Background on EvokeDx Fundamental Sciences

EvokeDx is an advanced, integrated system for recording and analyzing visual electrophysiology responses from VEP and ERG. In 2014, Konan Medical acquired rights to a novel device from VeriSci Corp, "Neucodia", which has been rebranded and repackaged to contemporary medical device standards under the trademarked name "EvokeDx".

1. Background, Terms, and Definitions of Visual Evoked Potential (VEP)

VEPs are minute electrical signals (on the order of microvolts), elicited by visual stimuli, that are measured usually from the surface of the head. They originate primarily in the cerebral cortex and are extracted from the relatively large ongoing brain waves (electroencephalogram, EEG) by means of signal averaging or by methods of frequency analysis (Regan, 1989). Typically, three sensors are placed on the head to measure the signal that arrives in the visual cortex following generation in the retina of the eye and modification in the lateral geniculate nucleus (LGN) of the thalamus. VEPs can be produced by simple stimuli, such as a flash of light, or by a spatial pattern presented on an electronic display with its contrast modulated in time. Unlike other neuro-assessment tools (e.g., magnetic resonance imaging and behavioral measures) VEPs reflect real-time brain processes with dynamics on the order of milliseconds. Thus, the integrity of functional connections and mechanisms in the eye and brain can be evaluated.

Electrogenesis

The EEG is a measure of the electrical potentials recorded from the scalp that originate in the brain and are then volume-conducted through the neural tissue and non-neural layers that surround the brain. It reflects extracellular currents that are generated by both excitatory and inhibitory postsynaptic potentials occurring on apical dendrites of pyramidal cells (Eccles, 1951; Purpura, 1959; Creutzfeldt & Kuhnt, 1973; Zemon et al., 1980, 1986; Speckmann & Elger, 1987). These morphological structures dominate the superficial layers of the visual cortex and provide the major input to the cortical neurons classified neurophysiologically as "complex" (Gilbert & Wiesel, 1979). The VEP is that part of the EEG that is time-locked to the visual input. Animal experiments involving pharmacological manipulations of visual cortex, demonstrated the significant role of GABAergic ($GABA_A$) intracortical inhibition in generating VEPs (Zemon et al., 1980, 1986).

Typically, the VEP waveform is plotted on a graph with amplitude in microvolts (µV) along the Y axis and time in milliseconds (ms) along the X axis. The conventional VEP is called a **transient VEP (tVEP)** because it is elicited by an abrupt stimulus change (e.g., flash of light, sudden reversal of contrast) with sufficient time provided for the response to be completed before the next stimulus change. The tVEP waveform has a series of peaks and troughs (maxima and minima) that are used to measure the **magnitude** (peak-to-trough amplitude) and **latency** (time from the stimulus change to the peak or trough) of the response. One latency measure has been shown to be of some value in identifying dysfunction in neural disorders – most notably, in individuals with multiple sclerosis. Evidence indicates that the major generators of the early components of the tVEP to contrast reversal (often labeled P60, N75, P100, and N135, with a nomenclature based on polarity and latency) reside mostly in primary visual cortex (Ducati et al., 1988; Nakamura et al., 2000; Shigeto et al., 1998).

An alternative approach to VEP measurement is to transform the time-domain waveform into the frequency domain by means of a mathematical technique known as Fourier analysis, and to express the entire response as a set of **frequency components** – each one quantified in terms of **sine** and **cosine coefficients**, or in terms of the derived measures of **amplitude** (microvolts, µV) and **phase** (degrees, deg). Through the use of stimuli designed to match the properties of particular types of neurons within the visual system, these VEP measures are capable of examining somewhat selectively the functional integrity of various neural pathways and mechanisms (e.g., M/P ON and OFF pathways). These novel VEP methods provide more accurate and sensitive assessment tools for disorders that target particular neural functions, and work has been conducted with these methods in the fields of glaucoma, amblyopia, multiple sclerosis, macular degeneration, retinitis pigmentosa, diabetic retinopathy, etc. Other advantages of these VEP tests over conventional VEPs and other means of assessment include the following: 1) they yield objective, noninvasive measures of brain processes, and they can quantify the entire response (not just a few select time points); 2) they are conducted with rapid data collection procedures – individual responses can be obtained in a few seconds, and an entire test can be completed in under one minute following attachment of the sensors to the scalp; 3) No behavioral response is required from the patient, and therefore, it enables clinicians to test preverbal children, infants, and patients with communication difficulties.

Electroencephalogram (EEG)

The EEG is the recording of electrical activity (potentials) via electrodes attached to the scalp. It is on the order of tens of microvolts, and the signal (measured at one scalp location relative to a second, reference location) is increased by a differential amplifier ~20,000 times, digitized by an analog-to-digital converter (ADC), and stored in a computer for subsequent analysis. It reflects ongoing activity throughout the cerebral cortex, including the visual response time-locked to a particular stimulus.

VEP Frequency component

A visual stimulus is usually displayed repetitively over time, and the VEP elicited by the stimulus contains periodic components at the stimulus frequency and/or at multiples of that frequency (depending on the stimulus type). Extracting a dominant response frequency component from the EEG recording can enhance the signal strength relative to ongoing, unrelated electrical activity (noise).

Mathematically, the frequency component can be expressed by either a pair of cosine and sine coefficients or by corresponding amplitude and phase measures. A plot of the individual and mean sine and cosine coefficients for a single frequency component, along with corresponding vector mean amplitude (magnitude) and phase, are depicted in **Figure 1**.

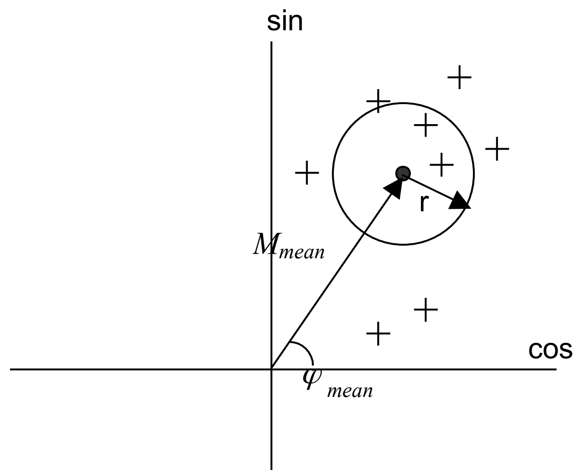


Figure 1 - Sine : Cosine plot of the individual and vector mean VEP responses at a given frequency.

