at three different retinal eccentricities: fixation, nasal 8 degrees, and nasal 14 degrees. At fixation, the 2 degree 18' field (2.3 degrees) was used. Based on calculations using the magnification factor of Cowey and Rolls (1974), a 2 degree 18' field (2.3 degrees) at zero degrees retinal eccentricity activates 34.73 mm^2 of cortex. Thus, the size of the field at the other retinal eccentricities (nasal 8 and nasal 14 degrees) also needed to activate 34.73 mm^2 of cortex. A field of 16 degree 32' (16.53 degree) was used at 8 degree eccentricity and a field of 30 degrees was used at 14 degrees eccentricity. Three subjects were tested with this paradigm. Results showed that the amplitude of the evoked potentials at 8 degree and 14 degree nasal eccentricities was almost the same when the field size was M-scaled. At zero degree eccentricity, the amplitude of the evoked potential was approximately two times the amplitude of the potentials obtained at 8 degree and 14 degree eccentricities. According to this study, the amplitude difference was expected due to the activation of both occipital cortices with stimulation of the macula. In addition to this result, there also appeared to be an optimal check size for each retinal eccentricity. The highest amplitude responses were found at 8 degree eccentricity with a field size of 7 degree 41' (7.68 degrees) and a check size of 2 degree 33' (2.55 degrees). At 14 degree eccentricity, the highest amplitude responses were produced with a field size of 13 degree 40' (13.67 degrees) and a check size of 3 degree 28' (3.46 degrees). Also, retinal eccentricity affected the amplitude of wave P1— a decrease in the amplitude of wave

P1 was noted with a peripheral stimulus as compared to the same stimulus located at the fixation point (Meredith and Celesia, 1982).

Baseler et al. (1994) conducted two studies that investigated VEP responses across the visual field. In both studies, participants viewed the stimulus binocularly in a dimly lit room. In the first study, visual evoked potentials to luminance and pattern reversal stimulation were derived using 64 equal-area patches throughout the central visual field. VEPs were recorded from six subjects with normal or corrected-to-normal vision. The stimuli were unscaled and consisted of an 8 x 8 square matrix of flickering squares (flash VEP) and squares containing reversing check patterns (pattern VEP). Four viewing distances were used—72, 142, 285, and 570 cm, so that the stimulus field subtended 16° x 16°, 8° x 8°, 4° x 4° and 2° x 2° respectively.   The size of each square changed as distance changed, ranging from 2° to 0.25^o in octave steps. The check size of the pattern stimulus was varied with distance so that it remained a constant ten minutes of arc on the retina. The responses obtained were robust and primarily near the center of the visual field. The proportion of the stimulus matrix that carried most of the response power changed little with the varying viewing distances. The ratio of the area of highest response relative to total area being stimulated was approximately constant at each of the four viewing distances (the only significant difference noted was at the farthest distance). This finding, according to the study, supports the model that cortical distance (V1) varies with visual field eccentricity as a logarithmic function. Field topographies were compared between and within the six subjects using different

electrode placement. Results showed that inter-subject variability existed due to inter-subject variations in gross cortical anatomy (Baseler et al., 1994).

The second study used luminance modulation of 56 patches across a 15 degree field and these patches were scaled to activate approximately equal cortical areas in area V1. Each patch stimulated 45 mm^2 of V1. One subject participated in the study. The results showed that the scaled stimuli produced robust signals at all eccentricities. Response amplitudes were comparable (not uniform) at positions in the fovea as well as in the periphery of the stimulus. Baseler et al. (1994) attributed the non-uniformity of response amplitudes to several factors: (1) scaling a stimulus is based on approximations of cortical magnification in the striate cortex, yet it is likely that other visual areas contribute to the responses; (2) estimates of human striate area and cortical magnification are based on a limited number of human brains; (3) no amount of eccentricity scaling can totally circumvent signal cancellation, particularly when the VEP wave forms are produced from the sums of multiple sources of separate anatomical origins; and (4) stimulus targets varied somewhat in area so that the shape of the targets can remain nearly the same at every location (Baseler et al., 1994).

CORTICAL MAGNIFICATION FACTOR

The cortical magnification factor is a value derived from a calculation that is used to adjust the size of an eccentric stimulus (a stimulus that is not projected in the fovea or at fixation) so that it occupies the same amount of cortical space as a foveal stimulus would occupy on the cortex (Virsu and Rovamo, 1979; Virsu et al., 1982). It is expressed

in terms of mm of visual cortex per degree of visual angle (Daniel and Whiteridge, 1961). The concept of cortical magnification is a way of describing the proportion of visual cortex that is devoted to processing a stimulus of a particular size, as a function of its visual field location (retinal eccentricity). For example, two stimuli that are equal in linear size will not stimulate the same amount of visual cortex if they are projected at different retinal eccentricities (Rovamo and Virsu, 1979). An object that is projected at zero eccentricity will stimulate a larger proportion of visual cortex than an object (same size) that is projected at, for example, 5 to 7 degrees eccentricity. The cortical magnification factor measured in human visual cortex, at ten degrees eccentricity, is estimated to be about 1/5 that in the fovea (Xing and Heeger, 2000). The reason for this difference in visual processing is due to the difference in the amount of neurons that is found at zero degree eccentricity compared to other retinal eccentricities. A larger number of neurons in the fovea (zero degree eccentricity) are devoted to visual processing than at other retinal eccentricities (Duncan and Boynton, 2003; Snell and Lemp, 1989; Thorpe et al., 1996).

Numerous studies have acknowledged that eccentricity effects can be minimized when eccentric stimuli (non-foveal projected stimuli) are scaled in size to foveal stimuli according to the cortical magnification factor using anatomical (Azzopardi and Cowey, 1993, 1996; Curcio et al., 1987), psychophysical (Duncan and Boynton, 2003; Xing and Heeger, 2000; Rovamo and Virsu, 1979; Strasburger et al., 1991) and electrophysiological (Popovic and Sjostrand, 2001; Slotnick et al., 2001) techniques. For example, accounting for cortical magnification neutralized the eccentricity effects in

visual search tasks which led to earlier target detection and faster reaction times

(Rovamo and Virsu, 1979). Minimum contrast required for detecting sinusoidal gratings

in the central and peripheral vision were measured in a study by Rovamo and Virsu

(1979). The results showed that almost all quantitative differences observed could be

removed and all gratings could be made equally visible by scaling the size of the stimuli

so that their calculated cortical representation became equivalent at different

eccentricities (Rovamo and Virsu, 1979).

Meredith and Celesia (1982) performed a study in which three field sizes were

calculated to activate the same amount of visual cortex at three different retinal

eccentricities (zero, eight, and fourteen degree eccentricities). In their experiment, the

cortical magnification factor of Cowey and Rolls (1974) was used. As the stimulus

moved outside zero retinal eccentricity, the linear size of the field had to be increased in

size in order to activate the same amount of visual cortex (also noted as M-scaling). The

field size at zero eccentricity was 2 degrees 18' (2.3 degrees) and contained a check size

of 0.05 degrees; field size at eight degree eccentricity was 16 degrees 32' (16.53

degrees) and contained a check size of 0.57 degrees, and the field size at 14 degree

eccentricity was 29 degrees 56' (29.93 degrees) and contained a check size of 1.15

degrees. After M-scaling, their results showed that the amplitude of the evoked

potentials was approximately the same at eight and fourteen degrees eccentricity. Also

a second variable, size of individual checks, was investigated to determine the optimal

check size for a particular retinal eccentricity. Results of the study showed that visual

resolution and receptive field size vary across the visual field. Small checks and fields

were optimal stimuli at the fovea (zero degree eccentricity), and larger checks and fields

at the periphery (beyond zero degree eccentricity).

In the current study, the parameters (stimuli sizes, cortical magnification factor)

were selected to focus on smaller field sizes. According to Horton and Hoyt (1991),

stimulating beyond the central 10 or 15 degree of visual field does not contribute

significantly to the amplitude of the visual evoked potential. The Horton and Hoyt

cortical magnification factor was used in the present study because its cortical scaling

factor (17.3 mm) is approximately the average of the values found in other cortical

magnification studies (Slotnick et al., 2001).

HORTON AND HOYT (1991) STUDY

Horton and Hoyt (1991) conducted a study to test the accuracy of the Holmes

retinotopic map that is found in many textbooks. The Holmes retinotopic map, created

in 1945 after G. Holmes and W.T. Lister examined soldiers wounded in World World I,

depicts an orderly topographic representation of vision in the striate cortex. The

Holmes map shows that the fovea has an expanded representation in the striate cortex

(central 15 degrees of vision represented by 25 percent of the surface area of the striate

cortex). The accuracy of the Holmes map was confirmed with the use of computed

tomography in early studies of occipital lesions in patients with visual field deficits. In

these pioneering studies, a strong correlation was reported between the

neuroradiological findings and the location of the occipital lesions predicted by the

Holmes map. However, these strong correlations were questionable due to the poor

resolution of early computed tomography (Horton and Hoyt, 1991).

Scientific and technological advances of electrophysiologic equipment with

better resolution enabled the striate cortex to be carefully mapped and studied in other

species (primates), as well as in humans. Horton and Hoyt (1991) compared the reports

of topographic maps of Old World primates and the Holmes map of humans and found

that a difference existed in the topographical representation of central vision on the

striate cortex. In macaque monkeys, the central 15 degrees of vision was allotted

approximately 70 percent of the total surface area of the striate cortex (Daniel and

Whiteridge, 1961). This finding far exceeded the Holmes map representation of the

visual field in human striate cortex (central 15 degrees of vision was allotted 25 percent

of the surface area of the striate cortex). The discrepancy in human and monkey data

suggested that the Holmes map needed to be revised or that the striate cortices in

humans and monkeys were different in terms of the topographical representation of

central vision. This led Horton and Hoyt to conduct a one year study to determine

whether the Holmes map should be amended or to confirm that differences exist in

human and monkey striate cortex (Horton and Hoyt, 1991).

The Horton and Hoyt (1991) study involved correlating magnetic resonance

images with visual field defects in three patients with occipital lobe lesions. The patient

cases were: a 30 year old woman with a delineated lesion in the left occipital lobe; a 28

year old woman with a right occipital lobe arteriovenous malformation with a left

homonymous hemianopia, and a lesion replacing the anterior portion of the right

calcarine cortex; and a 57 year old woman with bilateral infarcts involving visual cortex along the medial surface of the occipital lobe. They compared the patients' visual field defects to the Holmes map and found that the defects were incompatible to the Holmes map of the striate cortex. In all three patients, the Holmes map correlated poorly with the actual location of the lesion imaged by magnetic resonance and demonstrated that central vision occupied a greater proportion of the human striate cortex than what the Holmes map portrayed. The findings in these patients indicated that the relative magnification of central vision in the human striate cortex is very similar to laboratory data obtained from macaque monkeys and the Holmes map should be revised. The revised map, scaled to the cortical magnification of the macaque striate cortex, shows the fovea located at the occipital pole, and the extreme periphery of the visual field located anteriorly, at the junction of the calcarine and parieto-occipital fissures. Their revised map enabled Horton and Hoyt to localize more accurately the location of lesions in the striate cortex (Horton and Hoyt, 1991).

The retinotopic map of Horton and Hoyt and the Holmes map were developed from examining individuals that had sustained brain trauma or injury (Horton and Hoyt, 1991). Trauma can alter the structures and the function of the brain which could have had an impact on their findings. Also, it is important to note that these patients were examined weeks and months after their injuries, and cortical plasticity could have had an effect on the results. Cortical plasticity is the capacity of the brain/nervous system to adapt and regenerate due to changes in the neurons, their networks and organization. Lastly, both studies were based on a limited number and type of subjects. The Horton

and Hoyt study used only three subjects, and the Holmes map was devised primarily

from data on wounded soldiers of World War I (Horton and Hoyt, 1991).

CALCULATION OF CORTICAL MAGNIFICATION FACTOR

The Horton and Hoyt human cortical magnification factor was based on adapting

the magnification formula for the macaque striate cortex to the dimensions of the

human striate cortex. A correction factor of 1.44 was incorporated and the expression

for the human cortical magnification factor is (Horton and Hoyt, 1991):

$$M_{linear} = \frac{17.3}{E + 0.75}$$

M = the linear magnification factor
17.3 is a constant, cortical scaling factor in mm
E = eccentricity in degrees
0.75 is a constant, eccentricity at which a stimulus subtends half the cortical distance as it does when foveated

The Horton and Hoyt (1991) cortical magnification factor, derived from magnetic

resonance imaging (MRI) and visual field measures (anatomic), differs from cortical

magnification values that are derived from VEPs (psychophysical measures). Stimulus

target sizes differ based on the cortical scaling factor in anatomic and psychophysical

studies. The foveal and perifoveal target sizes in this study, calculated using the Horton

and Hoyt (1991) cortical magnification factor, was two degrees and ten degrees. The

foveal target size would be slightly larger using the Cowey and Rolls (1974) and the

Engel et al. (1994) cortical magnification factors (2.3 and 2.01 degrees respectively); and

smaller with the Sereno et al. (1995) and Slotnick et al. (2001) cortical magnification

factors (1.79 and 1.76 degrees respectively). The perifoveal target size would be slightly

larger using the Cowey and Rolls (1974) and Engel et al. (1994) cortical magnification

factors (11.45 and 10.05 degrees respectively); and smaller with the Sereno et al. (1995)

and Slotnick et al. (2001) cortical magnification factors (8.96 and 8.82 degrees

respectively). In addition to stimulus target size differences, VEP amplitudes

(psychophysical) decrease and implicit times increase at a much greater eccentricity

than the one degree eccentricity of the Horton and Hoyt study (Horton and Hoyt, 1991;

Slotnick et al., 2001). This study utilized a cortical magnification factor that was derived

anatomically; however, this difference was reconciled by using targets (overall size) that

were larger than one degree which were comprised of pattern VEP check sizes that

were significantly smaller than one degree.

VISUAL PROCESSING

The fovea is represented by a large proportion of the visual cortex (V1) and has

the strongest contribution to the VEP (Stevens, 2002). The fovea contains the foveola, a

highly specialized region that provides the best detail-oriented vision and is 0.35 mm

(one degree) wide (Chiappa, 1997; Celesia and De Marco, 1994; Cohen, 1992). There

are approximately 160 times more striate cells per cone in the fovea than in the

periphery; thus, the surface area of the visual cortex would have to be increased by a

factor of 13 in order to support peripheral retinal sampling as fine as that of the central

retina (Azzopardi and Cowey, 1993).

Interneurons have a functional role in visual analysis and affects gamma

frequency activity. The human gamma oscillatory response mediating in cortical visual

information processing can contribute to the VEP waveform. However, it is thought to

reflect mechanisms that are partially independent of the VEP. The gamma mass response has a shorter latency than the VEP low frequency components (Lamme et al., 1998; Sannita et al., 2007).

Azzopardi and Cowey (1996) found that in rhesus monkeys, (whose striate cortex is very similar to humans), the cortical representation of the central retina was expanded two to three times more than could be accounted for on the basis of ganglion cell topography in the retina, and the expansion occurred between the retina and the dLGN of the thalamus and between the dLGN and the cortex (Azzopardi and Cowey, 1996).

Popovic and Sjostrand (2001) directly compared resolution thresholds and quantitative estimates of retinal ganglion cell separation in humans with fMRI estimates of the human linear cortical magnification factor. Their results indicated an expansion in devoted cortical distance per central ganglion cell that could not be attributed to variances in ganglion cell concentrations across the retina nor peripheral scaling, but rather by an expanded representation of the fovea in the retino-cortical pathway (Popovic and Sjostrand, 2001). Ganglion cells near the fovea are allocated three to six times more visual cortex (V1) tissue than those in the periphery (Azzopardi and Cowey, 1993; Curcio and Allen, 1990) and there are four times more dLGN cells per ganglion cell afferent in the fovea than in the periphery (Connolly and Van Essen, 1984).

Additionally, there are ten times more striate cells for every incoming LGN projection from the fovea compared to the periphery (Connolly and Van Essen, 1984). Azzopardi, Jones, and Cowey (1999) provided evidence that the central retina is

accompanied by selective expansion of central vision in the parvocellular dLGN. Sample

ratios of parvocellular and magnocellular inputs to the visual cortex were computed

from counts of neurons in the dLGN of macaque monkeys that were labeled

retrogradely with WGA-HRP from the visual cortex at the cortical representation of

different retinal eccentricities. Parvocellular to magnocellular ratios decreased from an

average of 35:1 at the fovea to 5:1 at 15 degrees eccentricity (Azzopardi, Jones, and

Cowey, 1999).

Connolly and Van Essen (1984) determined the parvocellular and magnocellular

ratios to be 40:1 at the fovea and 4:1 in the far periphery (80 degrees eccentricity).

Based on results from several studies (Schein and de Monastero, 1987; Chatterjee and

Callaway, 2003; Connolly and Van Essen, 1984; Kaplan and Shapley, 1982), the general

consensus is that the ratio of parvocellular to magnocellular inputs to the striate cortex

decreases with eccentricity. These eccentricity effects cause stimuli that are equal in

size to be perceived differently when viewed with the central (fovea) and peripheral

areas of the retina (Cornsweet, 1970; Jacobs, 1979; Johnston and Wright, 1985; Juttner

and Rentschler, 1996). The difference in visual perception can sometimes be accounted

for by scaling stimulus size according to the cortical magnification factor.

One of the purposes of this study is to re-examine whether the cortical

magnification factor can be applied to VEP measures. Based on the spacing of the

photoreceptors in the fovea (retinal region that contains the foveola), the general

thought is that small checks in the fovea and large checks in the perifovea (retinal region

that subtends a visual angle of ten degrees or greater) will elicit the shortest VEP implicit

times (the time measured from stimulus onset to the peak of a response). However,

this may not always be the correct assumption to use clinically. Check size as well as

retinal location can affect implicit times and amplitudes of the VEP (Katsumi, Tanino and

Hirose, 1986) and using inadequate sized test stimuli may lead to a clinician missing

early signs of disease/defects. In the present VEP study, an original technique called

"double-scaling" was used. Double-scaling in this VEP study used both the overall size of

a stimulus and the check size within a specific stimulus to account for cortical

magnification. To obtain double-scaling, the following steps and calculations were

performed:

(1) The overall sizes of the foveal and perifoveal targets were scaled according to

the retinotopic map devised from the Horton and Hoyt study (1991).

According to this study, a two degree foveal stimulus and a ten degree

stimulus occupy equivalent proportions of cortical area. So, the first scaling

was the overall size of the two targets—two degrees and ten degrees (Figure

3). The overall size of each target is a diameter measurement.

Fovea (Center)   Perifovea (Annulus)   Full (Full Field)

Figure 3 shows the targets used for the fovea, perifovea, and full field stimuli.

(2) Three check sizes were selected for the foveal targets—1.78 degrees (largest

checks with a spatial frequency of 0.24 cpd); 0.23 degrees (smallest checks

with a spatial frequency of 2.18 cpd); and 0.52 degrees (intermediate size

checks with a spatial frequency of 0.97 cpd). The check size describes the size

of one check in the targets. These check sizes were selected based on the

sizes that were available on the equipment in the lab. The largest and the

smallest checks were projected in all stimulus targets (two degree, ten

degree annulus, and full field targets), but the intermediate checks were not

projected in all stimulus targets due to time and schedule constraints. The

intermediate size check (0.52 degrees or 0.97 cpd) was scaled again and

projected in the ten degree stimulus target.

(3) The second (double) scaling involved only the intermediate size check. In the

foveal stimulus target, the intermediate check size (0.52 degrees or 0.97 cpd)

was projected into it. In the perifoveal target (ten degree annulus), a check

size of 0.83 degrees (spatial frequency of 0.48 cpd) was projected into it.

This size was calculated by using the following cortical magnification formula

(Horton and Hoyt, 1991; Slotnick et al., 2001):

$$M = A/(E + E_2)$$

M = linear magnification factor
A = constant; cortical scaling factor in mm
E = eccentricity in degrees
E_2 = constant; eccentricity at which a stimulus
subtends half the cortical distance as it does when
foveated

M = 17.3 mm / 10 degrees + 0.75

M = 1.609 mm/degree

M (perifoveal check size) = 1.609mm x 9 mm = 14.48 mm = 1.45 cm

This formula uses a value of 17.3 for the constant "A" and a value of 0.75 degrees for the constant "E_2." Values for A and E2 can vary and several studies using MRI and VEP have estimated different values for these constants (Slotnick et al., 2001). Table 2 shows the estimated values for E_2 and A from previous studies on cortical magnification (Slotnick et al., 2001). Variance in the E_2 values and dual E_2 values for some of the subjects below may be attributed to the differences that exist in the gross cortical anatomy of individuals and methods of testing.

Table 2

Cortical Magnification Studies	E_2 – Values (degrees)	A – Values (mm)
Horton & Hoyt, 1991 (scaled macaque)	0.75	17.3
Cowey & Rolls, 1974 (n = 1)	1.5 +/- 1.6	15.1 +/- 1.4
Engel et al., 1994 (subject 1)	3.1 +/- 0.9	17.2 +/- 1.11
Engel et al., 1994 (subject 2)	11.2 +/- 2.2	20.4 +/- 1.9
Sereno et al., 1995 (n = 7)	0.4 +/- 0.7	19.3 +/- 2.6
Slotnick et al., 2001 (subject TC)	0.20 +/- 0.26; 0.92 +/- 0.28	21.1 +/- 1.5
Slotnick et al., 2001 (subject HB)	0.10 +/- 0.39; 0.48 +/- 0.18	19.6 +/- 2.1
Slotnick et al., 2001 (subject SD)	0.52 +/- 0.11; 0.68 +/- 0.49	32.3 +/- 3.81

Comparisons of the implicit times between the double-scaled stimuli and the other stimuli (the stimuli in which only the overall size is scaled) were performed.

HYPOTHESES

This study investigated the effects of stimulus check size (spatial frequency) and retinal eccentricity on the VEP response for the purposes of: (1) determining optimal sized VEP checks for foveal and perifoveal stimuli and (2) re-examining whether cortical magnification factor is applicable to VEP measures. The first hypothesis is that the fastest implicit times and highest amplitudes will occur for stimuli in which both the field size and individual check size are scaled based on the cortical magnification factor. The second hypothesis is that VEP response amplitudes generated from the fovea and perifovea (annulus) can be used to estimate the amplitude of the full field target.

METHODS

EXPERIMENTAL APPARATUS AND METHODS

Visual evoked potentials were recorded in ten subjects. Informed consent was obtained from all subjects using an UMSL IRB approved protocol. A Nicolet Biomedical 1015 visual stimulator was used to project the checkerboard pattern for the VEP onto a Panasonic CRT monitor. Testing was conducted monocularly on each subject's dominant eye. Eye dominance was determined by using the Miles test. Viewing distance was 100 cm and room illumination was 8 lux. One hundred sweeps per average were conducted and a sweep duration of 200 ms was used. A reversal rate of 1.8 Hz was used for all testing. These parameters were chosen based on guidelines from

the ISCEV standard for clinical visual evoked potentials--2009 update (Odom et al.,

2009). The ISCEV standards for clinical VEP testing are presented in Table 3.

 Two VEP recordings from each of the eight experimental conditions (16 trials) were

performed. Each test session per subject lasted approximately 35 minutes. Subjects

were given rest breaks between trials to avoid fatigue.

Table 3

VEP Test Parameters	ISCEV Standards
PVEP Checkerboard Stimuli Sizes	Large - 1.0 +/- 20% degree; Small – 0.25 +/- 20% degree
Stimulus Field Size	$\geq$ 15 degrees in its narrowest dimension and the aspect ratio between width and height should not exceed 4:3
Viewing Distance	50 – 150 cm
Mean Luminance of Checkerboard Pattern	40 – 67 cd/m^2
Reversal rate / sec	2.0 +/- 10%
Pattern Onset Duration	200 ms separated by 400 ms of background
Minimum Number of Sweeps per average	64
Amplification of Input Signal	20,000 – 50,000 times

The foveal stimulus was a circular field with a 3.6 cm diameter; the perifoveal

stimulus was an annulus with an inner diameter of 3.6 cm and an outer diameter of 17.5

cm, and the full field stimulus was a circular ten degree field with a diameter of 17.5 cm.