The individual responses are represented by '+' symbols, and the mean response is represented by a dot. The distance from the origin to the dot indicates the mean amplitude (magnitude) M_{mean}, and the angle φ_{mean} formed by the vector arrow and the positive X-axis (cosine-axis) indicates the phase of the response. The error circle with radius r represents the 95% confidence region around the mean response, computed using the T^2_{circ} statistic.

Figure 2. VEP frequency response. VEP frequency component (blue) plotted along with the stimulus modulation signal (red). The component's amplitude (magnitude) and its 90° phase lag relative to the stimulus are depicted.

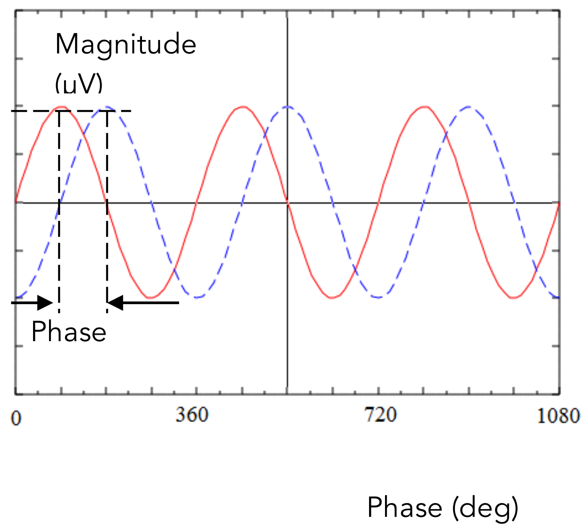


Figure 2 illustrates the relation between a sine-wave stimulus modulation and a VEP response at the same (fundamental) frequency.

Frequency response

The frequency response is a VEP signal expressed in terms of its frequency components.

F statistic

The *F* statistic is used in EvokeDx to test for a significant difference between two VEP response functions. For example, this statistic is employed to determine if fellow monocular responses are matched or differ sufficiently to raise concerns about a unilateral condition such as amblyopia. An observed *F* value obtained from the two functions being tested is compared to a critical *F* value set for a specified significance level (e.g., .05).

We are not aware of any other device that includes these quantitative features.

T^2_{circ} statistic

This is a multivariate *t* statistic (Victor & Mast, 1991) calculated on the sine and cosine coefficients of a VEP frequency component to estimate the variability (noise) in the set of responses at that frequency collected during a test. It is represented in a **sine-cosine plot** as the radius of the noise (confidence) circle. A two-sample T^2_{circ} statistic is used in EvokeDx to test for a significant difference between two individual VEP frequency components (e.g., two responses obtained from fellow-eye tests).

Noise circle

The noise (error) circle is established by the T^2_{circ} statistic to indicate the 95% confidence region that encompasses the mean vector response. If the circle includes the origin in the **sine-cosine plot** (see **Figure 1**), the response is not significant at the .05 level.

Signal-to-noise ratio (SNR)

SNR is defined as the vector mean amplitude ($\bar{A}$) of a frequency component divided by the radius of the noise circle *r* (see **Figure 1**):

$$\text{SNR} = \bar{A}/r \equiv M_{mean} / r$$

The magnitude of the VEP signal, as well as the noise related to other brain activities and non-neural factors (e.g., movement artifacts and environmental noise) may vary from person to person and from test time to test time. SNR is used to determine if the VEP signal is reliably greater than the noise level.

Sweep VEPs

An entire VEP function can be obtained in a short period of time by varying a particular stimulus parameter (e.g., spatial element size, contrast, temporal frequency) in successive steps. These swept-parameter VEPs ('sweep VEPs') are highly efficient and enable the assessment of a visual domain in only several seconds. When the parameter manipulated is size of spatial elements (e.g., width of bars in a striped, i.e. grating, pattern reduced step by step from thick to thin, see **Figure 4**), the test is known as a **spatial frequency sweep VEP (sfVEP)**. **Spatial frequency** is the number of pairs of light and dark bars in the grating pattern per degree of visual angle, which is the angle (measured in degrees) formed from the eye to the outer borders of the pattern (visual field size). The units of spatial frequency are cycles per degree (cycles/deg), and one cycle is a single pair of light and dark bars. The sfVEP is useful for obtaining an estimate of visual (grating) acuity in infants and young children and for testing for significant differences between fellow eyes that might indicate a developmental disorder (amblyopia).

Contrast sweep VEPs, in which contrast is parametrically increased in octave steps during each successive second of a test, have been obtained as well to examine contrast response functions under conditions designed to emphasize contributions from ON- and OFF-cell subdivisions of subcortical M and P neural pathways (Zemon & Gordon, 2006). This kind of sweep VEP has been shown to be of value in the assessment of patients with neural disorders such as glaucoma (Greenstein et al., 1998), retinitis pigmentosa (Alexander et al., 2005), schizophrenia (Butler et al., 2001, 2005), Alzheimer disease (Siegfried et al., 1995), and autism (Weinger et al., 2012).

Transient VEP (tVEP) response

A typical tVEP waveform elicited by a checkerboard pattern contrast-reversed in time (1 Hz, 2 reversals per second) is shown in **Figure 3**. The two halves of the waveform are identical because the odd harmonics, considered to contain only noise given the symmetrical contrast-reversal stimulus, are filtered out of the response. The remaining even harmonics necessarily produce identical waveforms to each contrast-reversal. The prominent positive peak in the waveform is denoted as P100 or P_1, and it typically has a latency of around 100 ms. Its magnitude is usually measured from the preceding negative trough, N75 or N_0, which has a latency of about 75 ms. An early, small positive peak is often observed and usually has a latency of about 60 ms (P60 or P_0).

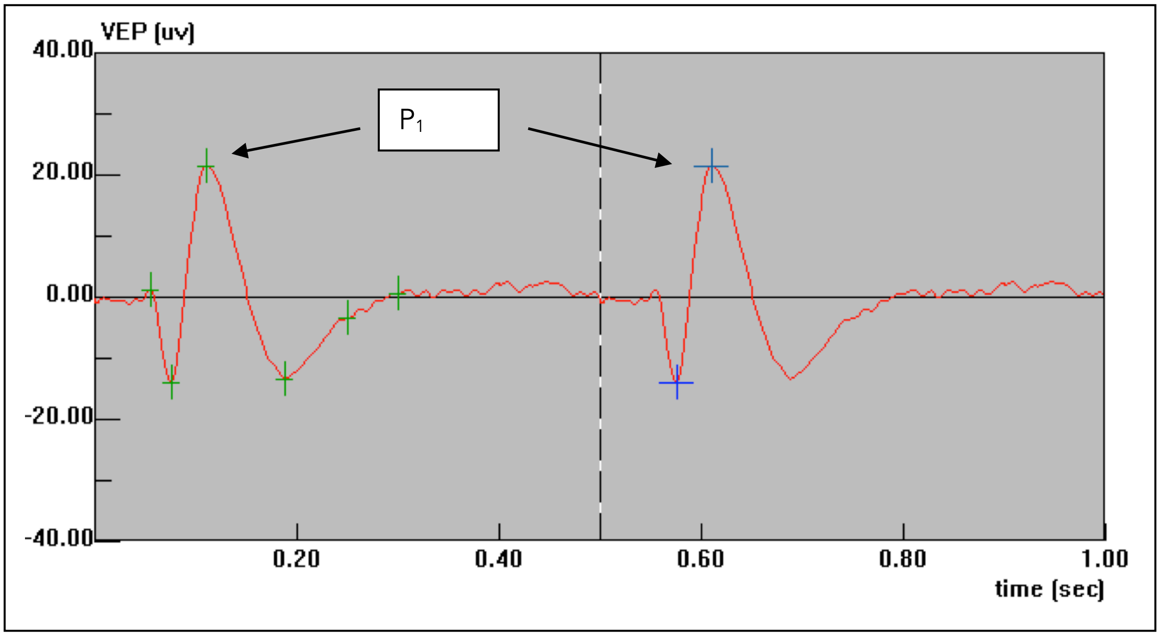


Figure 3. Transient VEP from a 7-yr-old child elicited by a contrast-reversing checkerboard.

Magnitude-Squared Coherence (MSC)

MSC is a statistic used to estimate signal power relative to signal + noise power in a VEP frequency response. It is algebraically related to the T^2_{circ} statistic which is used to derive the SNR measure (given above) to indicate a significant response at the .05 level. It is used in EvokeDx to quantify the strength of the tVEP response in the frequency domain for each harmonic frequency component. Work in our laboratory demonstrated that the tVEP to a contrast-reversing pattern (checkerboard) consists of six distinct frequency mechanisms which can be examined by calculating mean MSC values for each respective frequency band (Zemon et al., 2009).

Synchronized Data Collection

Synchronized data collection is a feature of EvokeDx that involves sampling the EEG at fixed time points relative to each frame of the stimulus display, as opposed to asynchronous data collection in which the sampling and the stimulus frames are unrelated. Typically, commercial VEP devices use asynchronous data collection. This latter form of data collection increases the variability in the response measures as a result of **side-lobe leakage**, in which response components other than the one of interest can contaminate ('leak into') the measurement of the relevant frequency component.

2. EvokeDx Clinical Use

EvokeDx is an electrophysiological device that presents stimuli on a visual display, records the EEG time-locked to the stimulus, synchronizes the EEG sampling to the display's frame rate, and analyzes the digitized EEG signal to extract the VEP and quantify it through the calculation of several response measures. Data processing includes software algorithms for noise filtering (drift, power line, saturation), artifact rejection (eye movements, electromyographic signals), frequency and time domain analysis. Results that are displayed on the operator's monitor include the following: EEG epochs, frequency component in an amplitude/phase plot or in a sine-cosine plot, and statistical measures to estimate mean amplitudes and noise levels. Tests include stimulus conditions and data processing methods to tap the specific neural pathways and mechanisms for sensitive assessment of select visual dysfunction. All tests performed on EvokeDx are designed to provide automated, objective outcome measures to determine the true response in a short period of time. Thus, it does not require the expertise of a trained electrophysiologist to operate it.

> While evoked potentials can provide valuable information concerning the integrity of neural functions, the output of EvokeDx should be interpreted in the context of other test results and a full clinical examination of the individual patient.

Spatial frequency VEP (sfVEP)

This sweep VEP test is used to determine whether spatial functions are similar for fellow monocular pathways or whether there is evidence to suspect a unilateral deficit, which occurs in disorders such as amblyopia. The statistical tests applied to the data also yield estimates of visual (grating) acuity (Zemon et al., 1997). This technique has been applied in a randomized, double-blind, clinical study on nutritional supplements in infant formula and the effects on visual neural development in preterm infants, and the results demonstrated enhanced grating acuities and neural development with supplementation (O'Connor et al., 2001). (The test procedure is described in detail in a separate document entitled "EvokeDx Clinical Testing Procedure.")

Stimulus

Horizontal gratings (~ 100% contrast) are reversed in contrast with a 7.5 Hz temporal signal. The sweep stimulus starts with thick bars (low spatial frequency) and changes to thinner bars (higher spatial frequency) in successive steps. The stimulus is usually presented several times to generate response functions for the subsequent statistical analyses. Example patterns are shown in **Figure 4**.