The size of the stimuli was scaled to take into account the cortical magnification factor

(Horton and Hoyt, 1991). The two degree stimulus size was chosen as the foveal target based on a pilot study in which a significant VEP waveform could not be obtained using a target that subtended less than two degrees with the instrumentation that was available at the UMSL lab. Also, limitations of the size of the CRT screen precluded using a perifoveal target with a diameter much larger than 18 cm.

Differing check sizes of the pattern VEP were used (see Table 4). Checkerboard patterns were selected rather than gratings because checkerboards are commonly utilized in the clinical setting and larger amplitudes are elicited from checkerboards. The smallest checks were 0.23 degrees (2.18 cpd) in size and the largest checks were 1.78 degrees (0.24 cpd) in size. The largest check size was determined based on having a minimum of four checks into the two-degree foveal target. A central fixation target (2.0 mm black circular disc) was placed in the center of each stimulus target to maintain participants' fixation. Check contrast was 96 percent and the mean luminance of the screen was 52 cd/m^2.

Table 4

Types of Checks	Check Size (degrees)	Spatial Frequency (cycles per degree or cpd)
Smallest Checks	0.23 deg	2.18 cpd
Medium / Scaled Checks (fovea)	0.52 deg	0.97 cpd
Medium/Scaled Checks (perifovea)	0.83 deg	0.48 cpd
Largest Checks	1.78 deg	0.24 cpd

Eight experimental conditions were conducted to measure the amplitudes and implicit times of the visual evoked potentials. Amplitude was defined as the N1 to P1

amplitude and latency was defined as the time from stimulus onset to the peak of a

deflection. Visually inspecting a VEP waveform, the N1 to P1 amplitude occurs between

the first negative (at an implicit time greater than 50 msec) deflection of the waveform

and the peak of the waveform. N1 appears as the first deflection and P1 appears as the

first peak of the waveform as shown in Figure 1. Using software from the experimental

apparatus, the minimum time points for N1 and P1 were determined by moving a cursor

along the nadir and peak. Black and white checks that differed in size were used for the

foveal, perifoveal, and full field targets, as shown in Table 5.

Table 5

Stimulus Check Size (degrees)	Stimulus Target (Location)
1.78	Fovea (2.0 degrees)
1.78	Perifovea (10 degrees)
1.78	Full field target (10 degrees)
0.23	Fovea (2.0 degrees)
0.23	Perifovea (10 degrees)
0.23	Full field target (10 degrees)
0.52	Fovea (2.0 degrees)
0.83 (double-scaled)	Perifovea (10 degrees)

Ten subjects with the following inclusion criteria participated in the experiment:

- Ages 21-45

- Visual acuity 20/20 or better OD, OS, and OU (corrected or uncorrected)

- Normal, steady fixation and no signs of manifest or latent nystagmus

- No current use of medication or nutritional supplement affecting fovea and

  perifovea retinal areas such as Amiodarone, systemic steroids, etc.

- No ocular / systemic disorders that can affect retinal-cortical function

Subjects were recruited from the College of Optometry at University of Missouri St. Louis. They were paid a rate of $10/hour.

EXPERIMENTAL SESSION

On selection, each participant performed a practice VEP test to familiarize them with the task. After this session, a rest break was given, and data collection began.

Two VEP recordings were conducted for each of the eight experimental conditions. Participants were seated 100 cm away from the display screen and wore a black eye patch so that testing was conducted monocularly on the dominant eye. To ensure that the dominant eye was tested, each patient performed the Miles test to determine ocular dominance. To perform the Miles test, subjects extended both arms and brought both hands together to create a small opening. Next, subjects maintained both eyes open and viewed a distant object through the opening. Last, subjects alternated closing their eyes to determine which eye is actually viewing the object (i.e. the dominant eye) (Roth, Lora, and Heilman, 2002). After establishing eye dominance, an eye patch was placed over the non-dominant eye and participants were informed when testing began and when it ended. After each recording, N1, P1 and amplitudes were recorded. Comparisons of implicit times and amplitudes were performed to detect differences between foveal and perifoveal targets within and between participants.

PROCEDURE

VEPs were recorded from three electrodes placed on subjects' scalps relative to bony landmarks. The active electrode was placed on the scalp over the visual cortex (2.5 cm above the external occipital protuberance); the mid-frontal reference electrode was placed 7 cm above the nasion, and a third electrode was adhered to the top of the head along the midline (approximately 10 cm from the reference electrode). Electrode placement was based on the guidelines from the ISCEV standard for clinical evoked potentials—2009 update (Odom et al., 2009). Impedance (conduction of electrical impulses) was checked prior to each VEP test. Testing was conducted when impedance was less than 20 Kohms. Subjects were seated and instructed to maintain fixation on the central fixation target at all times during testing. Subjects viewed the display screen and fovea, perifovea, and full field checkerboard patterns were presented. The stimulus parameters were set from a circular apparatus constructed from black plastic and plexiglass (diffuser) that was attached to the front of the display screen. A diffuser comprised of plexiglass, obscured areas of the checkerboard pattern that should not be viewed during testing but kept the amount of illuminance approximately constant. The ten-degree perifoveal target (annulus) had a circular opaque disc adhered centrally to obscure the central two degrees, and the two degree target had an opaque annulus that obscured the peripheral checkerboard so that only a two degree central area was visible (Figure 4). Measurements of N1, P1, and amplitude were obtained.

Figure 4 shows the apparatus that was attached to the front of the display screen for the two degree, ten degree, and full field targets.

RESULTS

ANALYSIS

Three stimulation paradigms were conducted:

(1) Paradigm I consisted of 1.78 deg, 0.23 deg, and 0.52 deg check sizes (spatial frequencies of 0.24, 2.18, and 0.97 cpd respectively) projected in the two degree foveal target to determine which stimulus check size results in the fastest implicit time.

(2) Paradigm II consisted of 1.78 deg, 0.23 deg, and 0.83 deg check sizes (spatial frequencies of 0.24, 2.18, and 0.48 cpd respectively) projected in the ten degree perifoveal target (annulus) to determine which stimulus check size results in the fastest implicit time.

(3) Paradigm III consisted of using a full field target (comprised of 1.78 deg and 0.23 deg checks) and fovea and perifovea targets (comprised of 1.78 deg and 0.23 deg checks) to determine if the amplitudes of the fovea and perifovea

stimuli can be predictive of a full field stimulus (combined fovea and

perifovea stimuli) target's amplitude. Multiple regression analysis was used

to determine if the amplitudes of the fovea and perifovea can be utilized to

estimate the amplitude of the full field target. Linear and non-linear analyses

with SPSS software were performed.

RESULTS OF THE EXPERIMENTS

PARADIGMS I & II

The figures in Appendix A show the values of N1, P1, amplitude and the waveforms that

were obtained from each subject as well as the means of those values with standard

error bars (see Figures 1-12 in Appendix A). Different scales were used on the graphs to

reflect the pattern of subjects' responses. A repeated measures ANOVA was performed

using stimulus check size and retinal position as factors and the values of N1, P1, and

amplitudes as dependent variables to assess if a significant difference existed within

subjects when different check sizes were used for the fovea and perifovea stimuli. The

analysis showed that check size had a significant effect on the value of N1 (implicit time)

in the perifovea (F = 23.22; p = 0.00; partial eta squared = 0.72), but did not have a

significant effect in the fovea (F = 0.30; p = 0.75; partial eta squared = 0.03). There was

a significant effect of check size on the P1 implicit time in the fovea (F =3.97; p = 0.04;

partial eta squared = 0.31), but there was not a significant effect of check size on the P1

implicit time in the perifovea (F = 0.92; p = 0.42; partial eta squared = 0.09). Check size

had no significant effect on foveal (F = 1.80; p = 0.19; partial eta squared = 0.17) or

perifoveal amplitudes (F = 1.70; p = 0.21; partial eta squared = 0.16). The multivariate

test (Wilks Lamda) showed only a significant difference between the means of N1

(implicit time) when different check sizes were presented in the perifovea (p = 0.001).

Table 6 below shows the ANOVA results.

Table 6

ANOVA Statistics	N1 (Fovea)	N1 (Perifovea)	P1 (Fovea)	P1 (Perifovea)	Amplitude (Fovea)	Amplitude (Perifovea)
F-Statistic	0.30	23.22	3.97	0.92	1.80	1.70
p-value	0.75	0.00	0.04	0.42	0.19	0.21
Partial Eta Squared	0.03	0.72	0.31	0.09	0.17	0.16

*$p \leq 0.05$ is significant

A comparison of the double-scaled checks that were projected in both the fovea

and perifovea showed that check size had no significant effect on the mean implicit

time, but amplitude was affected. The double-scaled checks used in the perifovea

resulted in an amplitude value that was approximately 1.25 times higher than the foveal

amplitude--the mean amplitude was 4.63 mV for the fovea and 5.74 mV for the

perifovea.

PARADIGM III

Linear regression analysis (multiple regression) showed that the fovea and

perifovea did not predict the full field stimulus, with the exception of the small checks (F

= 6.60; p = 0.03; r^2 = 0.55). When the large check size was used, the amplitudes of the

fovea and perifovea were not predictive of the amplitude of the full field stimulus (F =

2.82; p = 0.13). A comparison of the predicted amplitude (the summed amplitude of the

foveal and perifoveal stimuli) to the amplitude of the full field stimulus revealed that the

full field stimulus was approximately 1.75x more than the summed amplitudes of the

foveal and perifoveal stimuli. The mean predicted amplitude (summed foveal and

perifoveal amplitudes) was 4.76 mV and the amplitude of the full field stimulus was 8.10

mV for the large check size. For the small check size, the mean predicted amplitude

(summed foveal and perifoveal amplitudes) was 3.70 mV and the amplitude of the full

field stimulus was 6.50 mV.

Figures 1-11 in Appendix B show the values and the waveforms of the predicted

amplitudes and the real amplitudes. The predicted amplitudes were obtained by adding

the VEP waveforms of the fovea and perifovea together. The real amplitude is the value

taken from the full field stimulus waveform. The three VEP waveforms were derived

from the predicted, the real full field stimuli and the difference between the two. A

multiple regression was performed using the amplitudes of the fovea and perifovea as

factors and the amplitude of the full field target as the dependent variable to assess if

the combined fovea and perifovea amplitudes could predict the amplitude of the full

field target. Only the smallest and largest check sizes were used due to time and

schedule constraints. Separate analyses were performed for the small and large check

sizes. For the small check size, the amplitudes of the fovea and perifovea predicted the

amplitude of the full field target (F = 6.60; p = 0.03; r^2 = 0.55). The perifoveal amplitude

was the strongest predictor of the full field stimulus amplitude. The effect size was

large, 55.4 percent, and 65 percent of the variability with the variables was accounted

for. For the large check size, the amplitude of the fovea and the perifovea did not significantly predict the full field amplitude of the full field target (F = 2.82; p = 0.13).

The paired T-test was performed on the small and large check sizes using the amplitude, N1, and P1 as factors to assess if a significant difference exists between the populations—the predicted and the real full field stimuli. The paired T-test showed that there was a significant difference between the means of the predicted full and the real full amplitudes for the small check size (p = 0.001) and the large check size (p = 0.001).

OTHER MODELS

A quadratic nonlinear regression was performed and this analysis compared the relationship of each predictor variable (foveal and perifoveal amplitudes) individually to the criterion variable (amplitude of the full field stimulus). Analysis was performed with SPSS software and the quadratic equation: $Y = b_0 - b_1x - b_2x^2$.

The first analysis used the foveal amplitudes generated from both the small and large check size and compared it to the full field amplitudes that were also derived from the small and large check sizes. The results showed that a significant non-linear relationship existed between the amplitudes of the fovea and full field stimulus (F = 6.94; p = 0.01) with a large effect size (r^2 = 0.45) as shown in Figure 5.
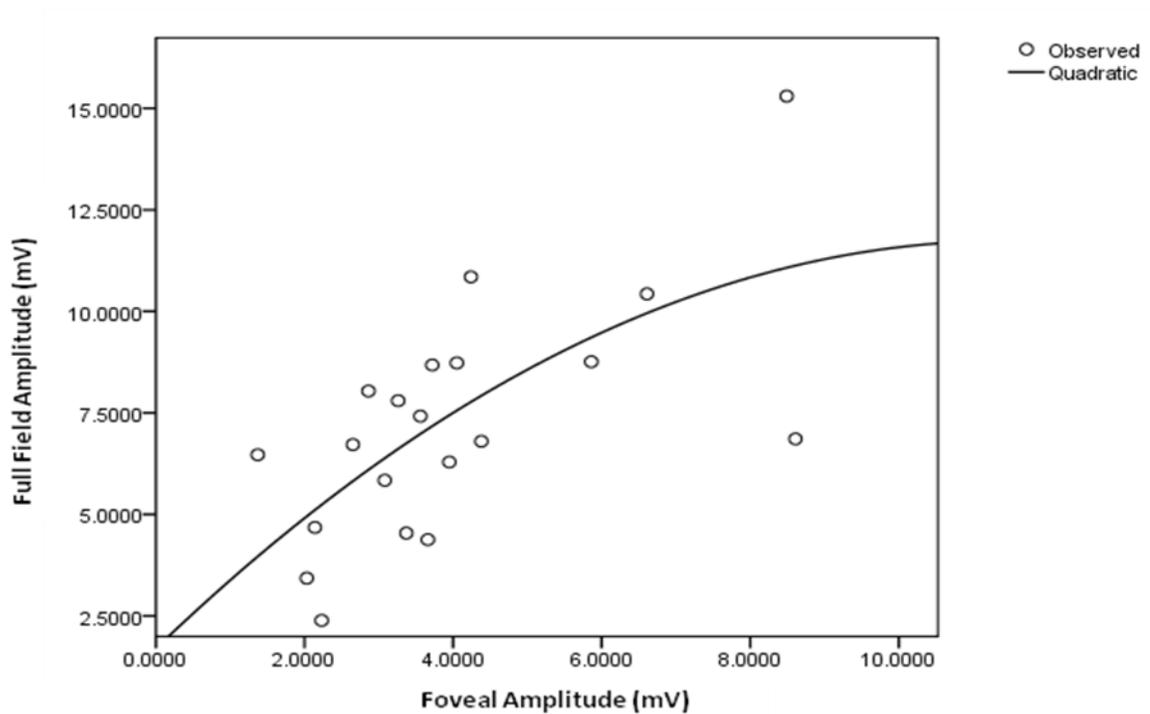
Figure 5 shows a comparison of the foveal amplitude (mV) to the amplitude of the full field stimulus (mV) that was generated from both the large (1.78 degree) and small (0.23 degree) check sizes. The amplitudes of the fovea and full field stimuli have a significant non-linear relationship.

The second analysis compared the perifoveal amplitudes that were derived from both the small and large check size to the full field amplitudes that were also derived from both the small and large check sizes. This analysis also demonstrated that a significant nonlinear relationship existed between the amplitudes of the perifovea and full field stimulus (F = 8.70; p = 0.003) with a large effect size (r^2 = 0.51) as shown in Figure 6.
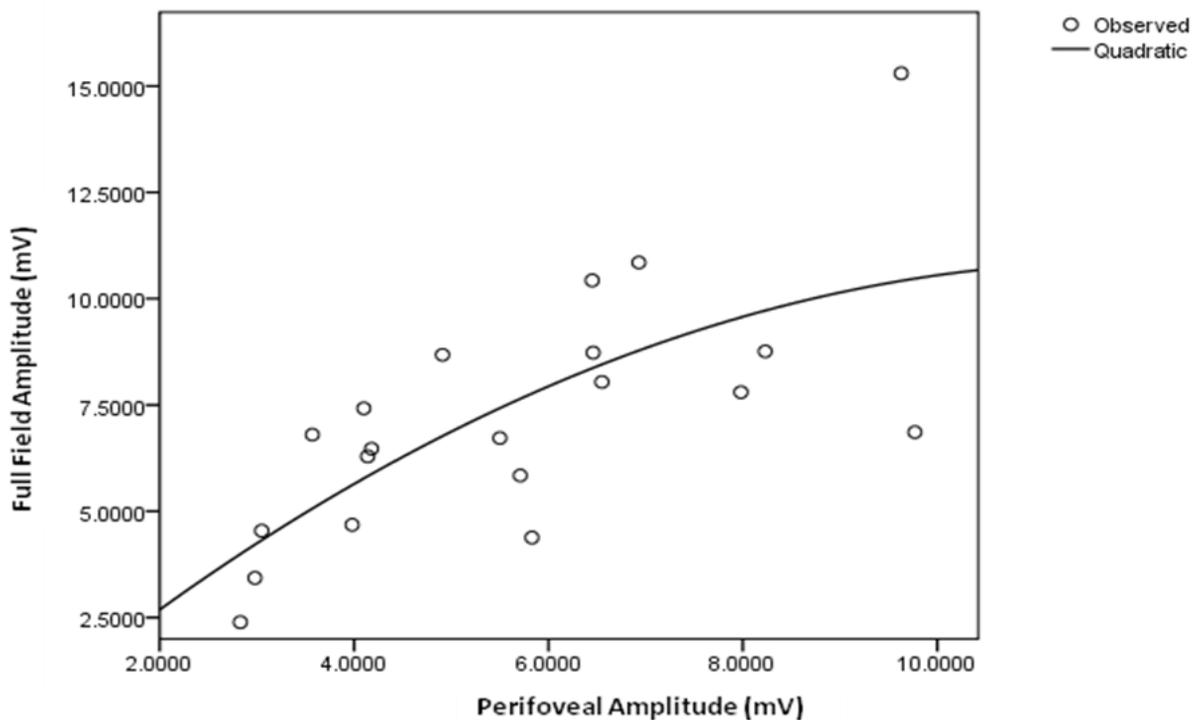
Figure 6 shows a comparison of the perifoveal amplitude (mV) to the amplitude of the full field stimulus (mV) that was generated from both the large (1.78 degree) and small (0.23 degree) check sizes. The amplitudes of the perifoveal and full field stimuli have a significant non-linear relationship.

Next, several analyses were performed in which the foveal and perifoveal

amplitudes that were derived from a particular check size were compared to the

amplitude of the full field stimulus that was derived from the same check size. The

results of these analyses, like the results from the linear/multiple regression analyses,

revealed that a significant nonlinear relationship between the fovea, perifovea and the

full field stimuli only existed when the small check size was used to generate

amplitudes. When large checks were used to generate the foveal and perifoveal

amplitudes, a significant relationship did not exist with the full field stimulus (F = 2.47; p

= 0.15; r^2 = 0.42 for the fovea; F = 2.04; p = 0.20; r^2 = 0.37 for the perifovea). See Figures

7 and 8 below.
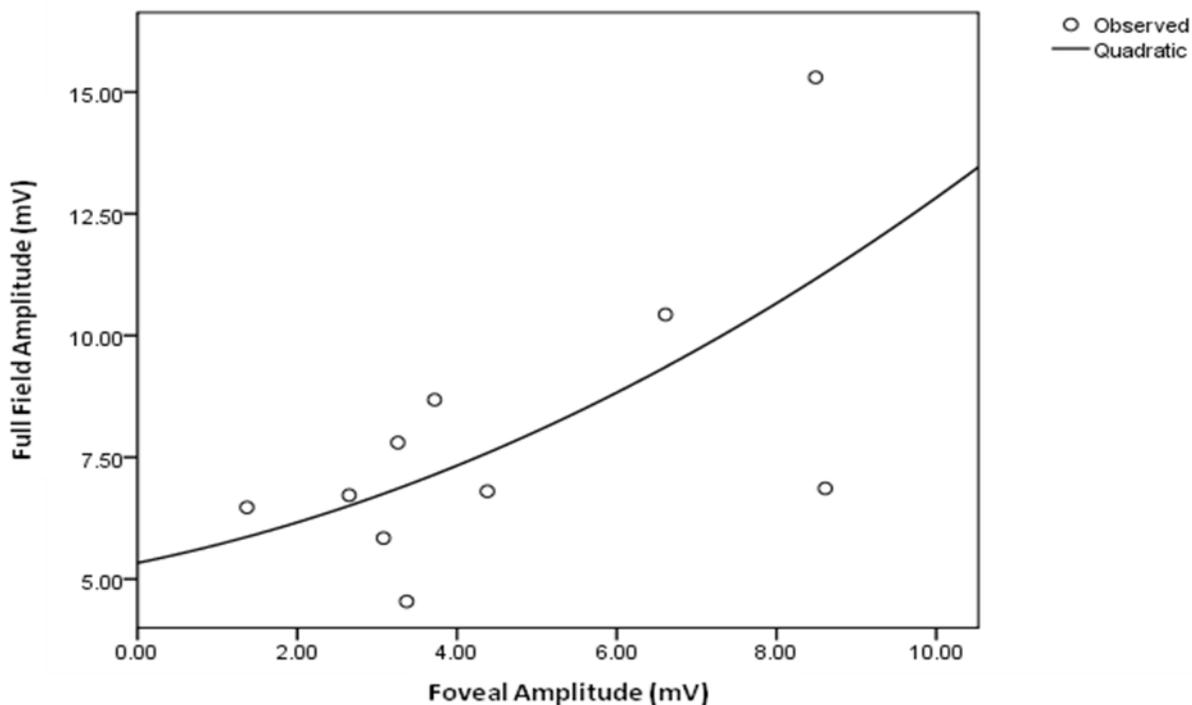
Figure 7 shows a comparison of the foveal amplitude (mV) derived from the large (1.78 degree) check size and the full field amplitude (mV) derived from the same large check size. A significant non-linear relationship between the foveal and full field amplitudes did not occur when the large check size was projected into the targets.
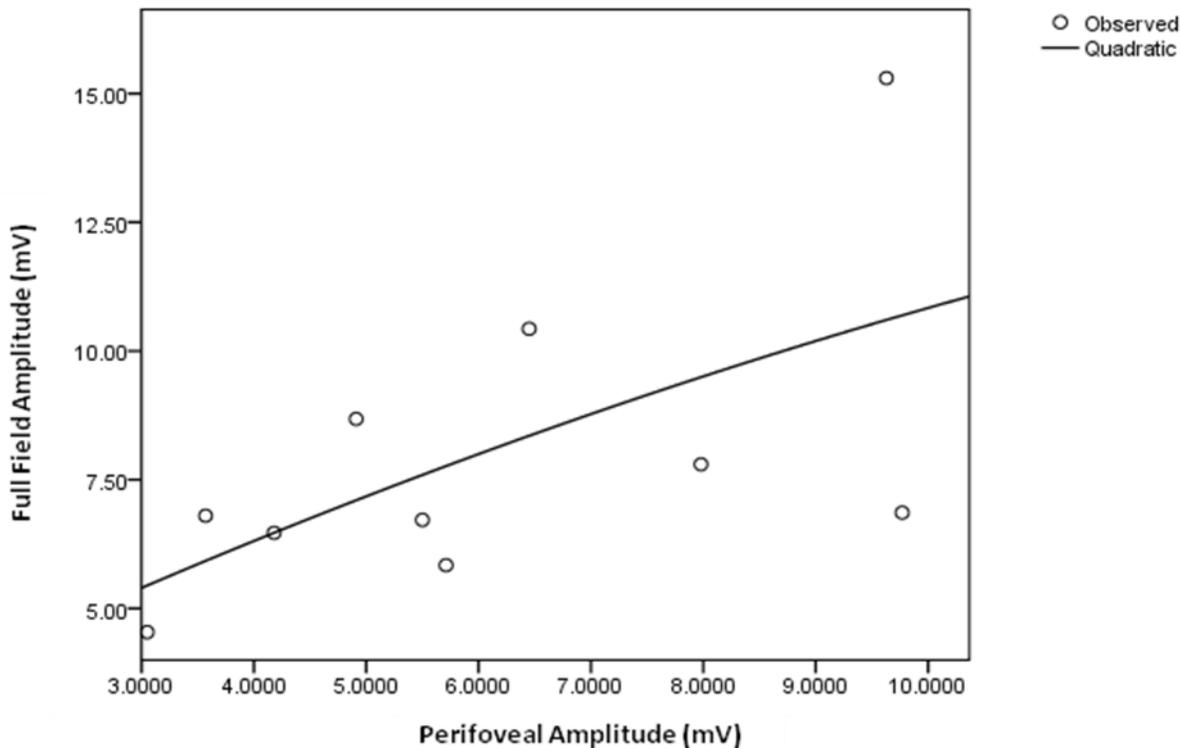
Figure 8 shows a comparison of the perifoveal amplitude (mV) derived from the large (1.78 degree) check size and the full field amplitude (mV) derived from the same large check size. A significant non-linear relationship did not occur when the perifoveal and full field targets were comprised of large checks.