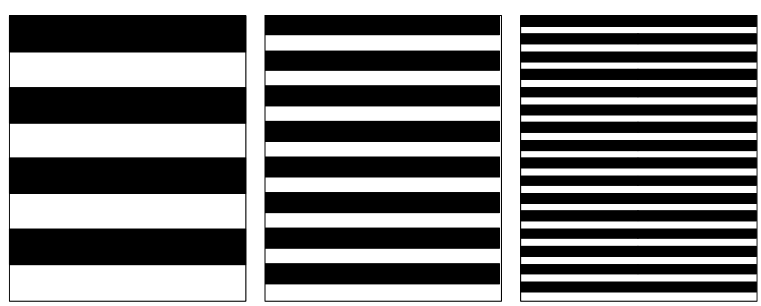
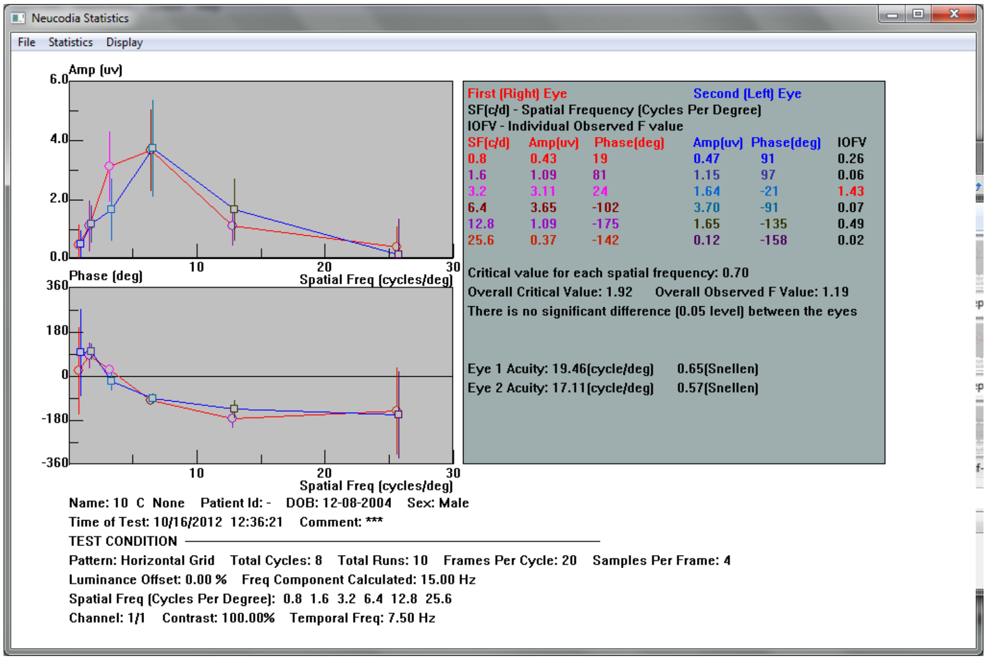
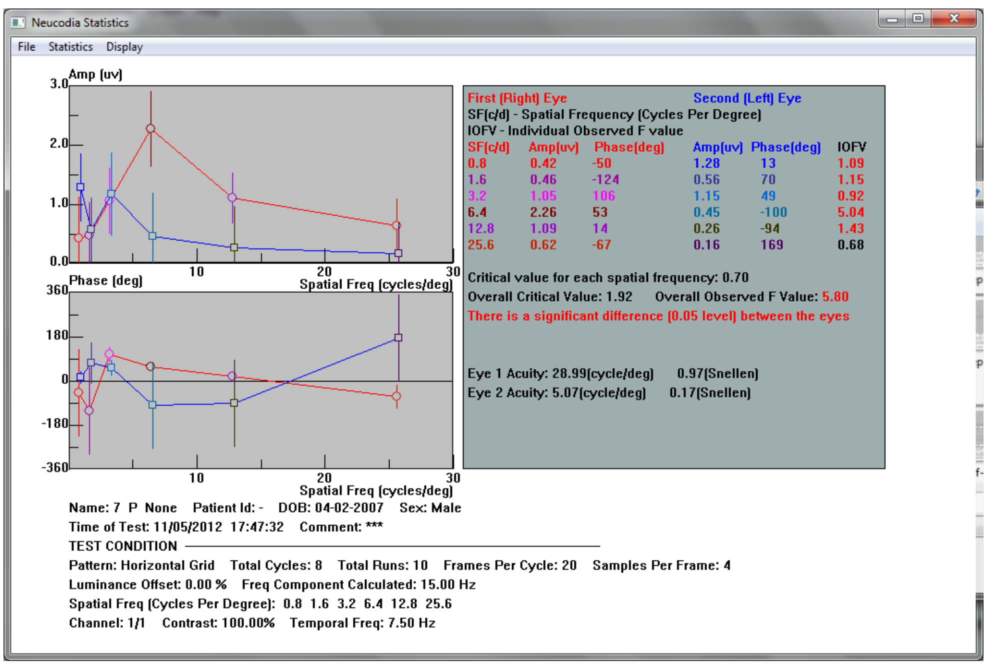


Figure 4. Spatial Frequency Sweep: horizontal gratings of high contrast (contrast-reversed at 7.5 Hz) are halved in width (doubled in spatial frequency) in successive 1-s steps to elicit steady-state VEPs in a test of spatial function. Statistical analyses determine



(a)



(b)

Figure 5. Comparison of spatial frequency sweep VEPs elicited by stimulation of fellow eyes. Amplitude and phase are plotted vs. spatial frequency. Symbols represent the mean response and error bars represent 95% confidence limits. (a) Data from an individual with matched monocular functions, and (b) data from an individual with amblyopia. The individual observed F values (IOFV) are calculated for each spatial frequency and compared against the critical value. When the IOFV is smaller than the critical value, there is no significant difference between the two responses at that spatial frequency, and the value is printed in black. When the IOFV exceeds the critical value, there is a significant difference and the value is printed in red. In addition, an overall observed F value across all spatial frequencies is calculated and compared with the overall critical value. If it exceeds the critical value, a statement indicating a significant difference between the functions will be printed in red.

Data processing

The dominant frequency component in the response to this stimulus is the second harmonic at 15 Hz. A discrete Fourier transform is applied to extract this frequency component, and statistical analyses (T^2_{circ} and F tests) are performed to test for significant responses at each spatial frequency and for significant differences between two sfVEP functions (usually to assess the similarity between two fellow-eye monocular functions. Grating acuity estimates are also obtained through linear interpolation to an SNR = 1 (criterion for a significant response at the .05 level).

Display of Data

Data by default are displayed in amplitude and phase vs. spatial frequency plots. Examples of two sets of data for fellow monocular sfVEP functions are shown in **Figure 5**.

Isolated-check VEP, icVEP™

This test is based on studies designed to emphasize contributions to the VEP selectively from ON or OFF subdivisions of M or P neural pathways (Zemon et al., 1988; Zemon et al., 1995; Zemon & Gordon, 2006). This work demonstrated differences in ON and OFF pathways that were previously thought to be 'mirror-image' systems, which were confirmed by histological staining of the different cell types in human retina (Dacey & Petersen, 1992) and by single-cell recordings in primary visual cortex of monkeys (Yeh et al., 2009).

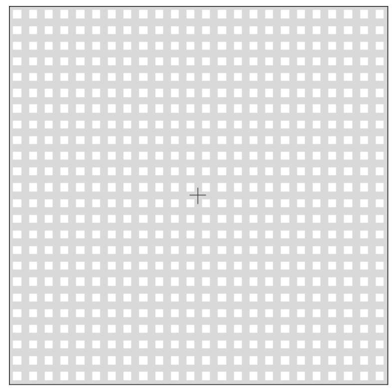


Figure 7. Isolated-check pattern.
The luminance of the checks varies sinusoidally in time such that the pattern appears and disappears. This bright-check pattern is used to test the ON pathway.

The version in EvokeDx is designed to assess low contrast processing in the visual system, which is deficient in various disorders, including glaucoma (Greenstein et al., 1998; Zemon et al., 2008). This icVEP work demonstrated high classification accuracy for early-stage glaucoma in a Phase I NIH-funded study (A'=94%) and in a multisite Phase II NIH-funded study (A'=89.2%).

A contrast sweep VEP technique using these stimulus patterns (Zemon & Gordon, 2006) was applied to the study of schizophrenia with selective deficits in visual processing discovered (Butler et al., 2001, 2005; Calderone et al., 2013).

Stimulus

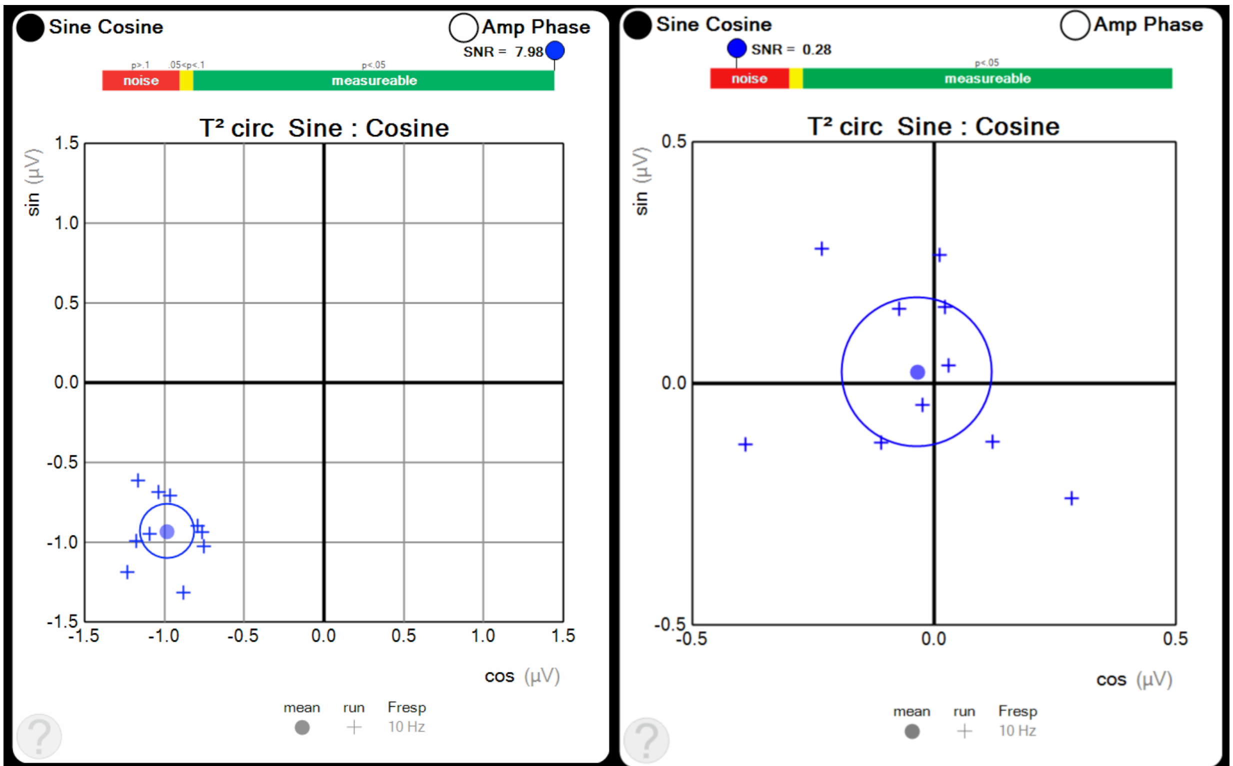
An example of a bright isolated-check pattern is shown in **Figure 7**. The contrast of the isolated checks is modulated from 0% (uniform field with no contrast) to a peak contrast (15%) with a temporal frequency of ~10 Hz. Thus, the checks appear and disappear at that frequency. A brief adaptation period precedes the stimulus in which the pattern is modulated to a peak contrast of 7.5%. This stimulus is designed to emphasize M-ON pathway activity.

Data processing

The fundamental frequency component of the steady-state VEP elicited by this type of stimulus is the dominant one in this test and the results are represented in a sine-cosine plot. The T^2_{circ} statistic is used to derive a signal-to-noise ratio for this component. An SNR > 1 indicates a significant response at the .05 level. Otherwise, a deficit in low-contrast processing is noted.

Display of Data

The values of fundamental frequency components obtained in individual runs are depicted along with the vector-mean responses and error circles in sine-cosine plots in Figure 8. In plot (a), SNR > 1 and the error circle a distance from the origin indicate a significant response; in plot (b), SNR < 1 and the error circle overlapping the origin indicate a lack of significance at the .05 level, and evidence for a low-contrast processing deficit.



(a) (b)

Figure 8. icVEP test results obtained with the bright isolated-check condition. Results are displayed in sine-cosine plots. The '+' symbol represents individual runs and the dot represents the vector-mean response. The error circle obtained with the T^2_{circ} statistic represents the 95% confidence region about the mean response. a) The error circle is a distance from the origin (SNR > 1), which indicates a significant response; b) Individual data points are scattered throughout the four quadrants of the plot and the error circle overlaps the origin (SNR < 1), which indicates the lack of a significant response at the .05 level.

Transient VEPs to a Contrast-Reversing Checkerboard Pattern

This method utilizes the conventional checkerboard pattern of high contrast, contrast-reversed with a 1 Hz square-wave temporal signal to elicit transient VEPs (tVEPs). The EvokeDx technique, however, differs from the conventional one in several ways. In EvokeDx, the test runs collect only ~2 s of EEG data, rather than the customary 60 s, and ten of these short runs are collected to yield independent estimates of the brain's true response to the stimulus. This enables proper statistical estimation, which is conducted on the entire response in the frequency domain. The conventional method is to examine the mean waveform in the time domain (averaged over the stimulus period) and determine subjectively a few time points to measure amplitude and latency values. EvokeDx also includes time-domain analysis with automatic measurement of amplitude and latency values of peaks and troughs in the waveform detected by preset window functions. A typical tVEP elicited by a contrast-reversing checkerboard stimulus is depicted in **Figure 3**. One longstanding role for this type of response is to aid in the diagnosis and monitoring of individuals with multiple sclerosis (e.g., Fuhr et al., 2001). A typical P100 latency measured in a healthy adult is around 100 ms. In many individuals with multiple sclerosis, P100 latency will exceed this value greatly.

Stimulus

The checkerboard pattern is shown in **Figure 9**. The 32x32 checks span 10° of visual angle at the viewing distance of 114 cm. The contrast is set to ~ 100% and the contrast-reversal frequency is ~ 1 Hz (2 reversals per second).