However, when small checks were used in the foveal and perifoveal stimuli, a significant relationship existed between the fovea and perifovea and the full field stimulus (F = 4.85; p = 0.05; r^2 = 0.58 for the fovea; F = 7.11; p = 0.02; r^2 = 0.67 for the perifovea). See Figures 9 and 10 below.
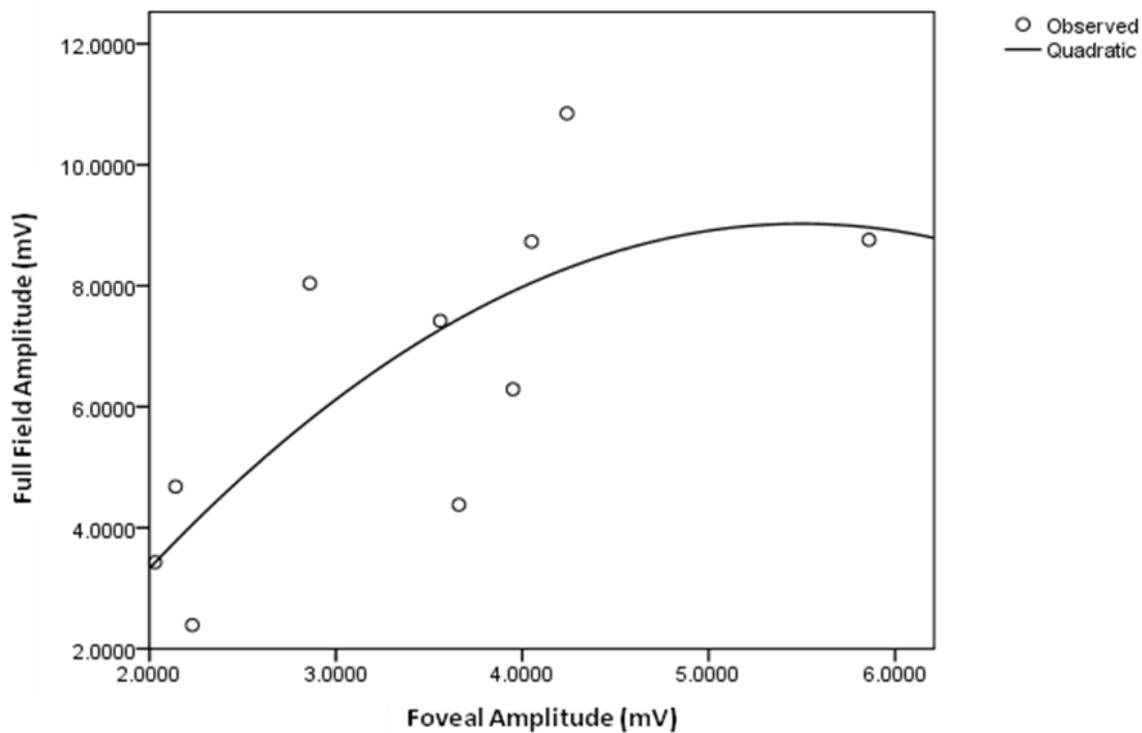
Figure 9 shows a comparison of the foveal amplitude (mV) derived from the small (0.23 degree) check size and the full field amplitude (mV) derived from the same small check size. A significant non-linear relationship exists between the foveal and full field amplitudes when small checks are projected into the stimulus targets.
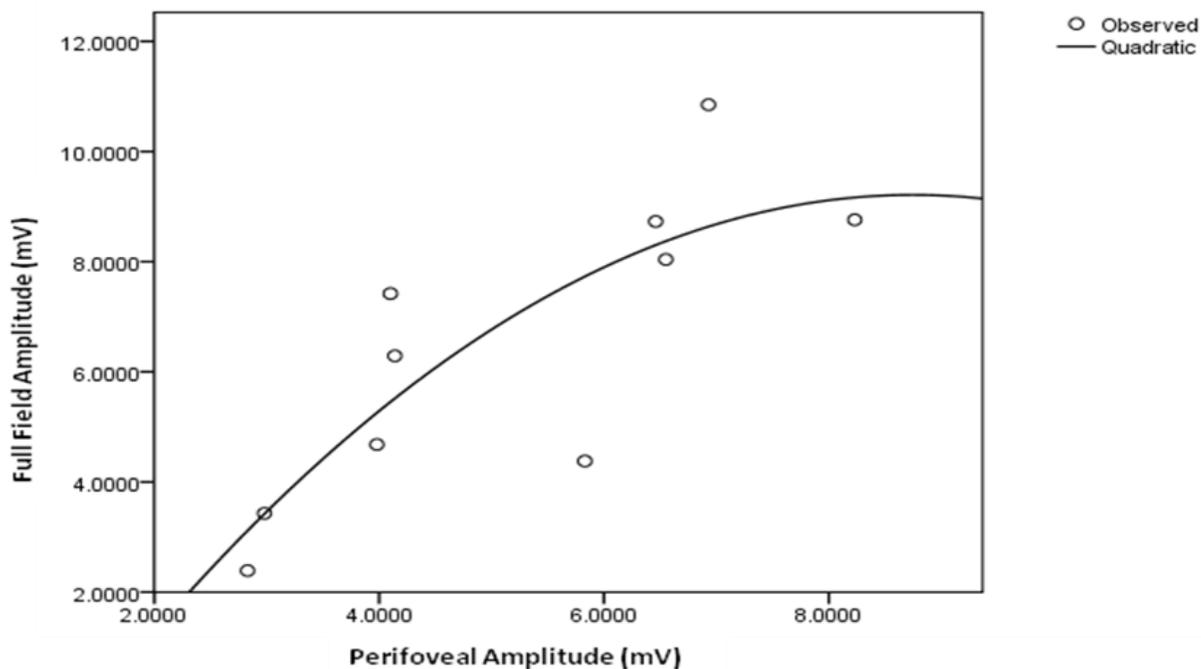
Figure 10 shows a comparison of the perifoveal amplitude (mV) derived from the small (0.23 degree) check size and the full field amplitude (mV) derived from the same small check size. A significant non-linear relationship exists between the perifoveal and full field amplitude when the stimulus targets are comprised of small checks.

Additional multiple regression analyses with SPSS software were performed

using the amplitudes of the fovea and perifovea as factors and the amplitude of the full

field target as the dependent variable to assess if the combined foveal and perifoveal

amplitudes could predict the amplitude of the full field stimulus. These analyses were

based on the amount of cortical area that is allocated to the photoreceptors of the

fovea and perifovea in order to have the same amount of retinal sampling.

Approximately 13 times more striate surface area is devoted to central retinal sampling

than peripheral retinal sampling (Azzopardi and Cowey, 1993); there are four times

more dLGN cells per ganglion cell afferent in the fovea than in the periphery (Connolly and Van Essen, 1984); and ganglion cells near the fovea are allocated three to six times more visual cortex tissue than those in the periphery (Azzopardi and Cowey, 1993). To perform the multiple regression analysis, the ratio of the foveal amplitude to the perifoveal amplitude was calculated using the factors 13x, 4x, and 6x for the striate, dLGN, and ganglion cells respectively. For example, calculation of the amplitudes using striate cells was:

13/14 (Foveal amplitude) + 1/14 (Perifoveal amplitude) = 1 (Full field amplitude).

Multiple regression analysis showed that the fovea and perifovea did not predict the full field stimulus, with the exception of the small check size (striate cells, F = 6.56; p = 0.03; r^2 = 0.55; dLGN, F = 6.56; p =0.02; r^2 = 0.55; ganglion cells, F = 6.61; p = 0.02; r^2 = 0.56). When the large check size (1.78 degrees) was used, the amplitudes of the fovea and perifovea were not predictive of the amplitude of the full field stimulus (striate cells, F = 2.80; p = 0.13; r^2 = 0.28; dLGN, F = 2.84; p = 0.13; r^2 = 0.29; ganglion cells, F = 2.81; p = 0.13; r^2 = 0.29). These values are shown in Table 7.

Table 7

Multiple Regression Statistic	Ganglion Cells (Small Checks)	dLGN Cells (Small Checks)	Striate Cells (Small Checks)	Ganglion Cells (Lg Checks)	dLGN Cells (Lg Checks)	Striate Cells (Lg Checks)
F Statistic	6.61	6.56	6.56	2.81	2.84	2.80
p - value	0.02	0.02	0.03	0.13	0.13	0.13
r^2 - value	0.56	0.55	0.55	0.29	0.29	0.28

*$p \leq 0.05$ is significant

Figures 11-16 show the graphs that had significant results (i.e., foveal and perifoveal amplitudes were predictive of the amplitude of the full field stimulus).
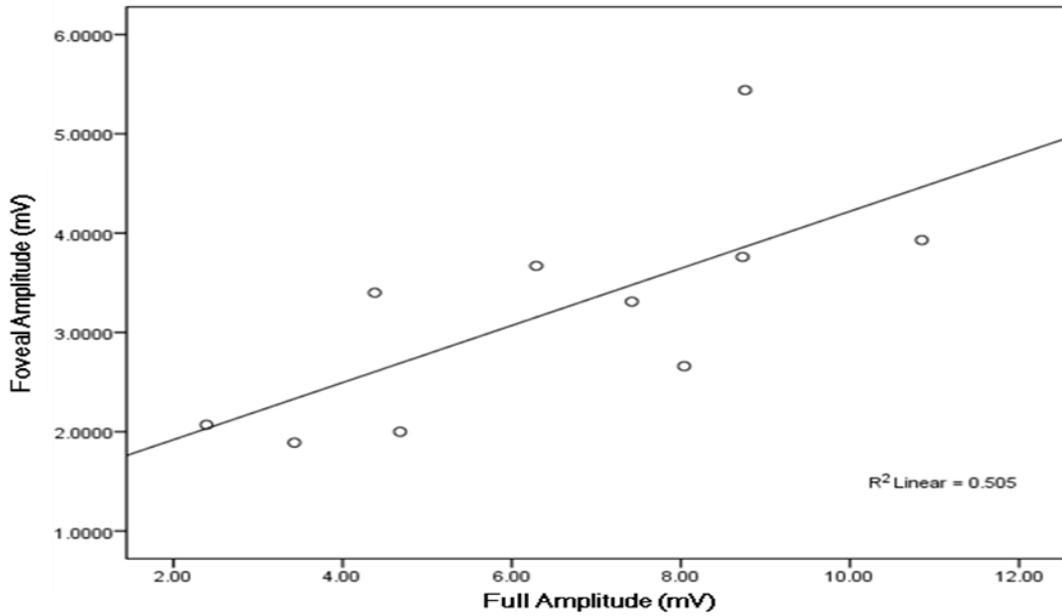
Figure 11 shows the full field amplitude and the foveal amplitude derived from using the small check size and striate cells.
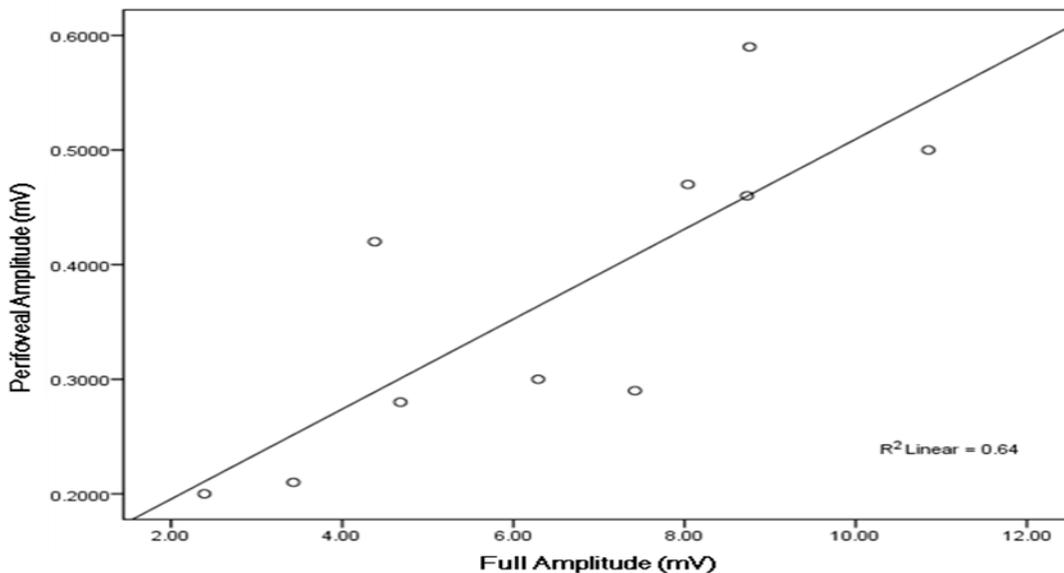
Figure 12 shows the full field amplitude and the perifoveal amplitude derived from using the small check size and striate cells. The amplitudes of the fovea and perifovea were predictive of the amplitude of the full field target (F=6.56; p=0.03; r^2=0.55).
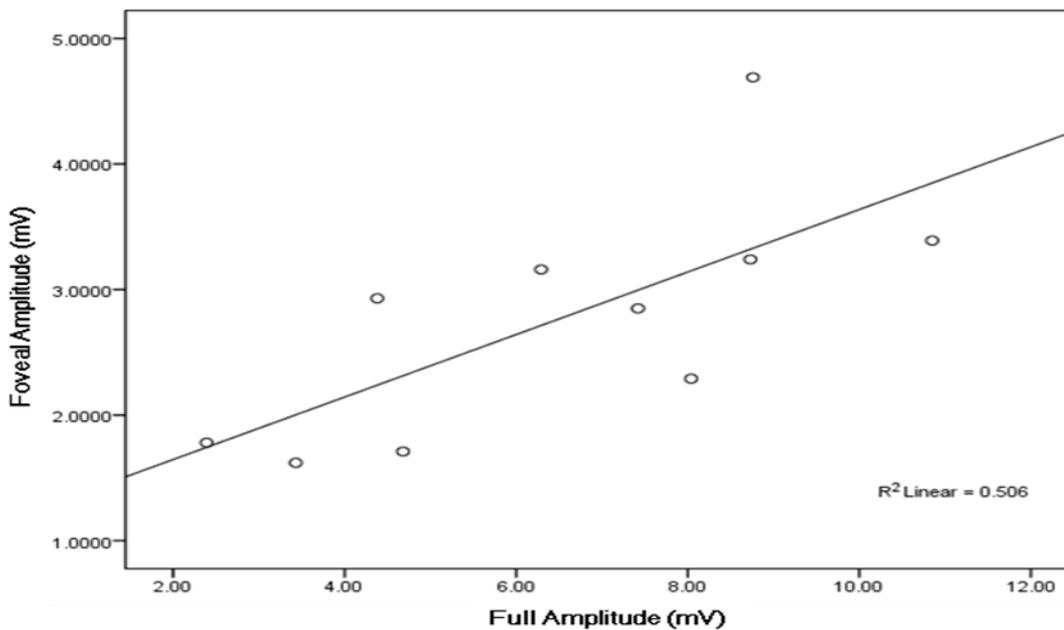
Figure 13 shows the full field amplitude and the foveal amplitude derived from using the small check size and dLGN cells.
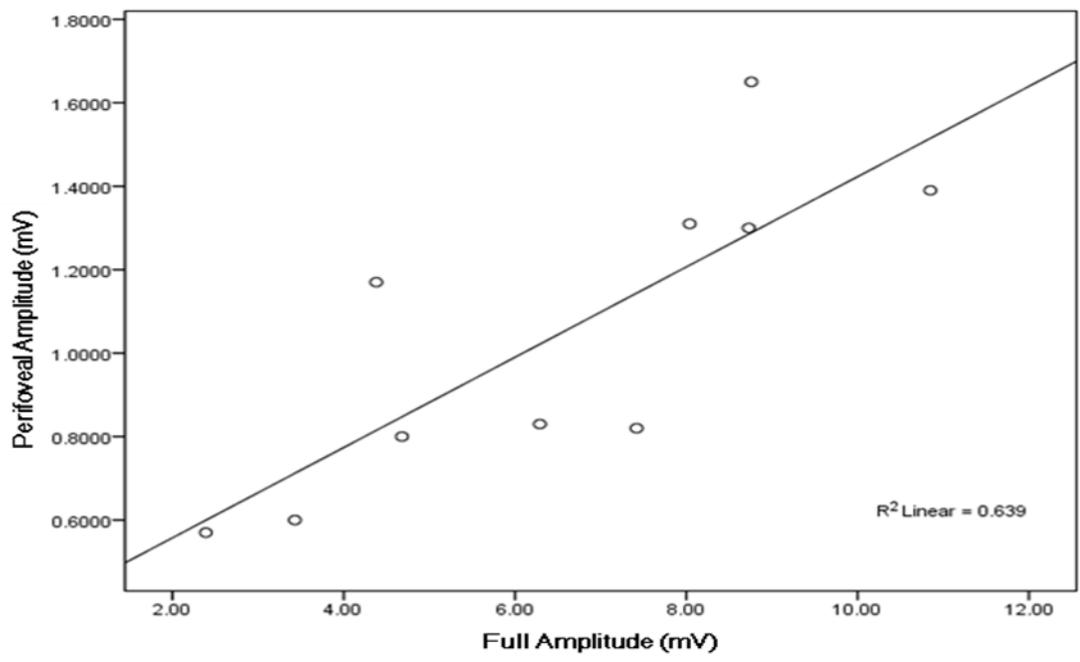
Figure 14 shows the full field amplitude and the perifoveal amplitude derived from using the small check size and dLGN cells. Perifoveal and foveal amplitudes were predictive of the full field amplitude (F=6.56; p=0.02; r^2=0.55).
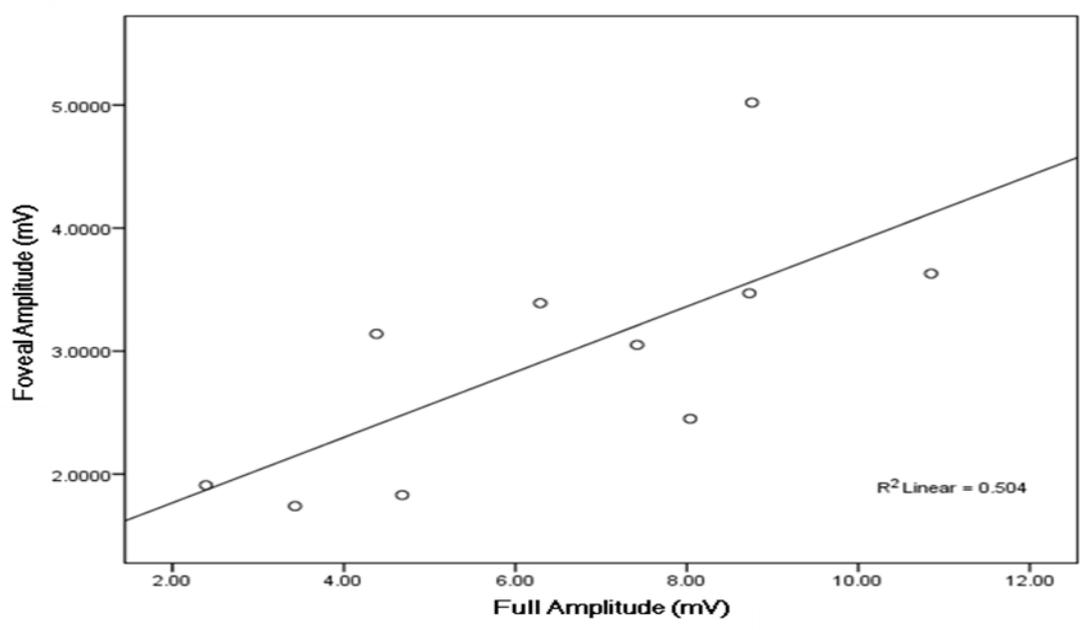
Figure 15 shows the full field amplitude and the foveal amplitude derived from using the small check size and ganglion cells.
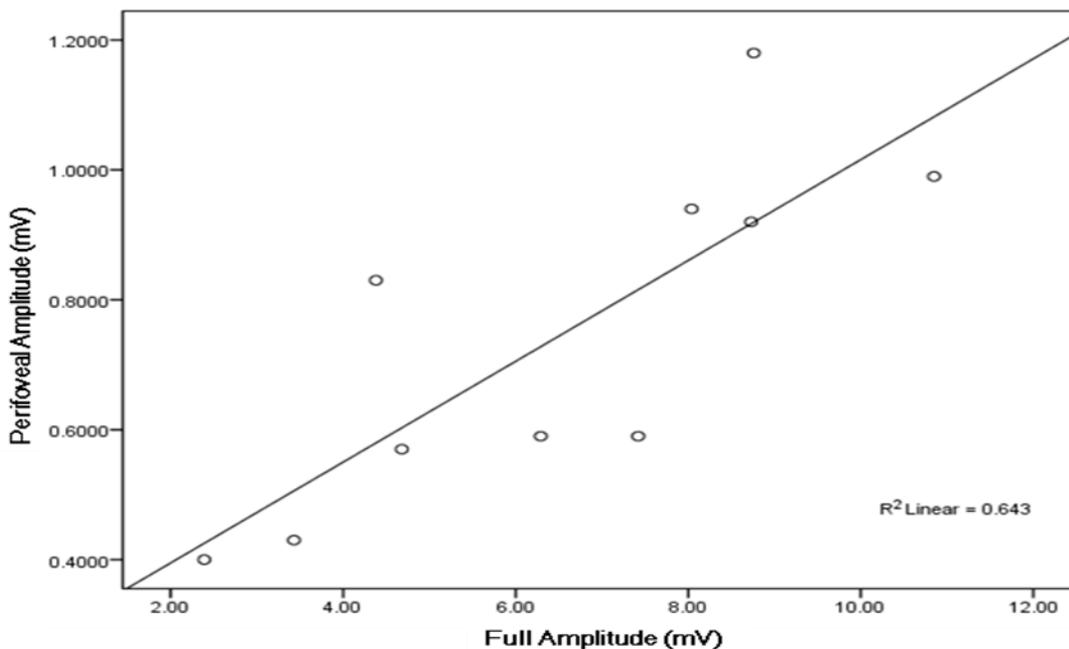
Figure 16 shows the full field amplitude and the perifoveal amplitude derived from using the small check size and ganglion cells. The amplitude of the full field target could be predicted from the foveal and perifoveal amplitudes (F=6.61; p=0.02; r^2=0.56).

DISCUSSION

Paradigms I and II involved assessing which stimulus check size (spatial frequency) would yield the fastest implicit time and the greatest amplitude. The hypothesis was that the fastest implicit time and highest amplitude would occur for stimuli in which both the stimulus field size and individual check size are scaled based on the cortical magnification factor. VEPs were recorded with a foveal target, a perifoveal annulus, and a full field target. The foveal target consisted of a two degree circle with a diameter of 3.6 cm; the perifoveal target, a circular ten degree annulus with an inner diameter of 3.6 cm and an outer diameter of 17.5 cm; and the full field target, a ten degree circle with a diameter of 17.5 cm. Different pattern VEP check sizes were

projected within the targets and implicit time and amplitude were assessed. Check sizes

of 1.78 or 0.23 degrees (0.24 cpd or 2.18 cpd respectively) were projected in the foveal,

perifoveal, and full field targets. An intermediate check size, 0.52 degrees (0.97 cpd),

was projected in the foveal target, and then scaled in size to 0.83 degrees (0.48 cpd) and

projected in the perifoveal target.