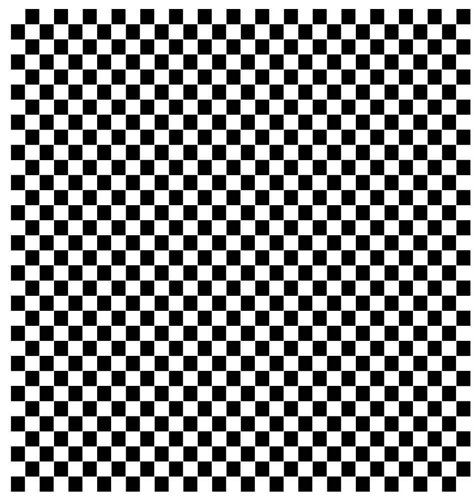


Figure 9. A checkerboard pattern with 32x32 contrast reversal checks

Data processing

After the set number of runs is completed, the data processing program performs data averaging, frequency analysis, digital filtering, and automatic peak detection for the given time windows.

Display of data

A tVEP from a child is displayed in **Figure 10**. The displayed waveform is post filtered in the frequency domain with odd harmonic components removed. Amplitudes and latencies of peaks and troughs in the waveform are automatically detected by the program and displayed on the right side of the plot. The P100 is usually the largest positive peak in the waveform. Its amplitude and latency can be found on the right side of the plot.

Low spatial frequency VEPs

These tests are designed to assess the status of low-vision patients. The stimuli are horizontal gratings or checkerboards of low spatial frequency (e.g., 0.4 cycles/deg) and high contrast (100%). The test procedures and data processing methods are the same as described above.

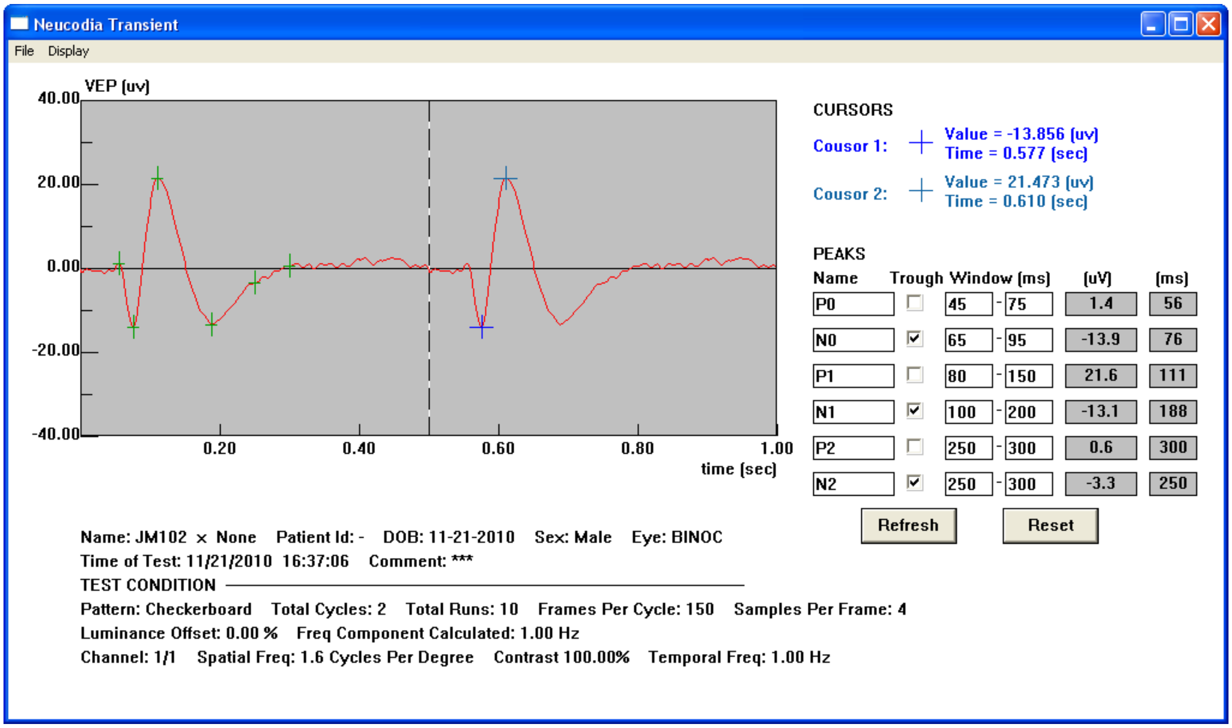


Figure 10. Transient VEP to a contrast-reversing checkerboard stimulus.
The averaged waveform is displayed over a full cycle of contrast reversal. The odd harmonic frequency components have been removed from the record based on the assumption that the responses to the two contrast reversals (half cycles) are identical.
Six preset peaks/troughs, denoted by P_0, N_0, P_1, N_1, P_2 and N_2, are marketed by green crosses on the waveform. The amplitudes and latencies of the peaks/troughs are displayed on the right side of the plot. The time windows in the display are set to search for the expected peaks/troughs. There are two additional cursors marketed by blue crosses which can be moved using the mouse to any time points to measure amplitudes and latencies.

Steady-State VEPs to Radial Stimuli

Partial-windmill and **windmill-dartboard** stimuli were designed to examine lateral interactions in the visual system. Two types of interactions were discovered: short-range and long-range (Zemon & Ratliff, 1982, 1984; Zemon et al., 1986b). The short-range interaction is measured in a fundamental frequency component in the steady-state VEP to the windmill-dartboard stimulus and it has been found to reflect GABAergic inhibitory activity in the visual cortex. These conditions were used in a study of pediatric seizure cases (Ratliff & Zemon, 1984) and in a clinical trial at New York Hospital for an antiepileptic drug (gabapentin, also known as Neurontin), and the results led to FDA approval (Conte & Victor, 2009). These VEPs were also used to assess neural function in patients with schizophrenia (Kim et al., 2005). A recent investigation used this technique to identify GABAergic dysfunction in the brains of migraine headache patients (Coppola et al., 2013). The lateral interactions measured with this technique are thought to be similar to the interactions observed in VEPs to vernier stimuli in a hyperacuity task (Levi et al., 1983) which have been shown to be indicative of dysfunction in patients with strabismic and anisometropic amblyopia (e.g., Hou, Good & Norcia, 2007). [EvokeDx also has the capability to measure VEPs to vernier stimuli.]

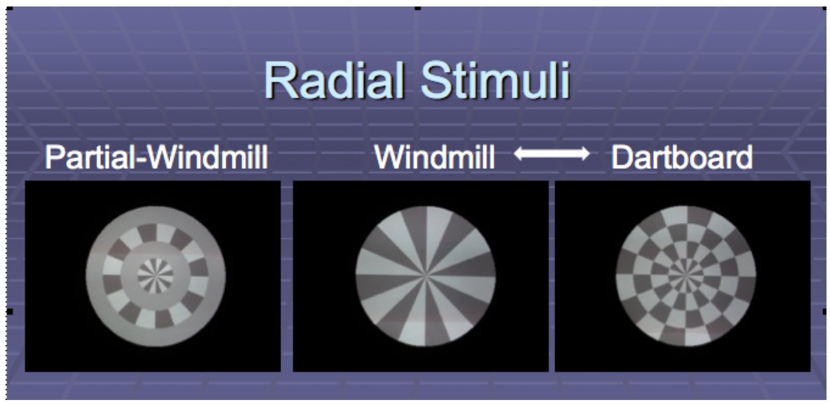


Figure 11. Radial stimuli: partial-windmill and windmill-dartboard. Dynamic elements in the central disc and second annulus are contrast-reversed sinusoidally at ~ 4 Hz. Static elements in the first and third annuli are matched in contrast to the peak contrast of the dynamic elements in the windmill-dartboard stimulus, and are replaced with uniform fields of light in the partial-windmill stimulus.

EvokeDx Features

- Innovative electrophysiological device for objective assessment of visual function
- High quality amplification – high common mode rejection ratio ≥ 130 dB
- Clinical studies conducted on early-stage glaucoma, macular degeneration, and diabetic retinopathy

Innovative

- Beyond conventional visual evoked potential (VEP) testing, our novel device with patented and proprietary technology can tap specific neural mechanisms within the visual system
- Isolated-check VEP (icVEP) technique to assess parallel ON/OFF and magnocellular / parvocellular (M/P) pathways selectively
- Spatial frequency sweep VEP testing to test for differences in fellow monocular functions which may indicate unilateral visual dysfunction (e.g., amblyopia) and estimate grating acuity
- Windmill-dartboard and partial-windmill stimuli to elicit steady-state VEPs that reflect nonlinear lateral interactions in the visual system, which have been shown to be of value in the assessment of various neural disorders (e.g., epilepsy, schizophrenia, autism, migraine headaches)
- Synchronized data collection with automated artifact rejection features and statistical algorithms that enable rigorous analysis and determination of a "pass" or "fail" test result
- Versatile – Easy to incorporate new test protocols (demonstrated to be of value in recent publications) with use of existing menu options

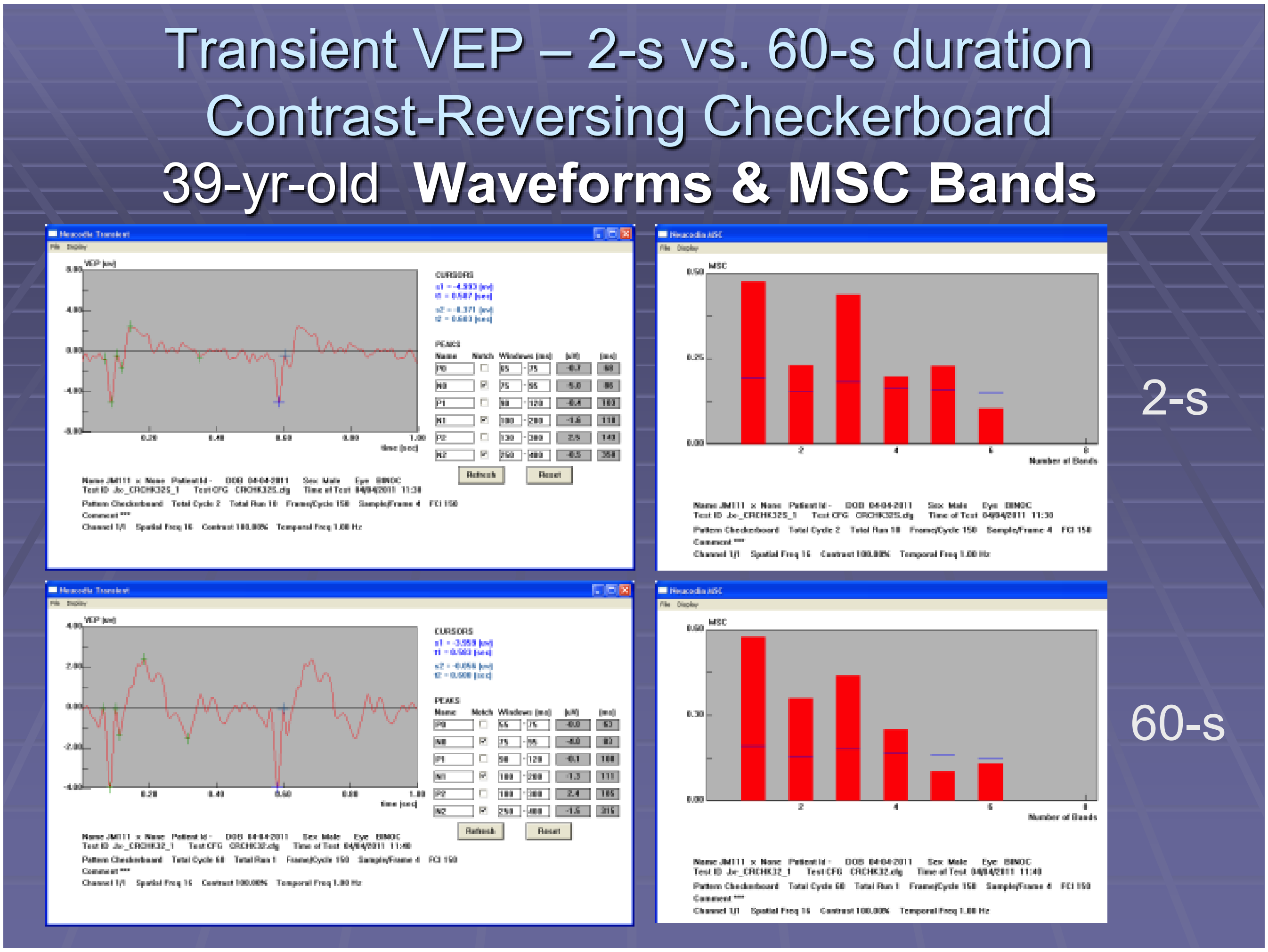
Objective

- Unlike conventional VEP devices, objective determination of the integrity of each mechanism that contributes to the VEP waveform is provided without requiring the subjective judgment of an expert electrophysiologist
- No verbal or other behavioral response (e.g., button pushing) is required
- Enables testing of infants, preverbal children, and patients with communication disabilities
- Automated estimation of grating acuity