The size of the foveal target and the VEP pattern check size that were used to

preferentially stimulate the fovea are comparable to stimuli that have been used in

previous studies (Celesia, 1984; Meredith and Celesia, 1982; Baseler et al., 1994). The

ISCEV Standards recommend using a pattern VEP check size of 0.25 +/- 20% degree to

stimulate the fovea (Odom et al. 2009). VEP pattern sizes that range between 0.17 and

0.25 degrees preferentially stimulate the fovea (Celesia, 1984). Meredith and Celesia

(1982) conducted experiments that used a 2.3 degree foveal target size and Baseler et

al. (1994) used a 2 x 2 degree field. The size of the perifoveal target was M-scaled

(linear size was adjusted/increased based on the cortical magnification factor and the

foveal target size) and this was also performed in previous studies (Celesia, 1984;

Meredith and Celesia, 1982; Baseler, et al., 1994; Horton and Hoyt, 1991). To stimulate

the peripheral retina, the ISCEV Standards recommend using a pattern VEP check size of

1.0 +/- 20% degree (Odom et al. 2009).

The results obtained from N1 and P1 implicit time measurements of the fovea

and perifovea are in agreement to the predicted outcome of this study and to previous

studies (Meredith and Celesia, 1982; Baseler et al., 1994; Bassi, 2002). For the foveal

VEP responses, the scaled checks resulted in a faster implicit time for N1 (72.4 $\pm$ 5.3 ms)

compared to both the small checks (74.24 $\pm$ 5.0 ms) and the large checks (74.96 $\pm$ 4.0

ms). However, presentation of the scaled checks to the fovea did not yield the fastest

P1 implicit time, although the implicit times were very close between the scaled and the

small checks (scaled checks, 104.08 $\pm$ 4.0 ms; small checks, 103.84 $\pm$ 2.9 ms; and the

large checks, 111.12 $\pm$ 4.8 ms). The findings for the foveal implicit time were expected—

large checks yield the slowest implicit time and scaled or small checks yield the fastest

implicit times.

In the perifovea, the scaled checks did not produce the fastest N1 implicit time

(scaled checks, 72.96 $\pm$ 2.0 ms; small checks, 80.56 $\pm$ 2.8 ms; and large checks, 69.44 $\pm$

3.0 ms); but they did produce the fastest P1 implicit times (scaled checks, 100.24 $\pm$ 4.0

ms; small checks, 103.52 $\pm$ 2.0 ms; and large checks, 102.24 $\pm$ 3.0 ms). This finding

reflects dissociation between N1 and P1, which is not uncommon, because N1 and P1

have different origins. It is common to see a slowing in the P1 than N1; however, it is

not common to see a slowing of the N1 with a decrease in the implicit time of the P1. A

possible explanation for this finding could be: (1) N1 is affected by the level of

attentional demand and processing effort and the scaled check size required more

processing effort than the large check size; and (2) the receptive fields of the retina and

visual cortex were stimulated differently by the scaled and large VEP check sizes. The

overall findings for the perifoveal implicit times were expected—small checks yield the

slowest implicit time and scaled or large checks yield the fastest implicit times.

The findings for the foveal and perifoveal implicit times were expected; however,

possible bias and error could have been produced by how the N1, P1 values were

determined. The N1 and P1 values were determined by positioning the cursor on the nadir and peak of the VEP waveform. If the peak or nadir of a waveform is not very distinct (very wide peak or nadir), bias and error can be produced by misplacement of the cursor on the waveform. A cursor that is placed farther to the left on the waveform will imply a faster implicit time (if placed to the right, a slower implicit time).

Meredith and Celesia (1982) showed that at the fixation point, smaller fields and smaller checks could elicit an evoked potential, but increasingly larger fields and checks were needed as the stimulus was moved from the fixation point to the periphery—eight and fourteen degree eccentricity. At fixation, a field size of 0.11-0.34 degrees and a check size of 0.05 to 0.16 degrees could elicit an evoked potential. At eight degree eccentricity, the field size and check size needed to be increased in order to elicit a VEP response (3.0 to 3.45 degree field and a check size of 0.57 to 0.86 degrees). At fourteen degree eccentricity, an even larger field size and check size was required to elicit a VEP response (4.6 to 6.9 degree field and a check size of 1.15 to 2.12 degrees). A second experiment by Meredith and Celesia (1982) showed that retinal eccentricity had an effect on the optimal check size for a particular retinal location. At fixation, a check size of 0.57 degrees within a field size of 2.3 degrees was optimal--produced the highest response; followed by a check size of 2.55 degrees at 8 degrees eccentricity within a field size 7.68 degrees, and a check size of 3.46 degrees at 14 degree eccentricity within a field size of 13.67 degrees (Meredith and Celesia, 1982).

Bassi (2002) demonstrated that small checks at the fixation point and large checks in the periphery would yield a faster P1 latency time. Pattern VEP check sizes of

0.23 degrees and 0.91 degrees were presented in a two degree stimulus field at zero

degrees eccentricity, in an 8.5 degree stimulus field (perifoveal annulus), and in a full

field target that subtended 8.5 degrees. In the two degree stimulus field, the smaller

check size (0.23 degrees) produced the fastest P1 latency time, 110 $\pm$ 0.5 ms, compared

to the larger check size (0.91 degrees). The P1 latency time for the larger checks was

115 $\pm$ 1.0 ms. In the 8.5 degree perifoveal annulus, the larger check size (0.91 degrees)

produced the fastest P1 latency time, 105 $\pm$ 0.5 ms, compared to the smaller check size

which had a P1 latency time of 114 $\pm$ 0.5 ms. In the full field target, the larger check size

yielded the fastest P1 latency time, 109 $\pm$ 0.5 ms, compared to the smaller check size

(0.23 degrees or 2.18 cpd) that produced a P1 latency time of 114 $\pm$ 0.5 ms (Bassi, 2002).

The results of the amplitude measurements of the foveal VEP were not in

agreement with previous studies (Meredith and Celesia, 1982; Celesia, 1984; Baseler et

al., 1994; Odom et al., 2009). The greatest amplitude in the foveal VEP was generated

from the largest check size (4.55 mV) instead of the scaled (4.45 mV) or the smallest

(3.45 mV) check size. In the perifovea, the largest checks produced the greatest

amplitude (6.07 mV) compared to the scaled (5.75 mV) and the smallest (5.20 mV)

checks, and this finding is in agreement with other studies (Meredith and Celesia, 1982;

Celesia, 1984; Baseler et al., 1994; Odom et al., 2009).

Celesia (1984) showed that check sizes that range between 0.17 and 0.25

degrees preferentially stimulate the fovea. The ISCEV standards recommend using

check sizes that subtend a visual angle of 0.25 $\pm$ 20% degrees to best stimulate the fovea

(Odom et al., 2009). In the current experiment, a check size of 0.23 degrees (2.18 cpd)

was presented in the foveal target, yet it did not yield the highest amplitude. The

highest amplitude in the foveal target was actually produced by the large check size.

Perhaps, this result occurred for several reasons. First, the VEP may reflect something

other than, or different than, magnetic resonance imaging (MRI) and psychophysics

measurements of the cortical magnification factor. Secondly, the possibility of the

temporal presentation (1.8 Hz) in tandem with the check size may have affected the VEP

measures. If a lower temporal rate (<1.8 Hz) was used in the study, perhaps, the

expected result (smallest checks have the highest amplitude in the foveal target) would

have occurred due to the spatiotemporal tuning of foveal neurons. For future studies,

varying the temporal rate and VEP check size could be performed to explore spatial

temporal interactions on the VEPs. Third, the scaling of the overall stimulus size (field

size) of the foveal and perifoveal targets may have affected the VEP response. Scaling of

the stimuli was performed using the cortical magnification factor of Horton and Hoyt

(1991). Horton and Hoyt (1991) derived their cortical magnification factor by correlating

magnetic resonance imaging with visual field defects in patients with occipital lobe

lesions (Horton and Hoyt, 1991). Thus, using this cortical magnification factor

represents an anatomic scaling, which is different from a psychophysics scaling of

stimuli. If the overall stimuli fields and check sizes were scaled using a cortical

magnification factor derived from psychophysics or scaled based on receptive field size,

then maybe the results of the experiment would have been different. Lastly, could

there be a possibility of the large checks in the fovea producing a flash VEP result. There

is very little possibility of this occurring because each stimulus consisted of multiple

checks (even the smallest target had four checks within it). Secondly, Bassi (2002) used

a blur overlay of similar sized stimuli that eliminated any response. The flash VEP

implicit times and amplitudes are more robust at N2 and P2 implicit times, not at N1 and

P1 implicit times. In flash VEPs, N1 implicit time is at 40-50 ms; P1, at 60-70 ms; N2, 90

ms and P2 peaks at 120 ms. The standard amplitude of a flash VEP, measured from the

positive P2 peak to the preceding negative N2 peak, is 4.3 µV (Odom et al., 2009).

Amplitudes derived from the perifoveal stimulus were expected—larger checks

produced the highest amplitude and smaller checks produced the lowest amplitudes.

These results were expected and Meredith and Celesia (1982) showed that larger check

sizes were optimal (produced the highest amplitude) as a stimulus is moved from

fixation to an eccentric location. At 8 degree eccentricity, a check size of 2.55 degrees,

and at 14 degree eccentricity, a check size of 3.46 degrees produced the highest VEP

amplitude.

Paradigm III was conducted to examine the second hypothesis--cortical VEP

amplitudes generated from the foveal and perifoveal (annulus) stimulus targets can be

used to estimate the amplitude of the full field target. Results of Paradigm III showed

that the cortical VEP amplitudes generated from the two degree target and the ten

degree annuli could not be used to predict the VEP amplitude of the ten degree (full

field) target, with the exception of the small checks. A comparison of the effect sizes in

the linear ($r^2 = 0.55$) and nonlinear ($r^2 = 0.58$ for the fovea; $r^2 = 0.67$ for the perifovea)

regression analyses showed that the nonlinear regression analysis was better at

predicting this outcome. The linear regression and the nonlinear regression analyses

revealed that the amplitude of the VEP generated from the ten degree annuli was a stronger predictor of the amplitude of the full field stimulus rather than the amplitude of the VEP generated from the two degree stimulus target. This is an unexpected result. Earlier studies have shown that the fovea comprises only 0.01% of the retina area, but takes up a large amount of the visual cortex--approximately eight percent (Engel, Glover and Wandell, 1997; Horton and Hoyt, 1991; Tootell et al., 1996). As visual targets are moved outside the fovea, the amount of cortical space allocated for the peripheral retina drastically reduces (Celesia and Brigell, 1999; Mishkin et al., 1983; Smith et al., 2001). Experiments conducted by Harter (1970) showed that eccentricity of stimulation influenced the VEP response amplitude, with the greater responses being obtained between 0 to 1.5 degrees eccentricity and with a check size of 0.25 to 0.50 degrees. The VEP waveform was only influenced by check size when the stimulus was projected centrally—0 to 7.5 degrees (Harter 1970).

The outcome of this experiment may be attributed to several factors. First, based on the size of the smallest check (0.23 degrees or 2.18 cpd), the perifovea had the most contribution because the small checks were relatively large when compared to resolution acuity (i.e., the perifovea was still able to resolve this check size relatively well). If the 0.23 degree checks (2.18 cpd) were smaller, the fovea probably would have been the strongest predictor of the full field amplitude because the perifovea would have been unable to resolve the spatial frequency of the smaller check size. Secondly, the cortical magnification factor that was used in this experiment was based on magnetic resonance imaging measures (Horton and Hoyt, 1991), rather than

psychophysical measures. Perhaps, if the overall sizes of the stimuli were re-computed/scaled using a cortical magnification factor that was derived from a psychophysical measure, the outcome may be similar to other studies (Meredith and Celesia, 1982; Celesia, 1984; Baseler et al., 1994; Harter, 1970). Lastly, other visual areas contribute to the VEP response. The VEP waveform is produced from the sums of multiple sources of separate anatomical origins and scaling a stimulus cannot completely preclude the possibility of signal cancellation (Baseler et al. 1994).

CONCLUSION

The aim of the present study was to examine how check size (spatial frequency) and retinal eccentricity affect VEP implicit times and amplitudes. Four VEP check sizes were projected into the foveal and perifoveal targets—1.78, 0.23, 0.52, and 0.83 degrees. The first hypothesis was that the fastest implicit time and highest amplitude would occur for stimuli in which both the stimulus field size and individual check size are scaled based on the cortical magnification factor. The results of this study demonstrated that M-scaling the overall size of the stimulus targets, projecting smaller checks in the fovea and larger checks in the perifovea would yield faster N1 and P1 implicit times. The most novel findings were obtained when scaled checks (0.52 and 0.83 degrees) were projected in the stimulus targets. In the foveal target, the scaled checks produced the fastest N1 implicit time but did not yield the fastest P1 implicit time. The highest amplitude derived from the foveal target was produced by the larger check size rather than the small or scaled check sizes. In the perifovea, the scaled

checks produced the fastest P1 implicit time, but did not produce the fastest N1 implicit time. Amplitudes derived from the perifoveal stimulus were expected—larger checks produced the highest amplitude.

The second hypothesis was that cortical VEP amplitudes generated from the foveal and perifoveal (annulus) stimulus targets can be used to estimate the amplitude of the full field target. Results showed that cortical VEP amplitudes could not be used to predict the VEP amplitude of the full field target, with the exception of the small checks (0.23 degrees). Linear and nonlinear regression analyses revealed that the strongest predictor of the full field amplitude was the amplitude produced from the perifoveal target, not the foveal target. This is an intriguing finding because it is in contradiction to earlier studies that have shown that the strongest contribution to the VEP response amplitude is from the fovea (Chiappa, 1990; Harter, 1970; Meredith and Celesia, 1982; Celesia, 1984).

These findings suggest that the VEP response may reflect something other than or different than MRI and psychophysical measurements of the cortical magnification factor. In addition, other visual areas contribute to the VEP response, and stimulus properties such as check size, eccentricity, contrast and temporal frequency may be processed differently in these visual areas. Results of this study have implications for the clinical use of VEPs. They imply that a single stimulus (check size) is not optimal for all measures (implicit time and amplitude) and a complex interaction occurs between visual targets and responses.

For future studies, using a cortical magnification factor derived from psychophysical measures (or scaling stimuli on the basis of receptive field size) in tandem with different check sizes would be relevant in assessing whether cortical magnification can be applied to VEP measures.

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Appendix A

SUBJECT #1- N1, P1

Table A1

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	56.8	68.8	64.8	76.8	71.2	71.2
P1 (ms)	114.4	109.6	113.6	100.8	90.4	104.0
Amplitude(µV)	5.86	4.12	6.61	8.23	8.09	6.45

Table A1 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
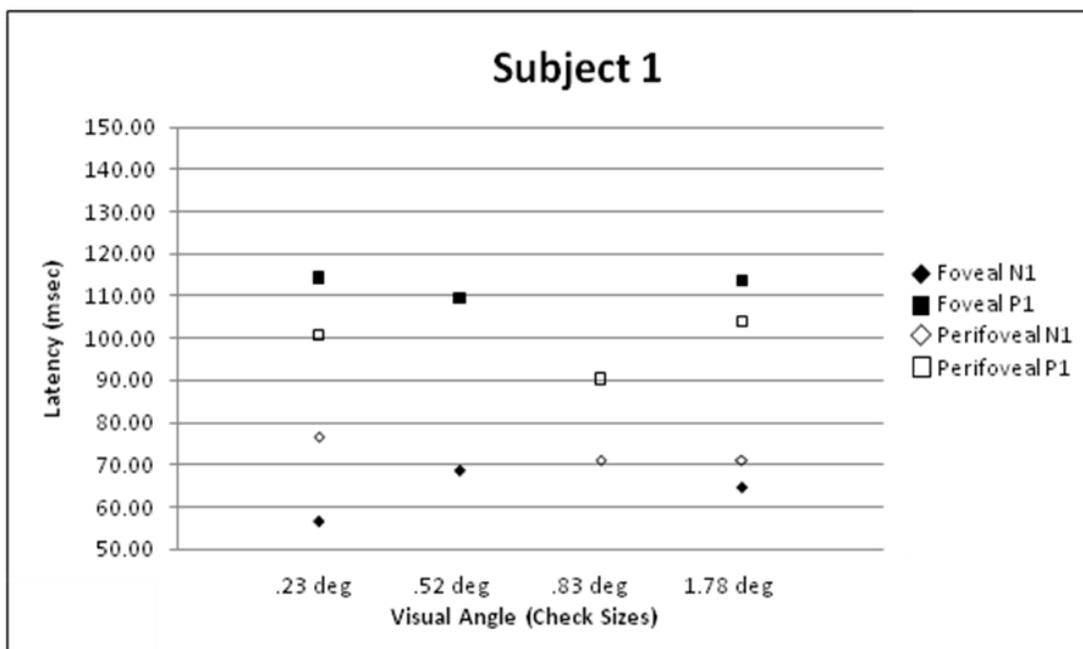
Figure 1a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occured with the 0.23 deg checks in the fovea, and the fastest P1 implicit time occured with the 0.83 checks in the perifovea.
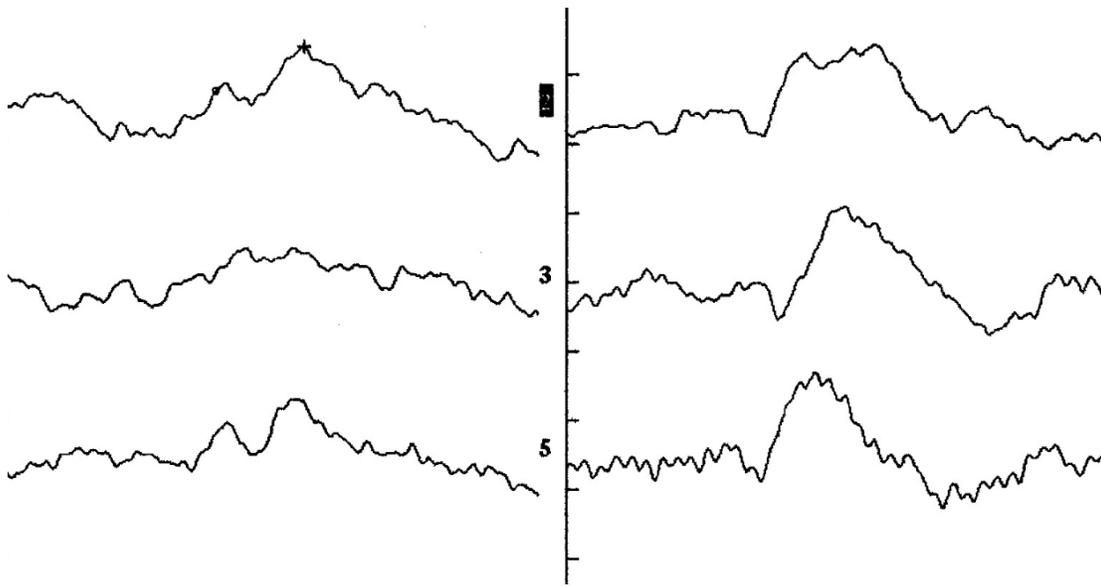
Figure 1b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), small (middle), and scaled (bottom)
checks

SUBJECT #2 – N1, P1

Table A2

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	77.6	76.8	77.6	80.8	69.6	69.6
P1 (ms)	96.0	100.8	95.2	99.2	100.8	99.2
Amplitude (µV)	2.23	2.77	1.37	2.83	4.67	4.18

Table A2 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
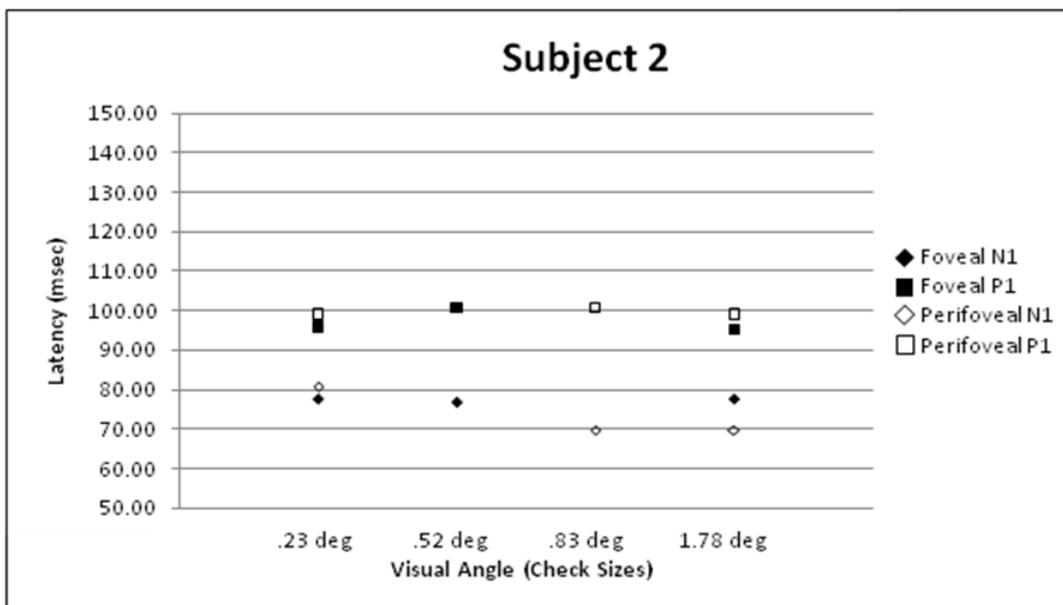
Figure 2a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occured with the 0.83 and 1.78 deg checks in the perifovea, and the fastest P1 implicit time occured with the 1.78 deg checks in the fovea.
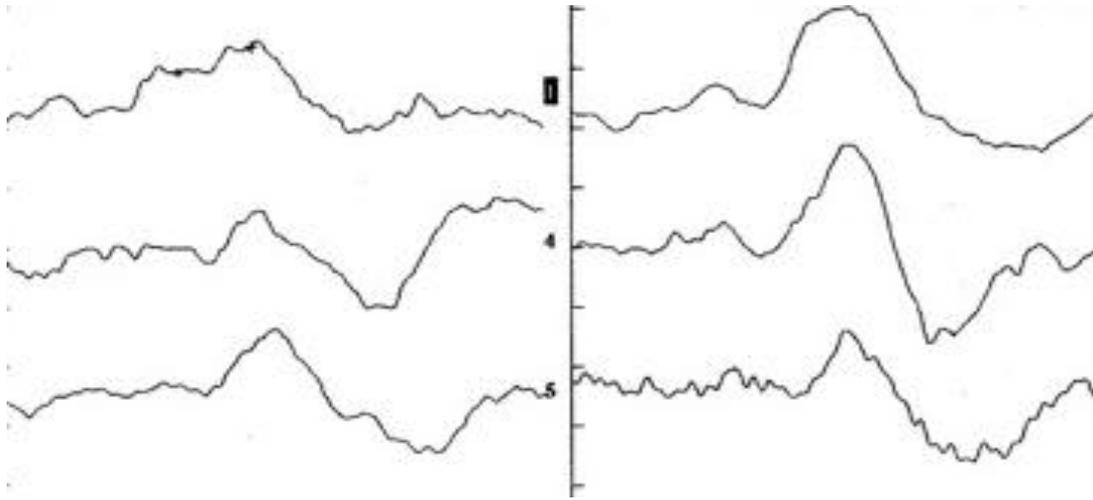
Figure 2b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), scaled (middle), and small (bottom) checks

SUBJECT #3 – N1, P1

Table A3

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	84.0	92.0	65.6	78.4	68.0	64.0
P1 (ms)	108.8	106.4	112.8	108.8	92.8	99.2
Amplitude (μV)	4.24	3.23	8.61	6.93	7.15	9.77

Table A3 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
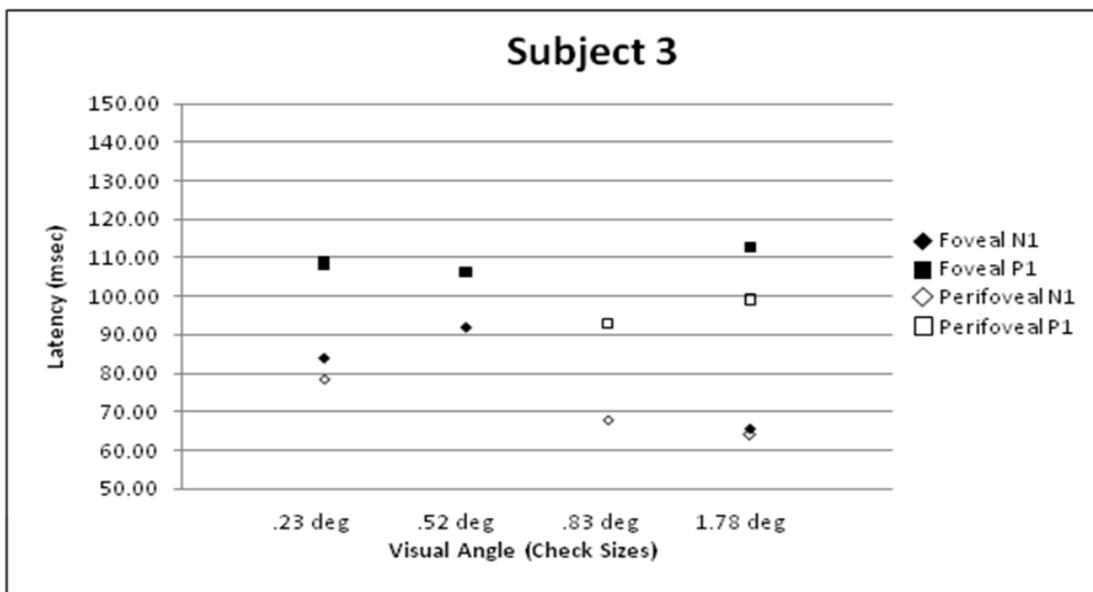
Figure 3a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occurred with the 1.78 deg checks in the perifovea, and the fastest P1 implicit time occurred with the 0.83 deg checks in perifovea. Note that the perifoveal and foveal P1 values for 0.23 deg checks are the same and are plotted on top of each other.
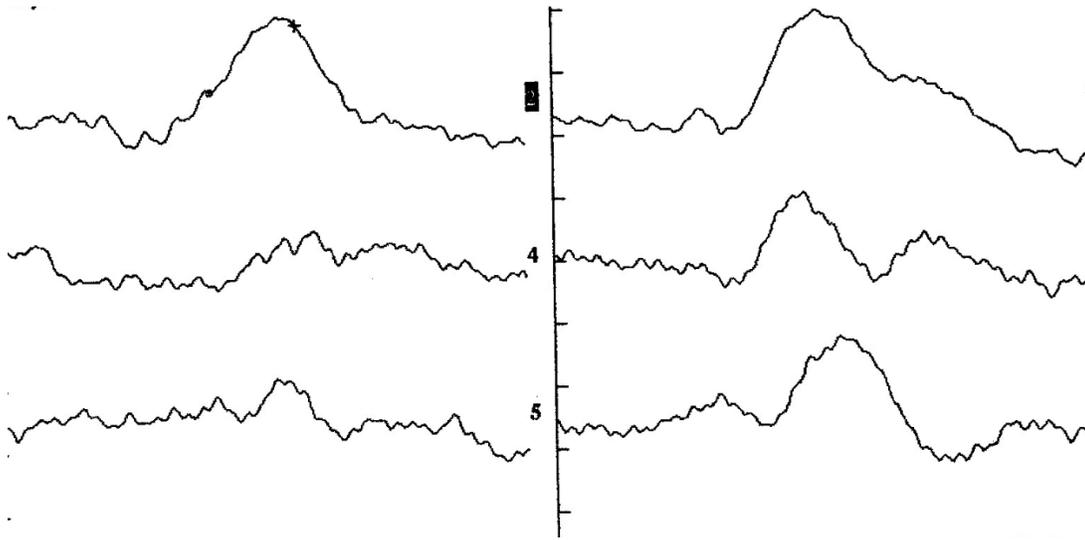
Figure 3b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), scaled (middle), and small (bottom) checks

SUBJECT #4 – N1, P1

Table A4

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	63.2	64.8	70.4	81.6	71.2	68.8
P1 (ms)	96.0	103.2	110.4	104.0	102.4	104.8
Amplitude (µV)	4.05	7.14	8.49	6.46	7.61	9.63

Table A4 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
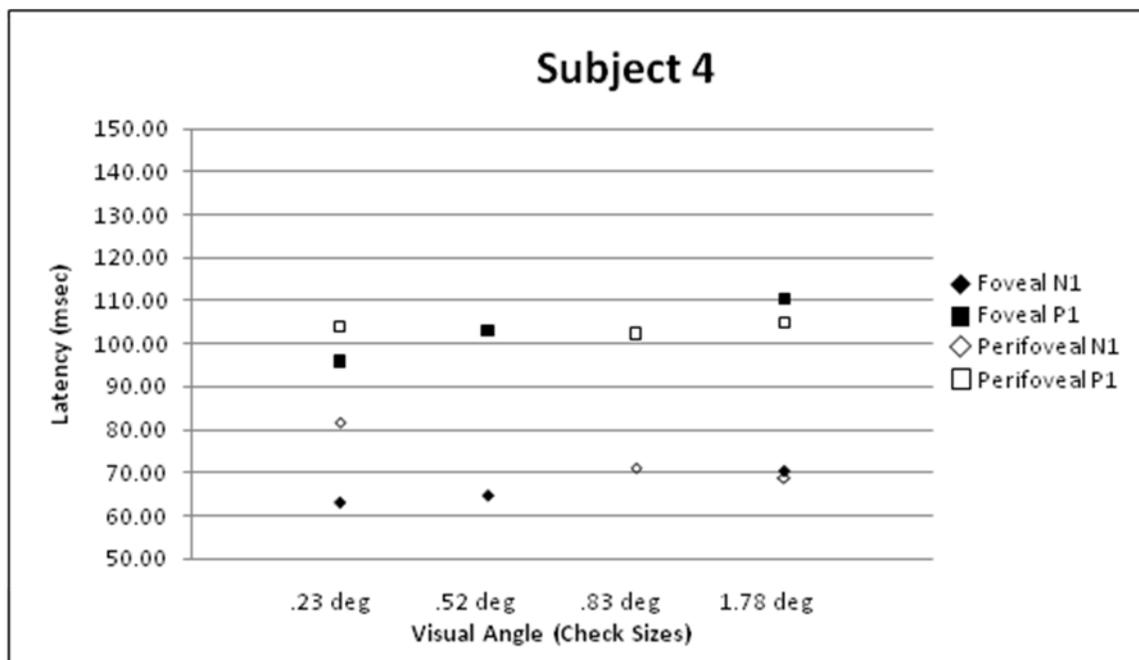
Figure 4a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 and P1 implicit times occurred with 0.23 deg checks in the fovea.
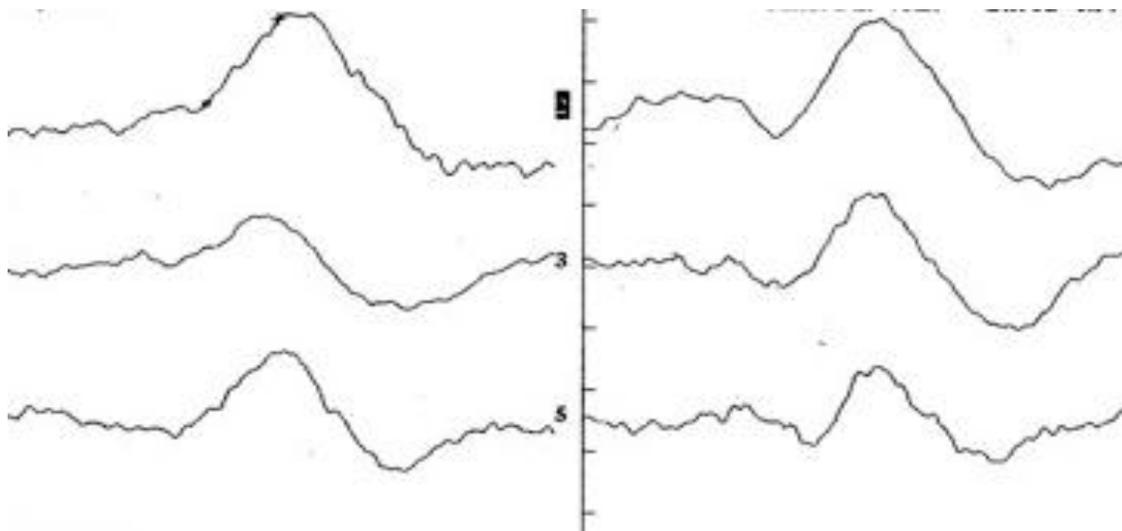
Figure 4b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), scaled (middle), and small (bottom) checks

SUBJECT #5 – N1, P1

Table A5

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	77.6	72.0	79.2	82.4	72.0	73.6
P1 (ms)	100.0	100.8	116.0	101.6	93.6	90.4
Amplitude (µV)	2.03	3.43	3.37	2.98	4.19	3.05

Table A5 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
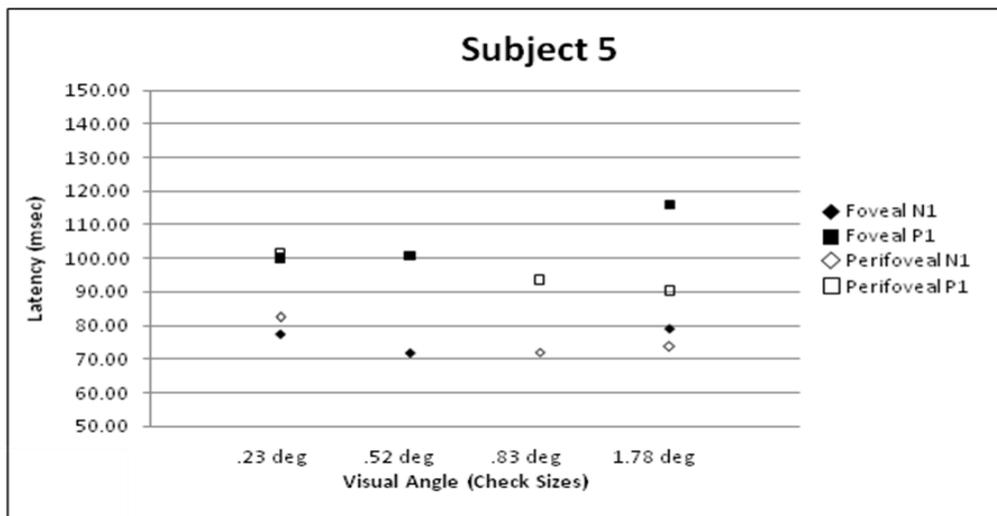
Figure 5a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occurred with 0.52 deg checks in the fovea and 0.83 deg checks in the perifovea, and the fastest P1 implicit time occurred with 1.78 deg checks in the perifovea.
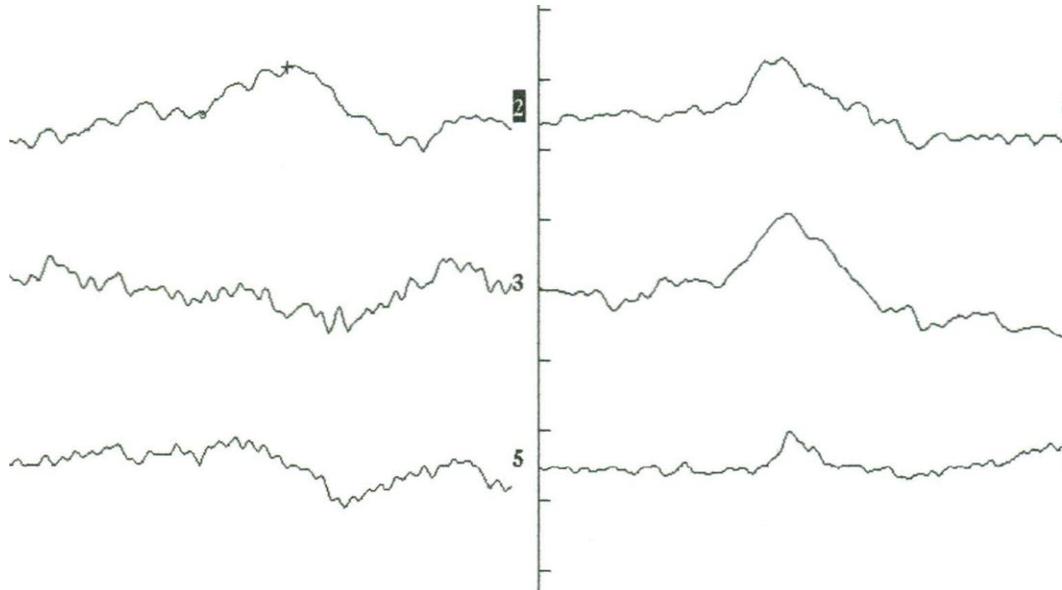
Figure 5b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), scaled (middle), and small (bottom) checks

SUBJECT #6 – N1, P1

Table A6

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	79.2	75.2	71.2	87.2	74.4	64.0
P1 (ms)	103.2	111.2	104.8	109.6	97.6	98.4
Amplitude (µV)	2.14	3.84	4.38	3.98	3.29	3.57

Table A6 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
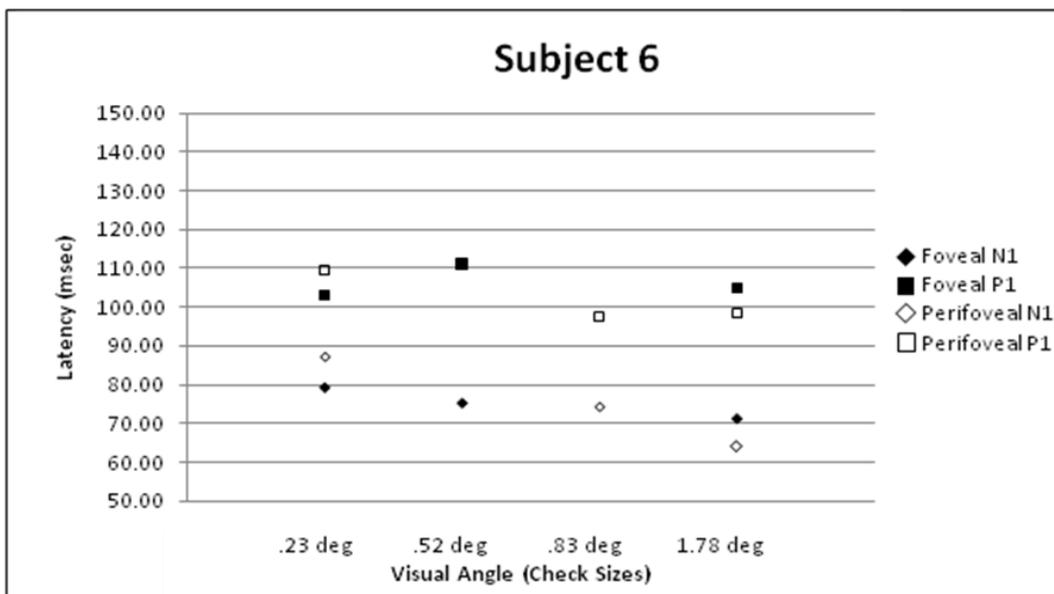
Figure 6a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occurred with 1.78 deg checks in the perifovea, and the fastest P1 implicit time occurred with 0.83 deg checks in the perifovea.
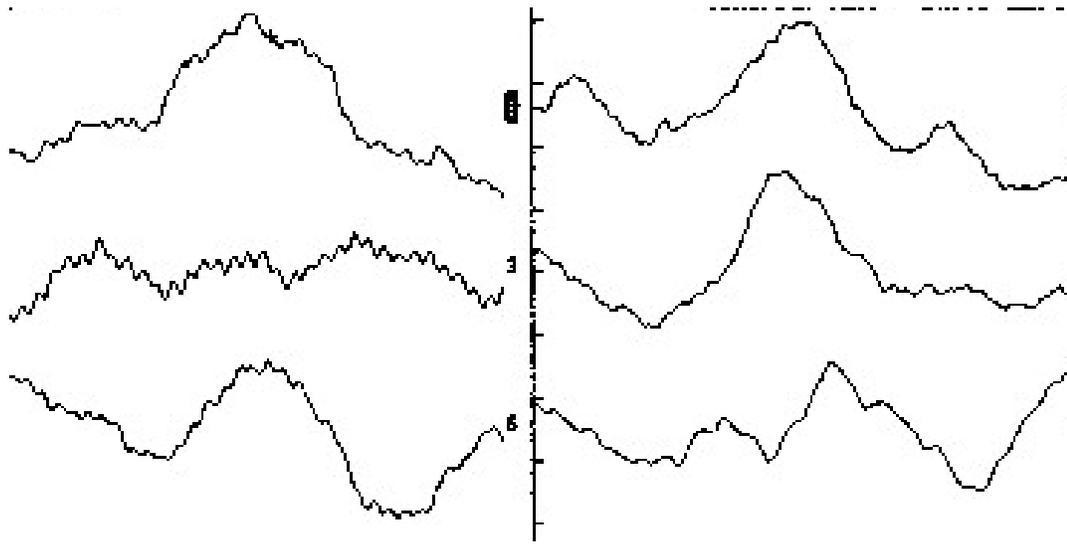
Figure 6b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), scaled (middle), and small (bottom) checks

SUBJECT #7 – N1, P1

Table A7

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	82.4	79.2	79.2	88.0	84.8	77.6
P1 (ms)	110.4	108.8	107.2	110.4	108.8	107.2
Amplitude (µV)	3.56	4.87	3.72	4.10	4.14	4.91

Table A7 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
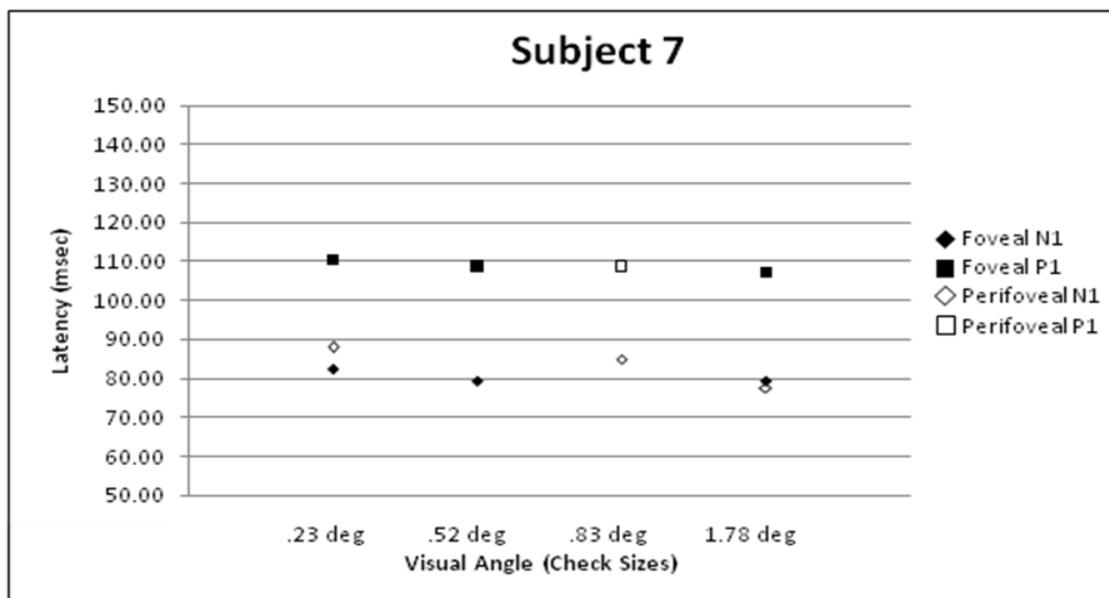
Figure 7a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occurred with 1.78 deg checks in the perifovea, and the fastest P1 implicit time occurred with 1.78 deg checks in the fovea and perifovea. Note that the foveal and perifoveal P1 values for the 0.23 and 1.78 deg checks are the same and are plotted on top of each other.
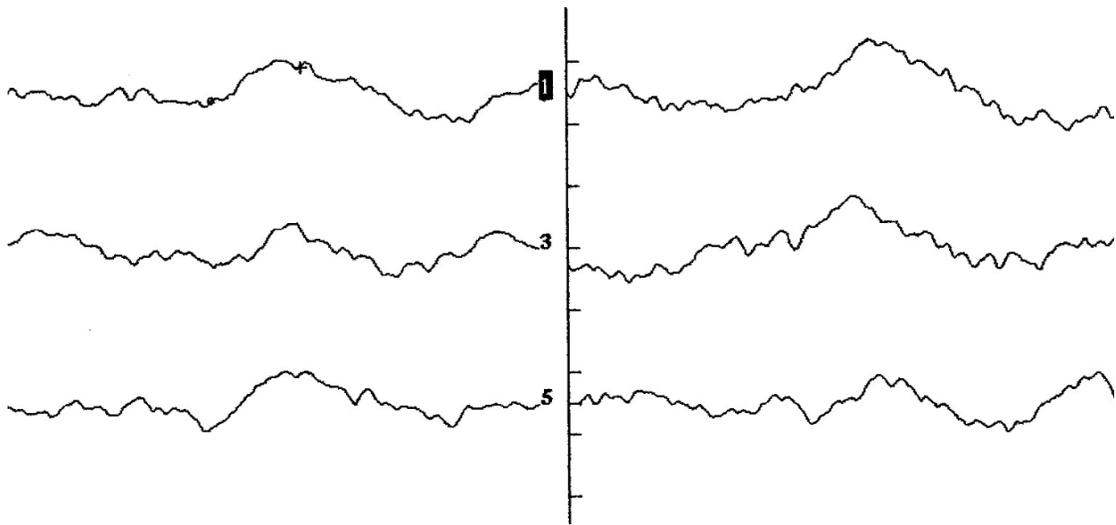
Figure 7b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), small (middle), and scaled (bottom) checks

SUBJECT #8 – N1, P1

Table A8

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	77.6	72.8	72.8	77.6	72.8	65.6
P1 (ms)	109.6	107.2	113.6	100.0	110.4	100.8
Amplitude (μV)	2.86	3.87	3.08	6.55	5.27	5.71

Table A8 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
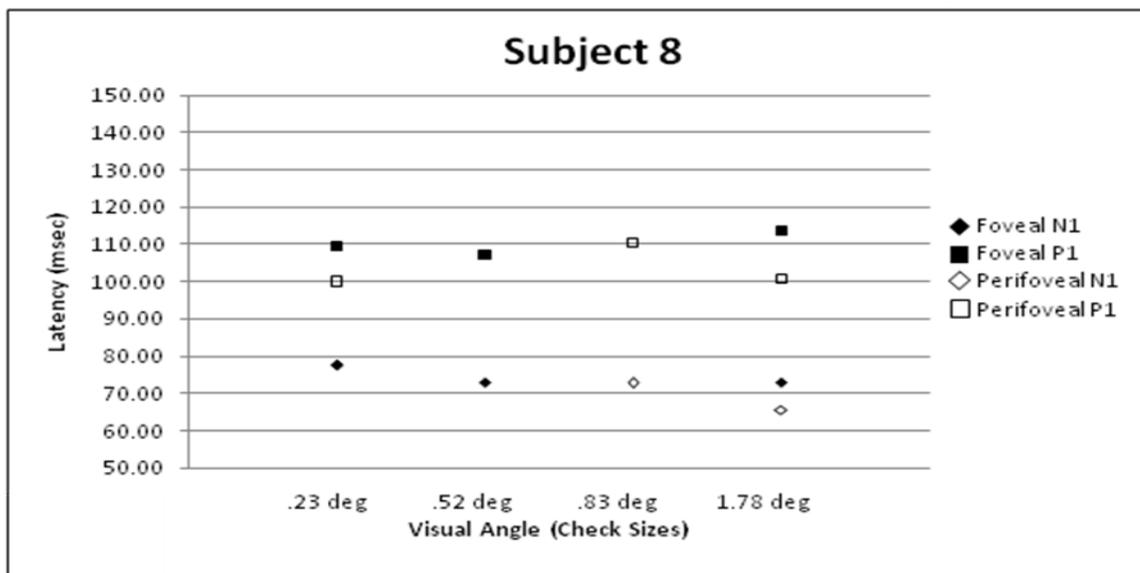
Figure 8a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occured with 1.78 deg checks in the perifovea, and the fastest P1 implicit time occurred with 0.23 deg checks in the perifovea. Note that the foveal and perifoveal N1 values are the same and are plotted on top of each other.
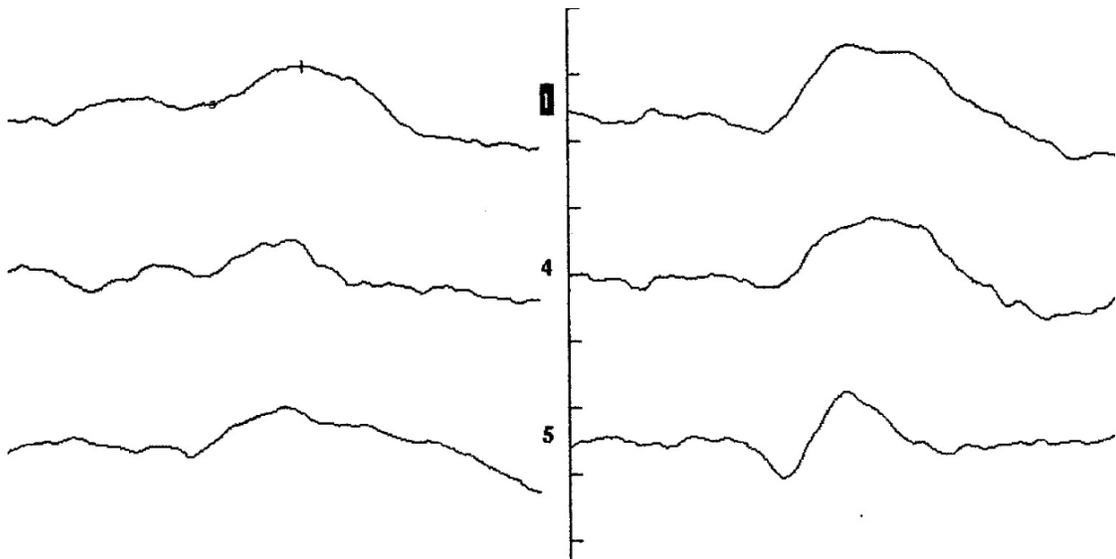
Figure 8b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), small (middle), and scaled (bottom) checks

SUBJECT #9 – N1, P1

Table A9

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	76.8	67.2	91.2	68.8	74.4	66.4
P1 (ms)	100.0	93.6	128.0	97.6	108.0	112.8
Amplitude (µV)	3.95	5.8	3.26	4.14	6.79	7.98

Table A9 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
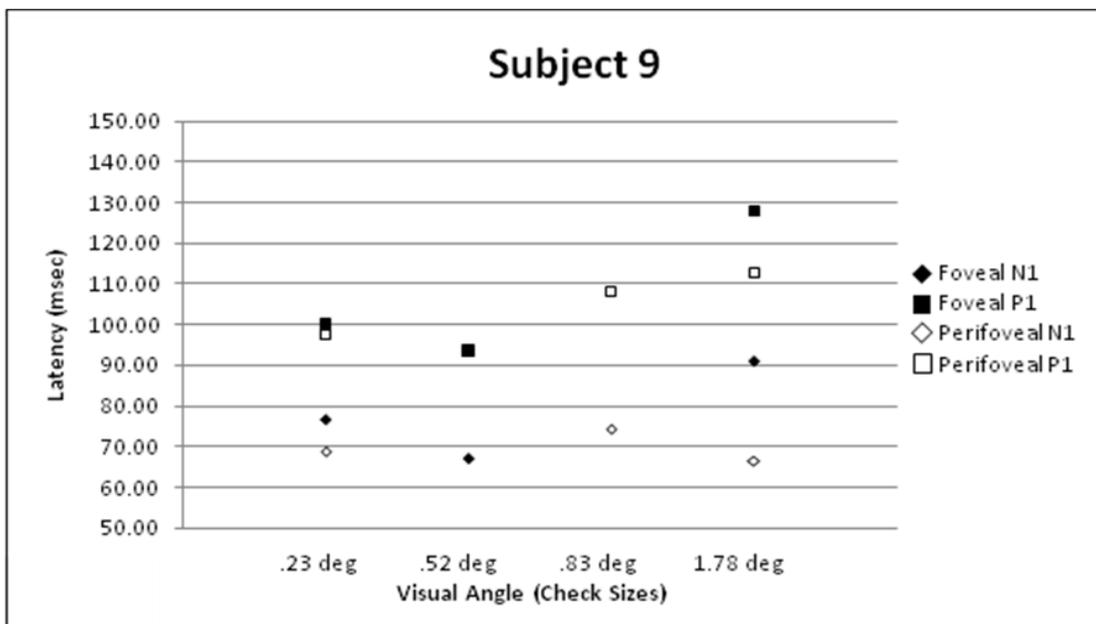
Figure 9a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occurred with 1.78 deg checks in the perifovea, and the fastest P1 implicit time occurred with 0.52 deg checks in the fovea.
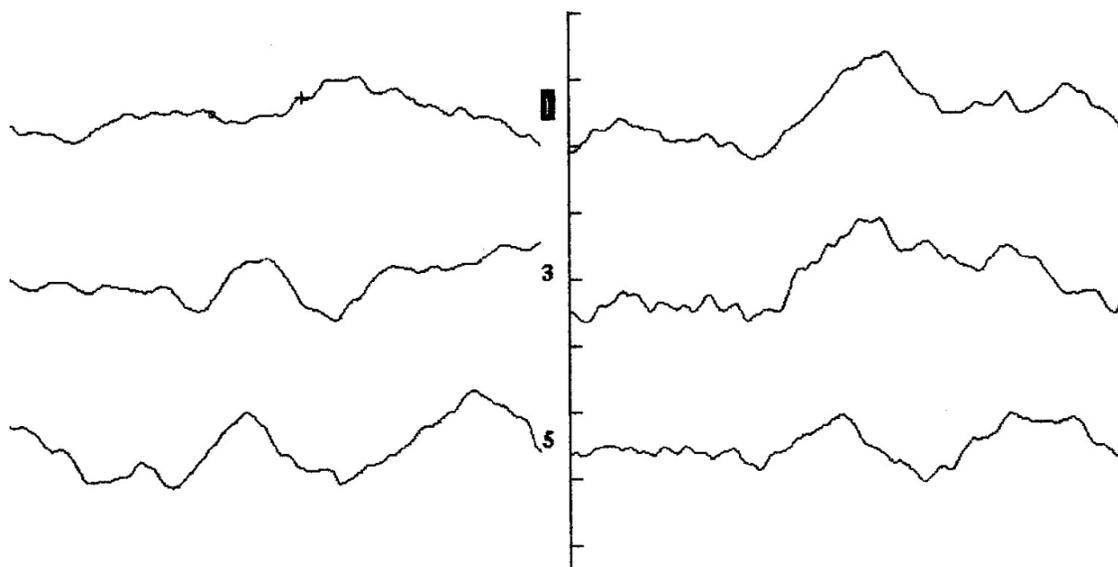
Figure 9b: Foveal waveforms (left side) of large (top), small (middle), and scaled (bottom) checks and Perifoveal waveforms (right side) of large (top), small (middle), and scaled (bottom) checks

SUBJECT #10 – N1, P1

Table A10

VEP Parameters	Fovea 0.23 deg Check size	Fovea 0.52 deg Check size	Fovea 1.78 deg Check size	Perifovea 0.23 deg Check size	Perifovea 0.83 deg Check size	Perifovea 1.78 deg Check size
N1 (ms)	67.2	55.2	77.6	84.0	71.2	73.6
P1 (ms)	100.0	99.2	109.6	102.4	98.4	104.0
Amplitude (µV)	3.66	5.4	2.65	5.83	6.28	5.5

Table A10 shows the N1, P1, and Amplitude values when different size checks were projected into the foveal and perifoveal targets.
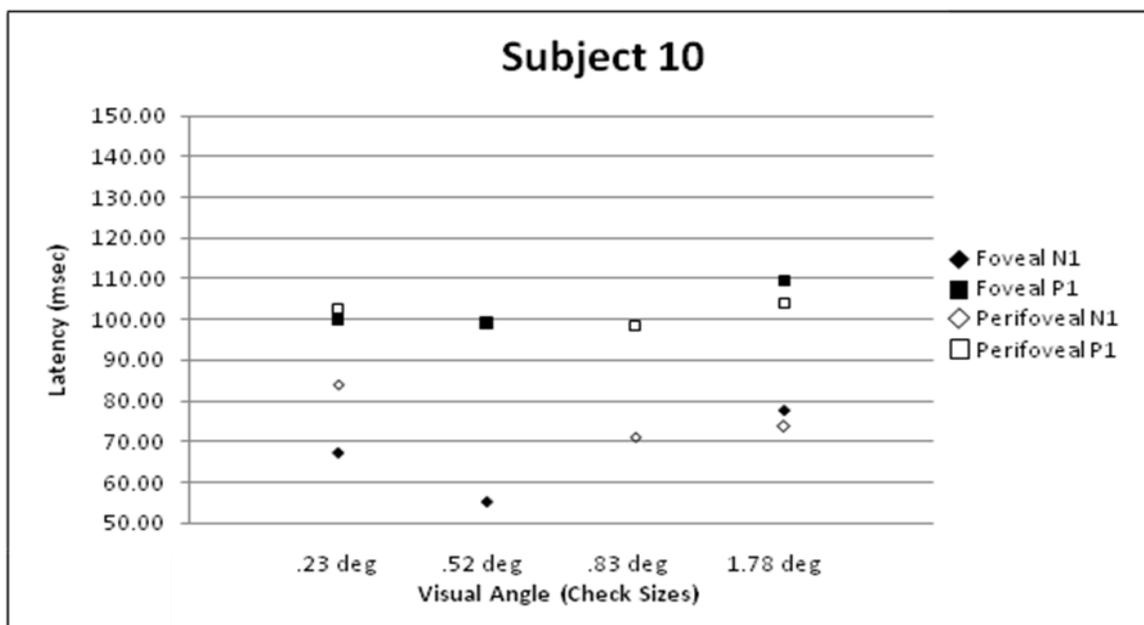
Figure 10a: Foveal and perifoveal latency (N1, P1) when different check sizes were projected into stimuli. The fastest N1 implicit time occurred with 0.52 deg checks in the fovea, and the fastest P1 implicit time occurred with 0.83 deg checks in the perifovea.
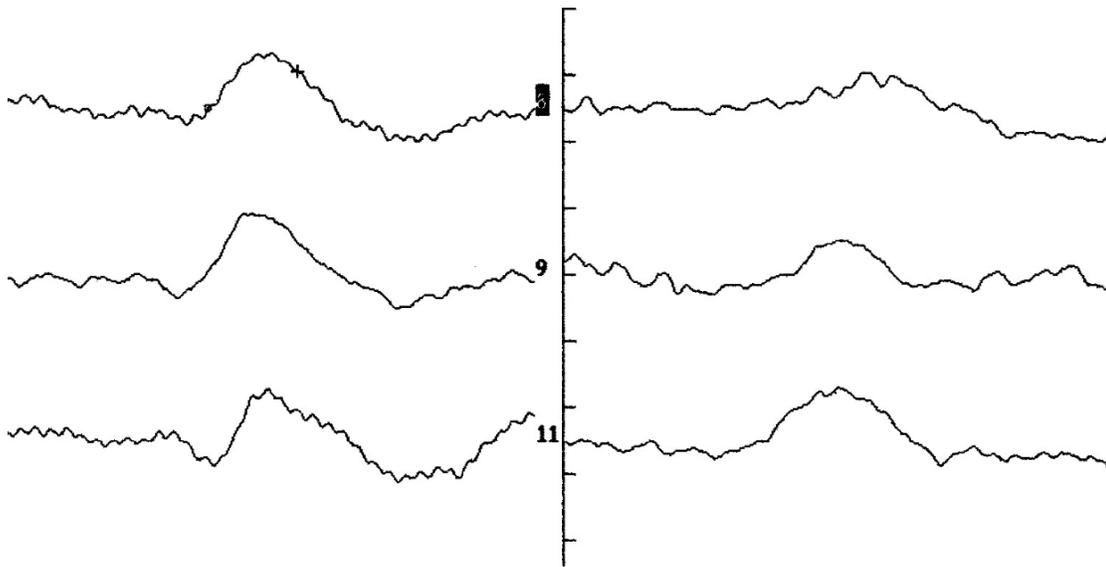
Figure 10b: Perifoveal waveforms (left side) of large (top), scaled (middle), and small (bottom) checks and Foveal waveforms (right side) of large (top), small (middle), and scaled (bottom) checks

SUMMARY GRAPHS- N1, P1, AMPLITUDE
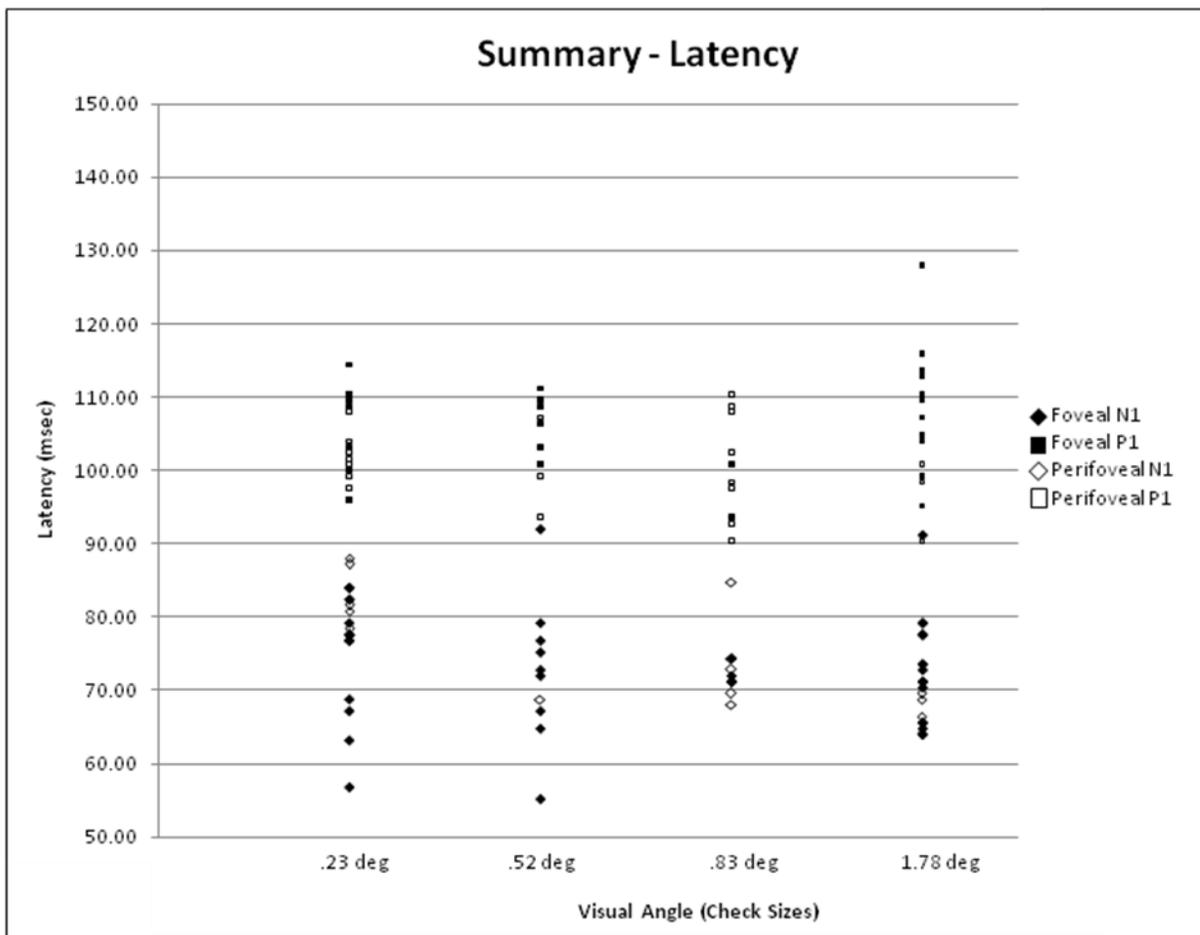
Figure 11a: Foveal and perifoveal latency (N1, P1) of all 10 subjects when different check sizes were projected into stimuli. The fastest N1 implicit times for all 10 subjects occurred most often with 1.78 deg checks in the perifovea. The fastest P1 implicit times of all 10 subjects occurred most often with 0.83 deg checks in the perifovea and the fastest P1 time occurred with 0.83 checks in the perifovea as well.

SUMMARY GRAPHS- N1, P1, AMPLITUDE
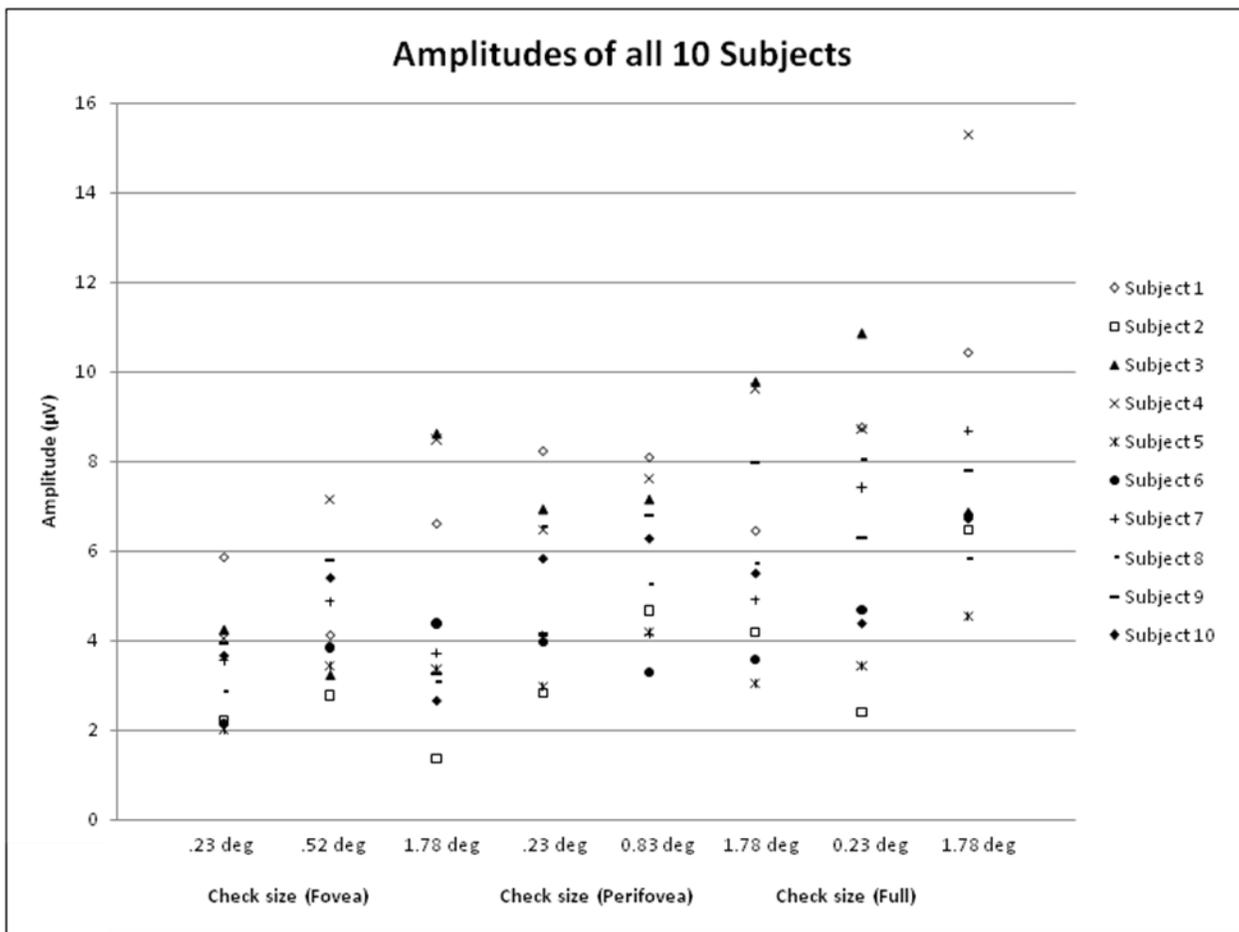
Figure 11b: Amplitudes of all 10 subjects when different check sizes were projected into stimuli. Mean amplitudes were highest when 1.78 deg checks were projected in the fovea, perifovea and full field stimulus targets.

Mean - N1
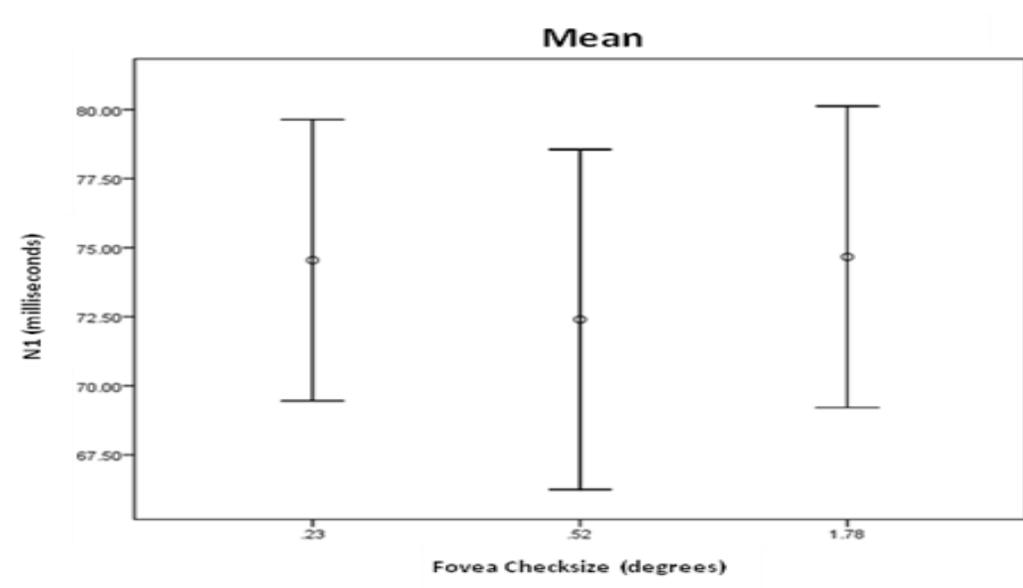
Figure 12a: Mean N1 of the Foveal target of all ten subjects.
Fastest N1 implicit time occurred with 0.52 deg checks in fovea.
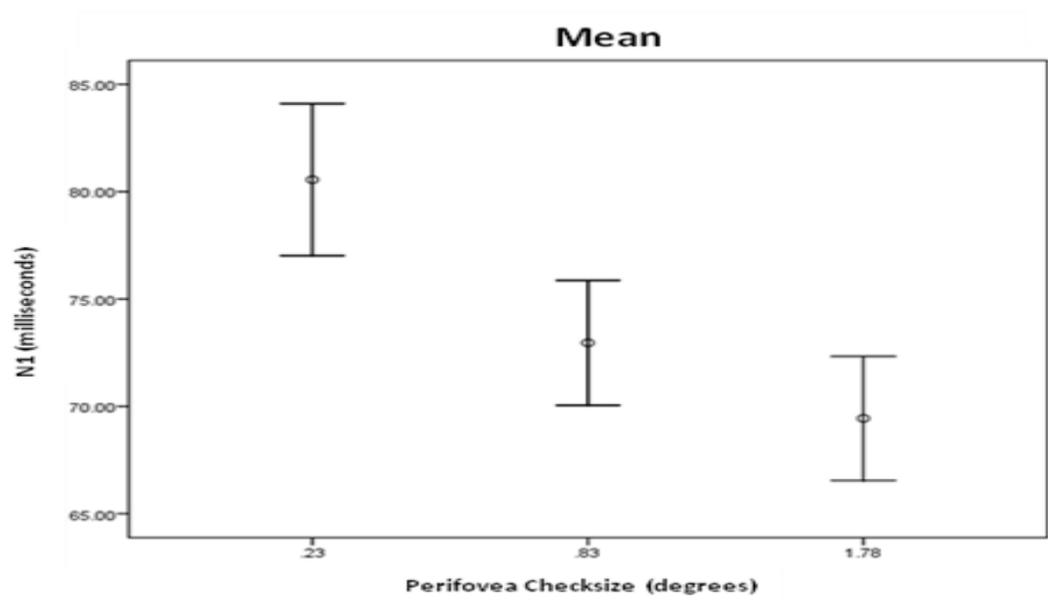
Figure 12b: Mean N1 of the Perifoveal target of all ten subjects.
Fastest N1 implicit time occurred with 1.78 deg checks in perifovea.

Mean – P1
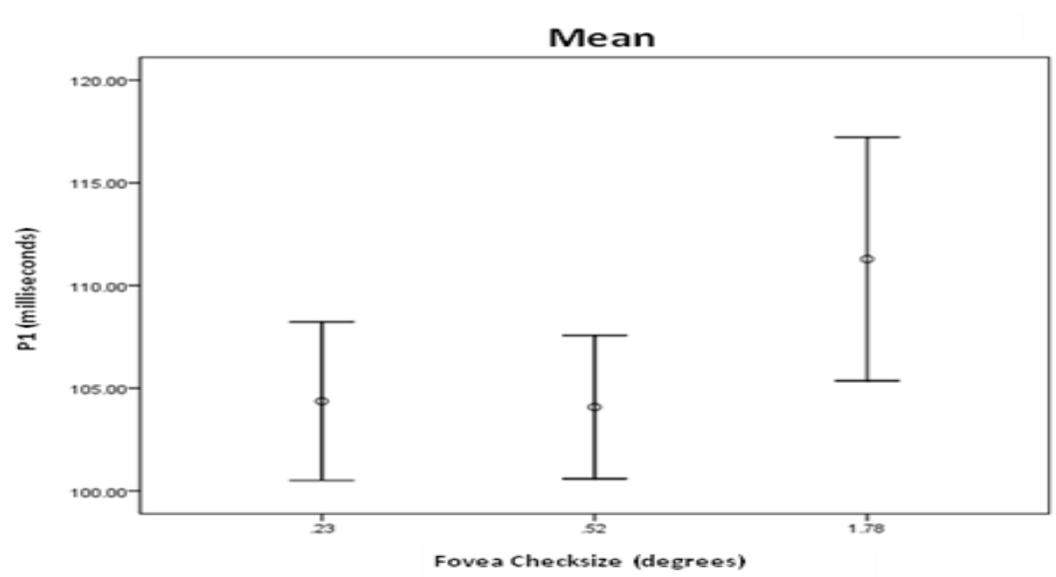
Figure 12c: Mean P1 of the Foveal target of all ten subjects. Fastest P1 implicit time occurred with 0.23 and 0.52 deg checks in fovea.
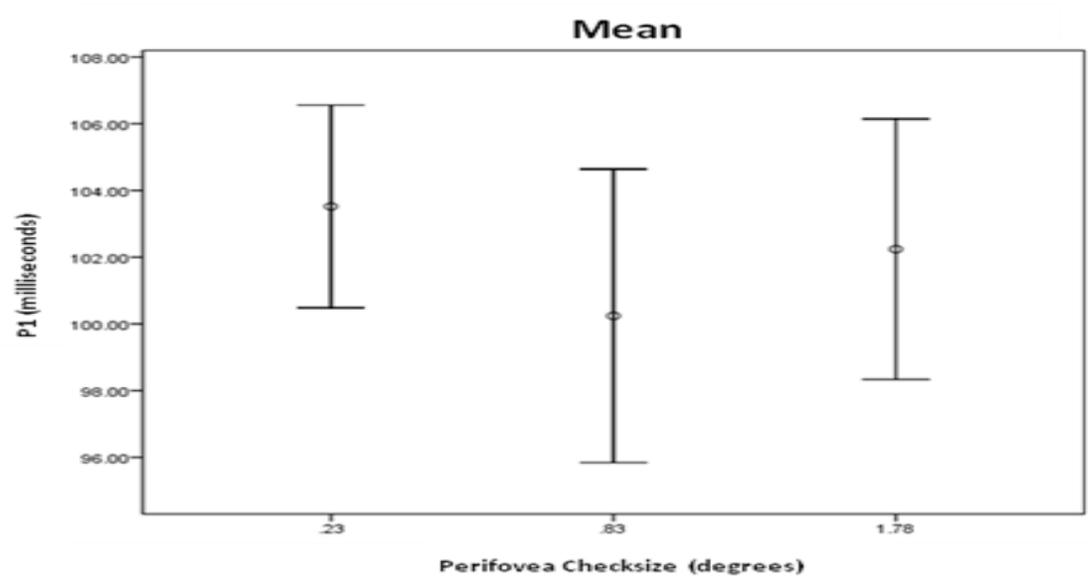
Figure 12d: Mean P1 of the Perifoveal target of all ten subjects. Fastest P1 implicit time occurred with 0.83 deg checks in perifovea.

MEAN – AMPLITUDES
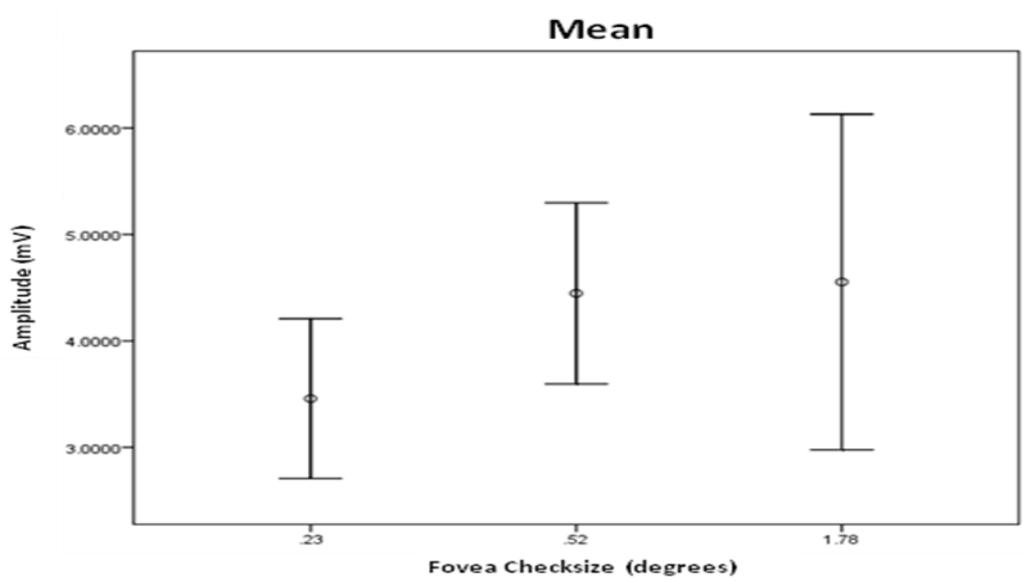
Figure 12e: Mean Amplitude of the Foveal target of all ten subjects. Amplitude is highest with 1.78 deg checks in fovea.
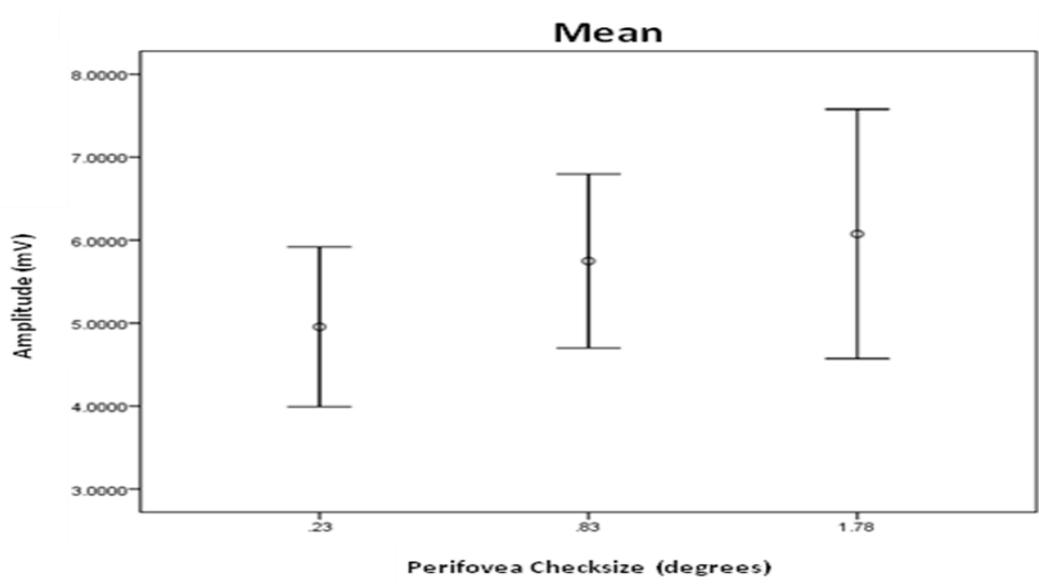
Figure 12f: Mean Amplitude of the Perifoveal target of all ten subjects. Amplitude is highest with 1.78 deg checks in perifovea.

Appendix B

SUBJECT #1

Subject #1
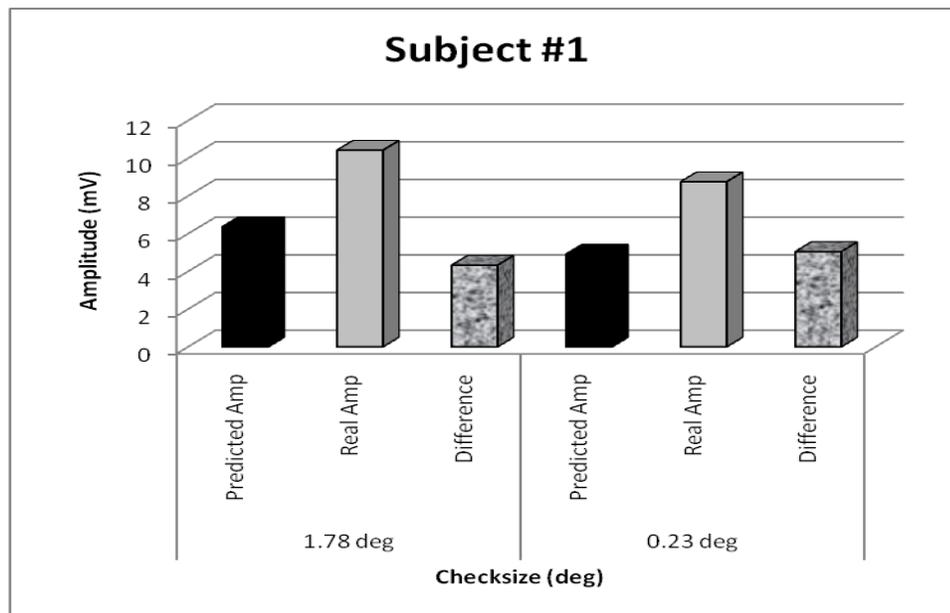
Figure 1a shows the predicted and real amplitude of the full field stimulus and the difference between them for the large and small check sizes.
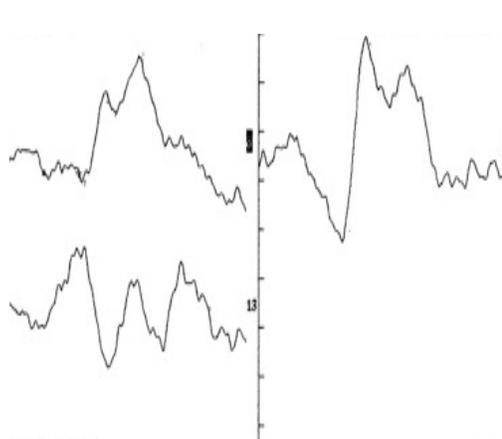
Figure 1b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
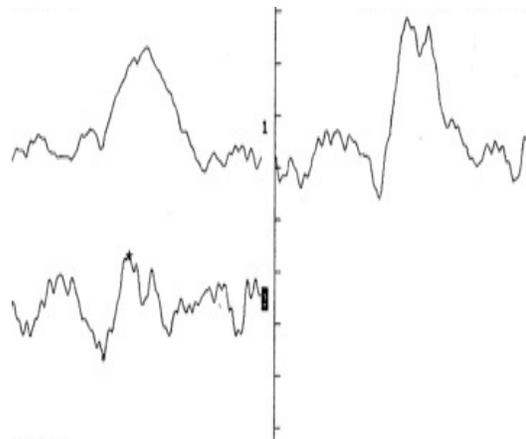
Figure 1c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #2
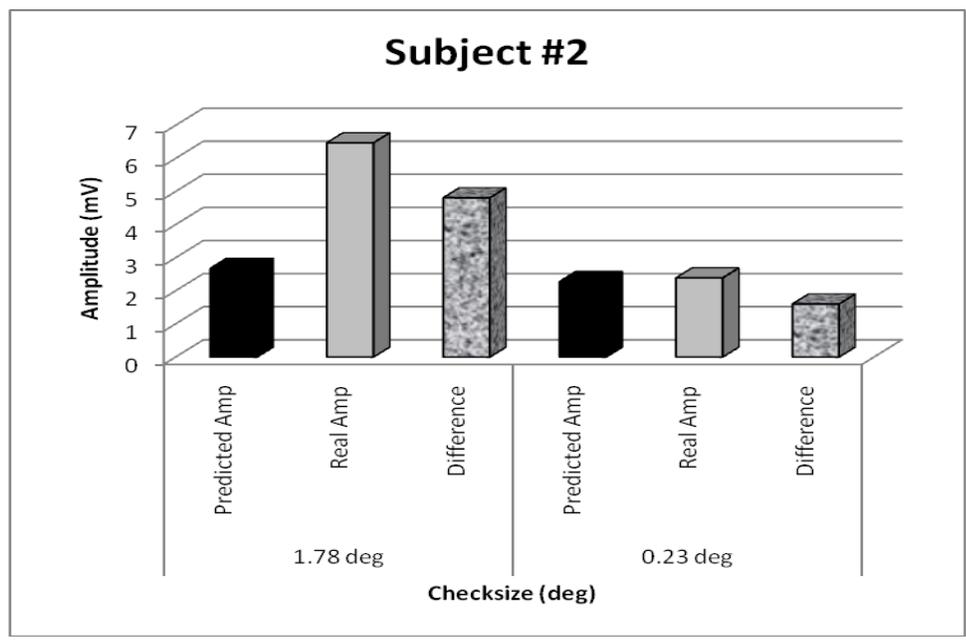
Figure 2a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
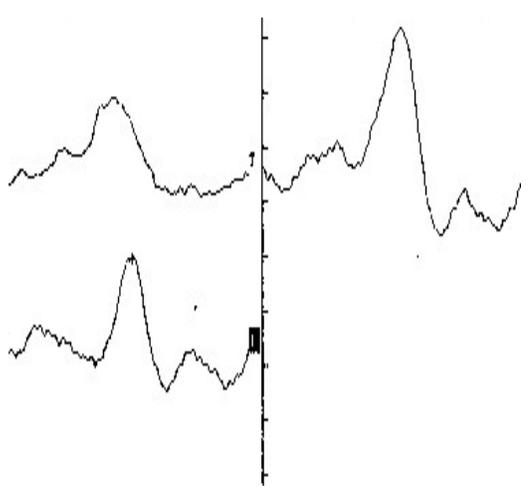
Figure 2b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
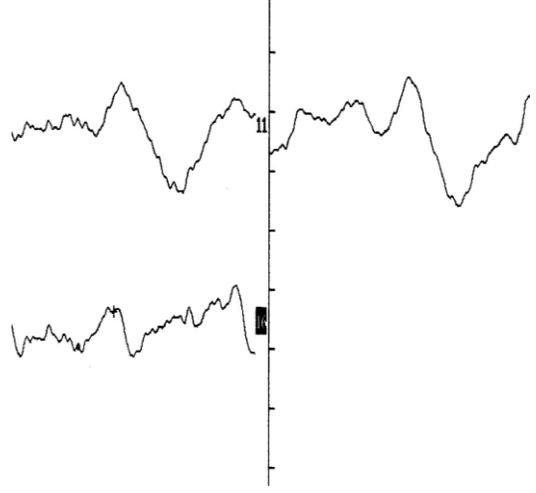
Figure 2c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #3
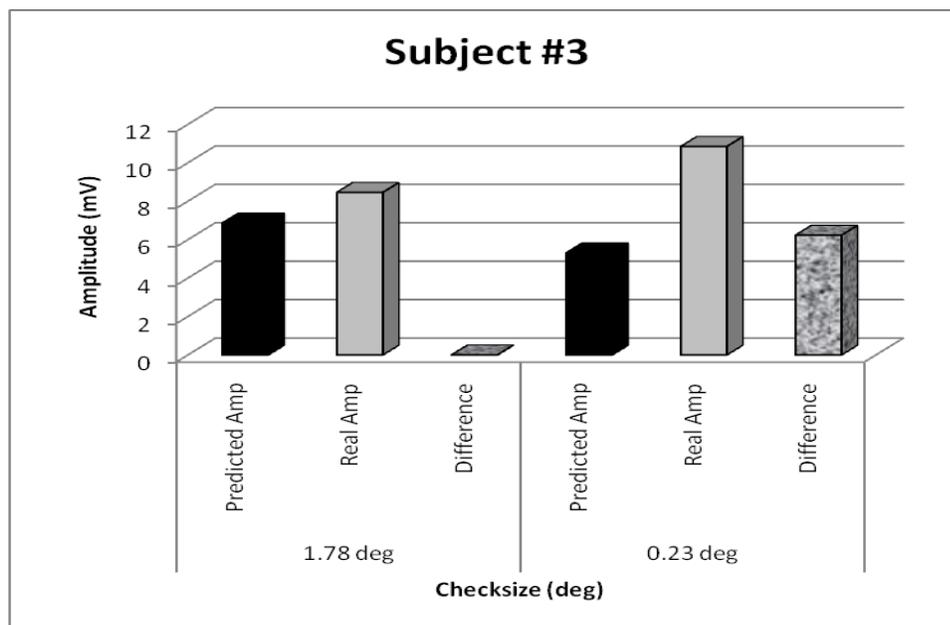
Figure 3a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
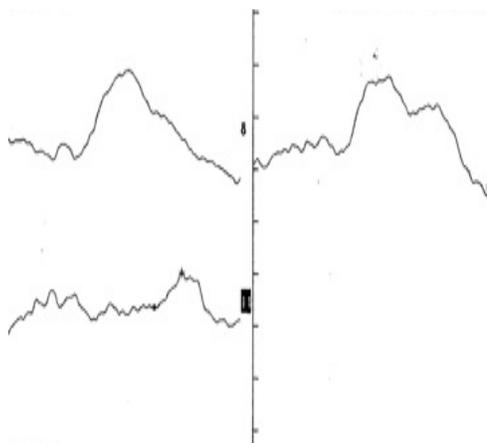
Figure 3b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks.
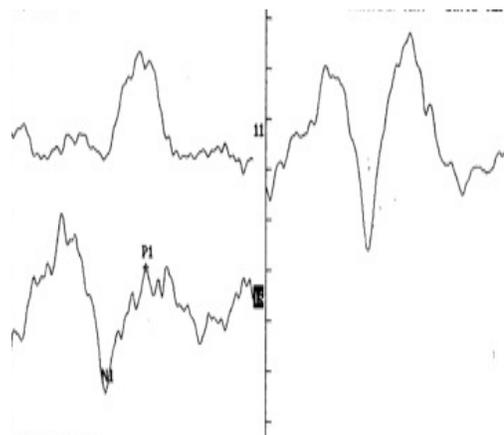
Figure 3c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks.

SUBJECT #4
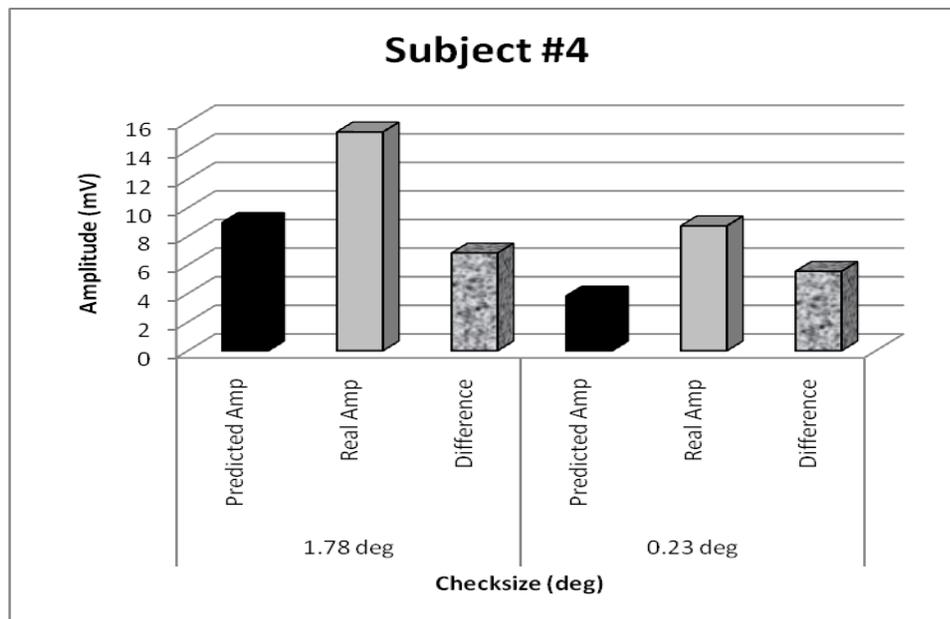
Figure 4a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
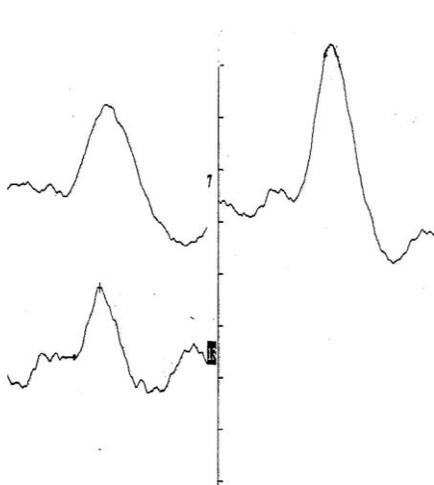
Figure 4b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
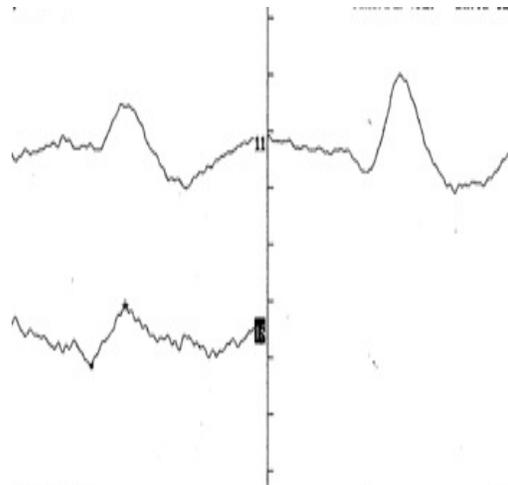
Figure 4c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #5
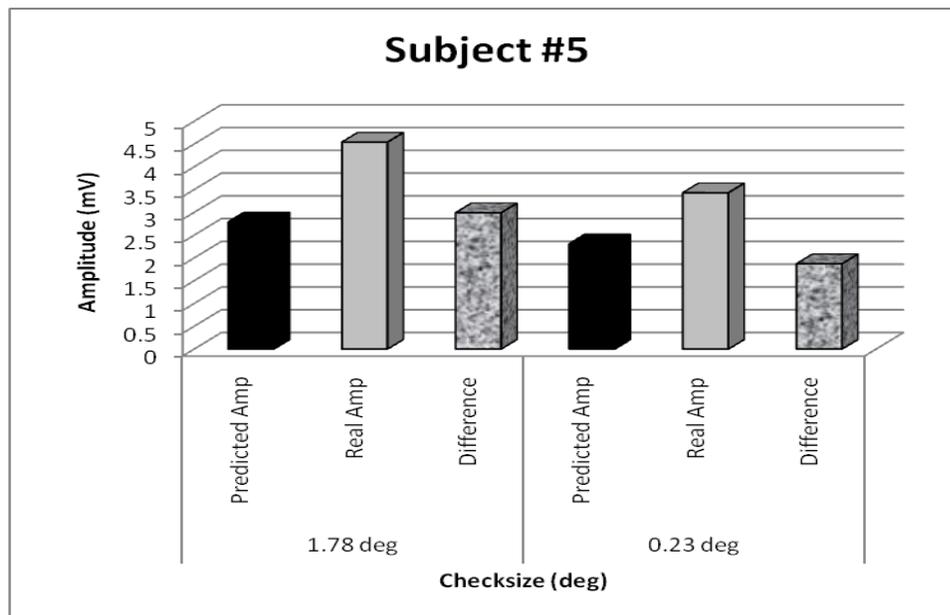
Figure 5a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
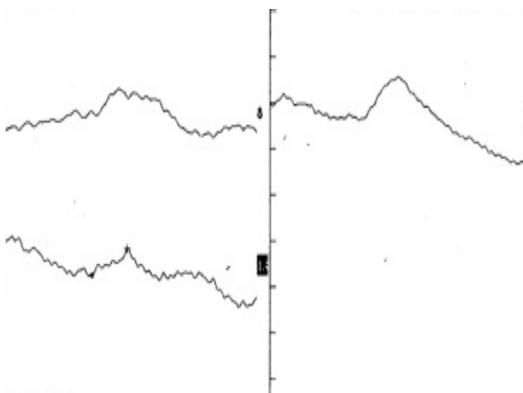
Figure 5b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
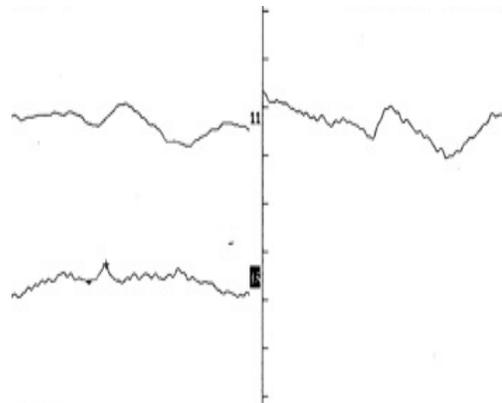
Figure 5c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #6
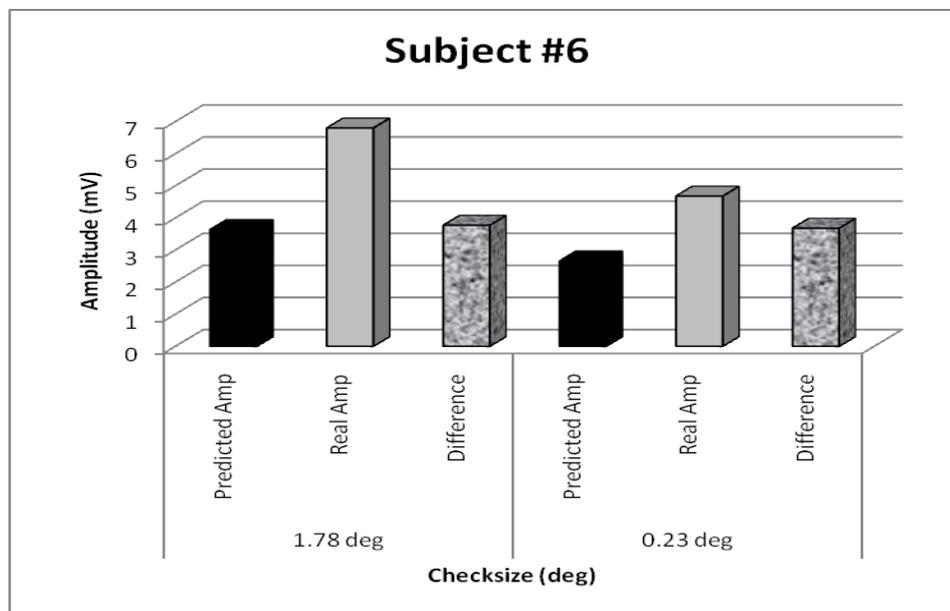
Figure 6a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
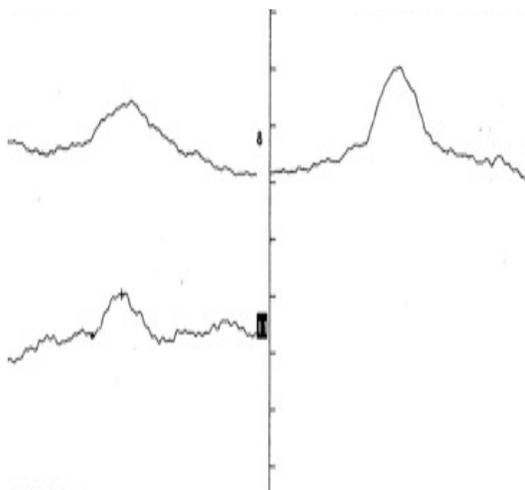
Figure 6b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
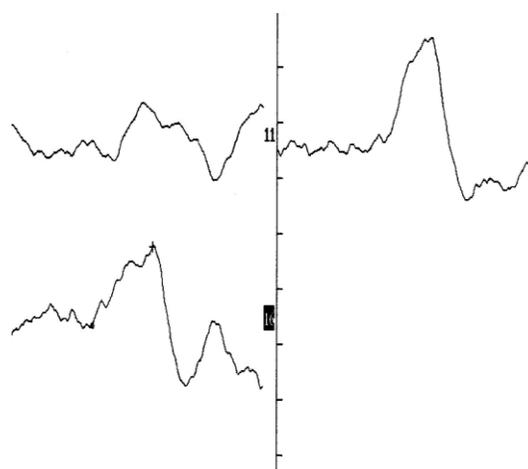
Figure 6c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #7

Subject #7
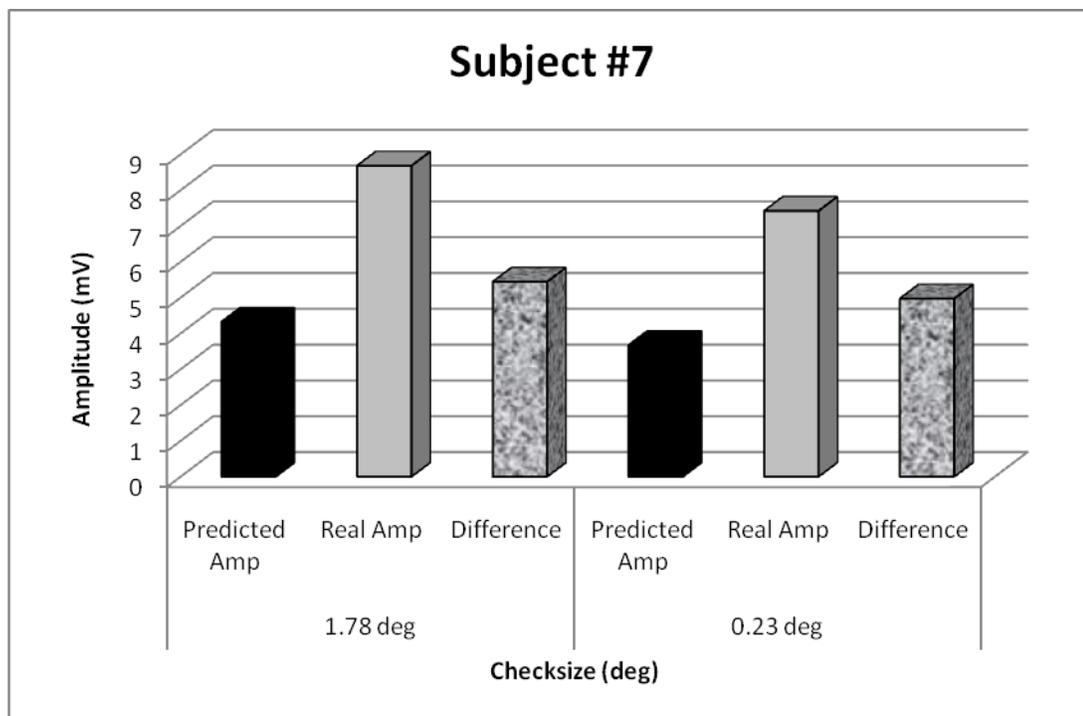
Figure 7a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
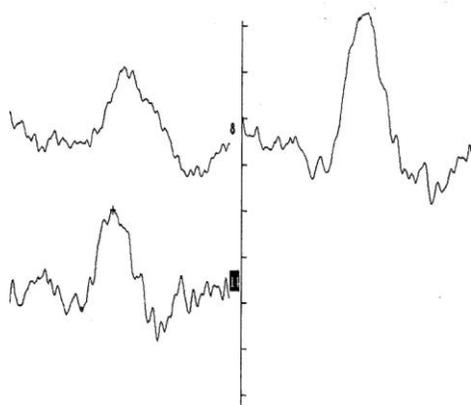
Figure 7b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
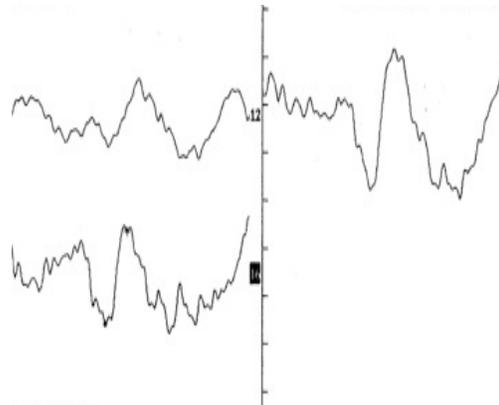
Figure 7c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #8

Subject #8
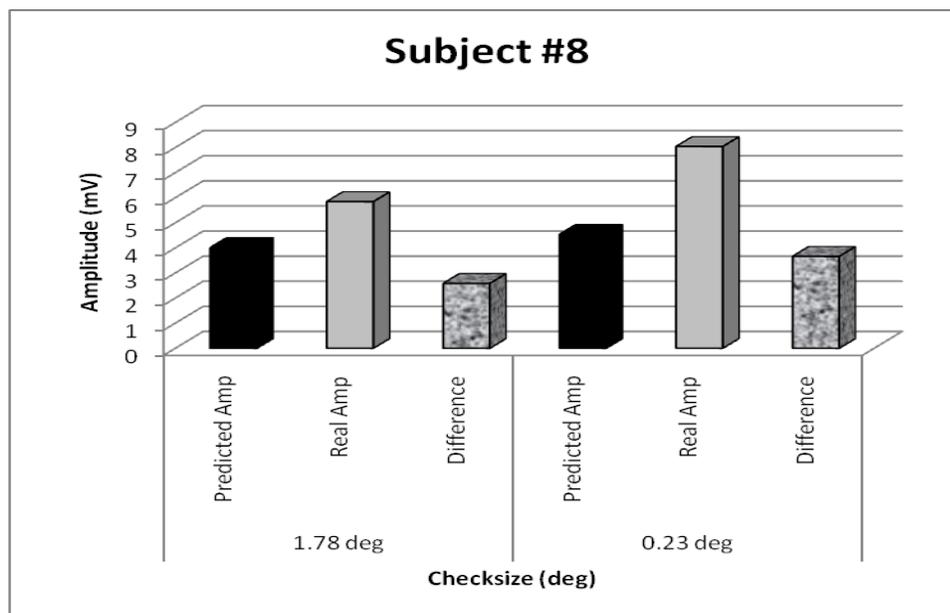
Figure 8a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
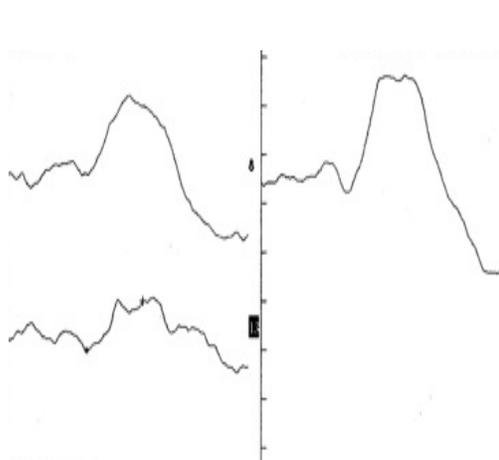
Figure 8b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
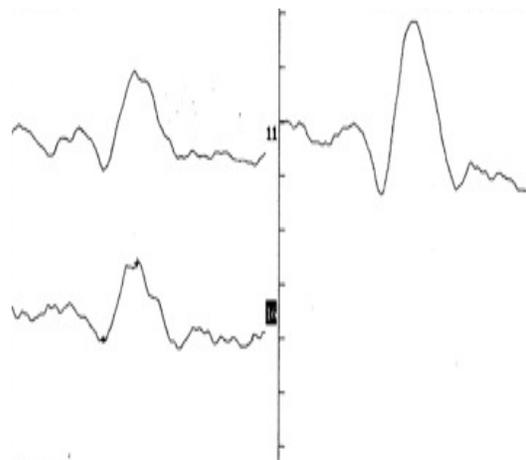
Figure 8c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #9
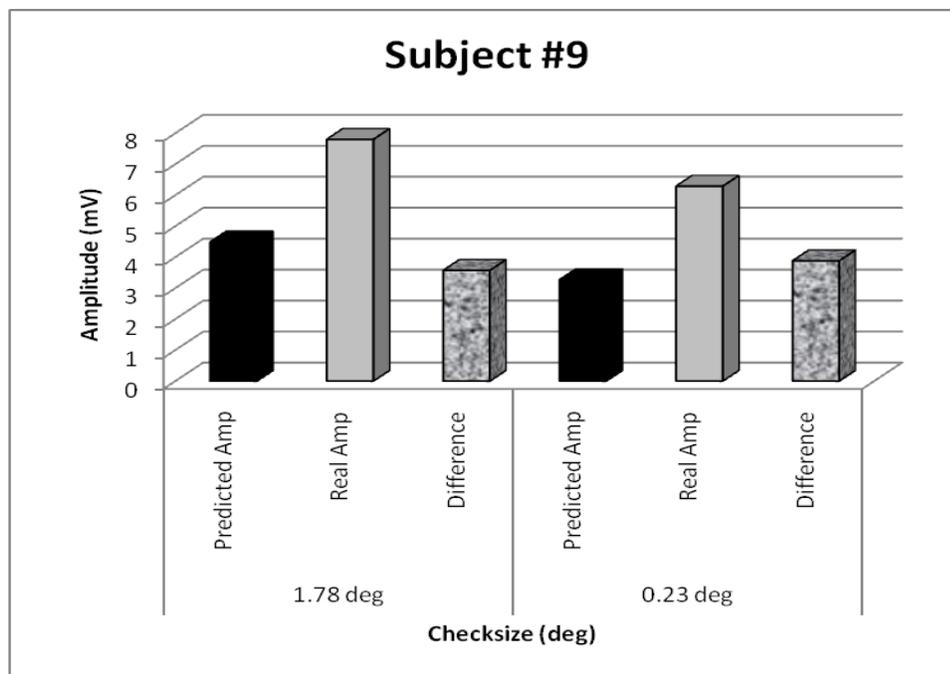
Figure 9a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
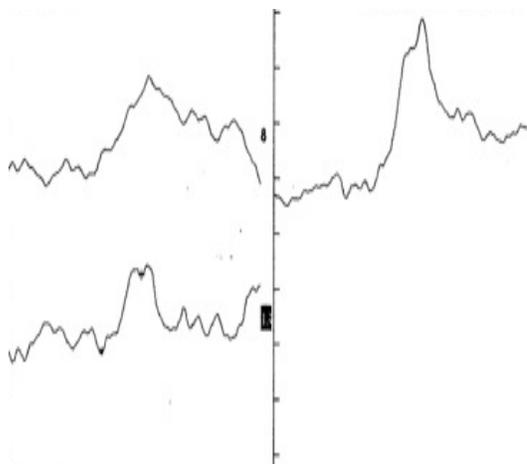
Figure 9b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
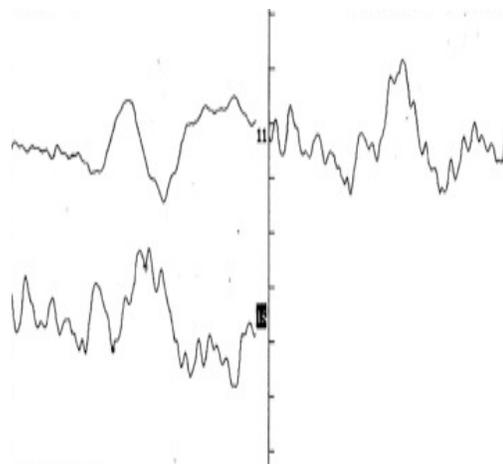
Figure 9c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

SUBJECT #10
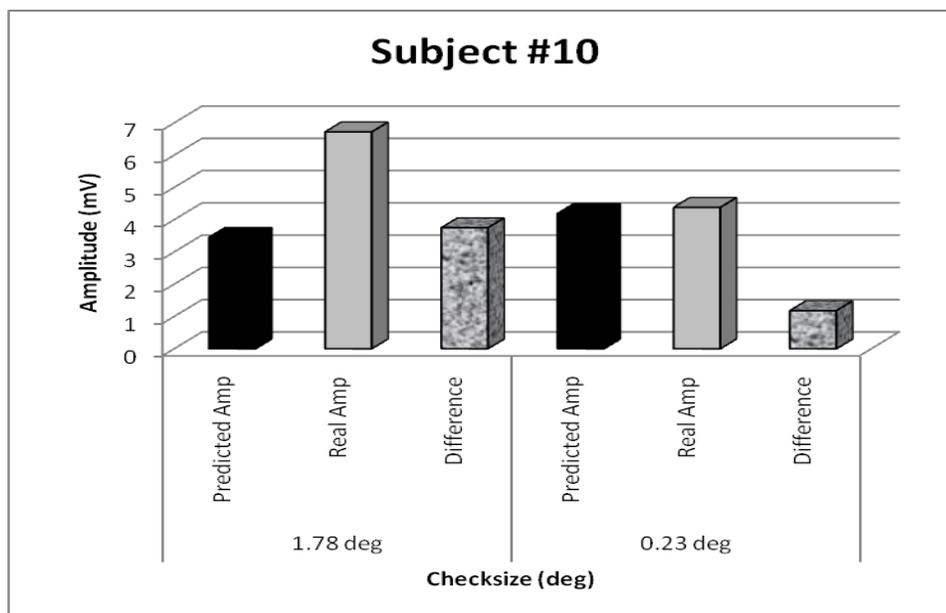
Figure 10a shows the predicted and real amplitude of the full field stimulus, and the difference between them for the large and small check sizes.
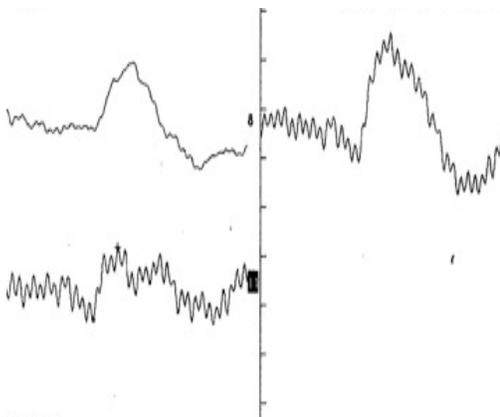
Figure 10b: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the large checks
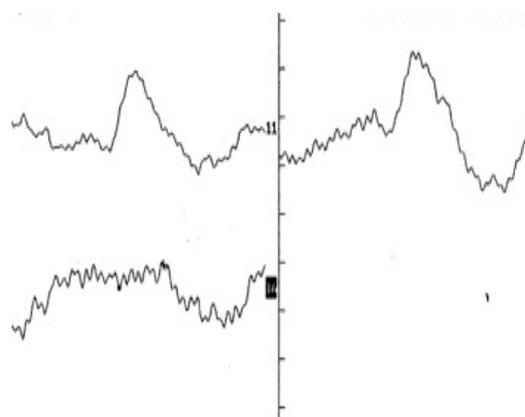
Figure 10c: Predicted (top left), Real (right side), and the Difference waveforms (bottom left) of the small checks

MEAN AMPLITUDE
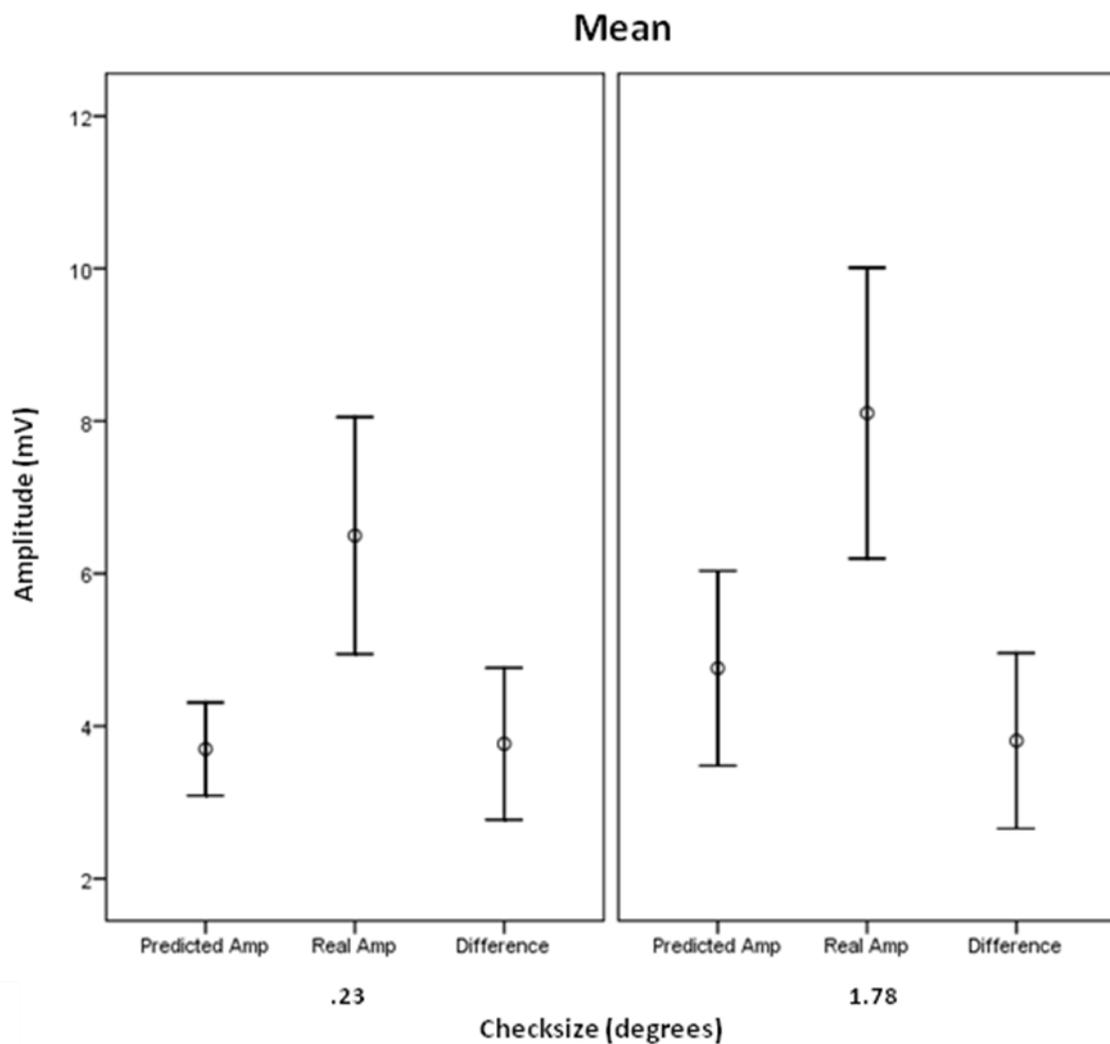
Figure 11 shows the mean of the predicted and real amplitude of the full field stimuli and the difference between them for all ten subjects. The graph on the left shows the mean amplitudes for the smallest check size (0.23 degrees) and the graph on the right shows the mean amplitudes for the largest check size (1.78 degrees). The error bars are standard error bars.