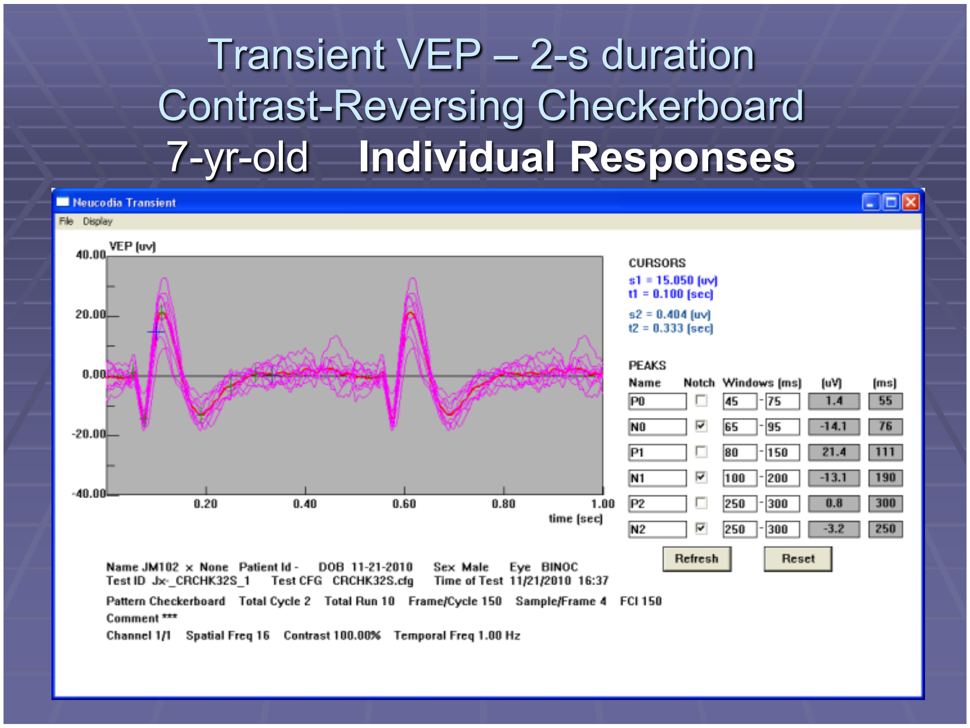
Easy

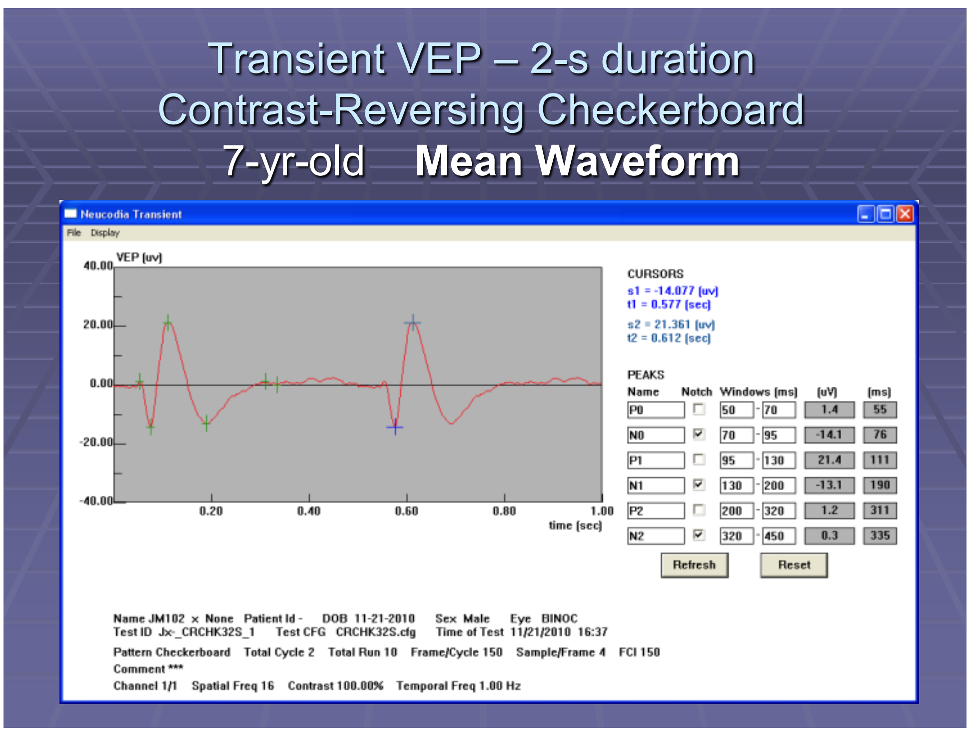
- Designed for use in a physician's office
- Both user- and patient-friendly
- Clear, automated reports for visual function assessment and monitoring
- Fast: A test can be completed in only a few minutes, and results are displayed immediately upon completion
- Testing is non-invasive

"icVEP can rapidly and effectively assess abnormalities in both the
"on" and "off" subdivisions of the magnocellular pathway in patients with glaucoma"
Tsai (2009), Glaucoma Today.

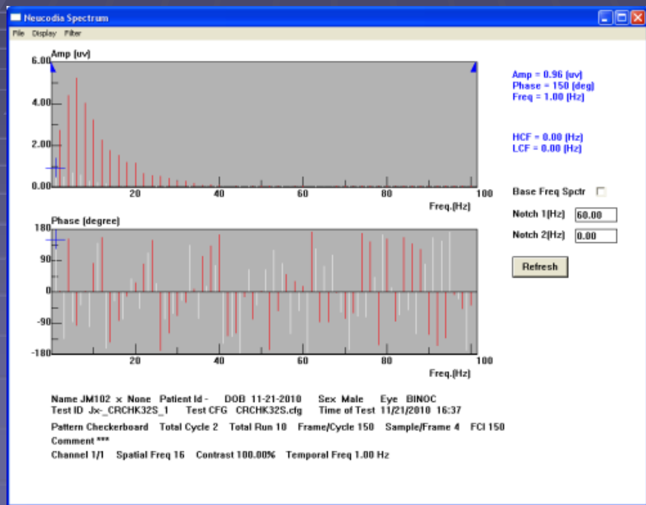

Transient VEP – 2-s vs. 60-s duration
Contrast-Reversing Checkerboard
39-yr-old **Waveforms & MSC Bands**
2-s
60-s

Example Data from 7-yr-old Child

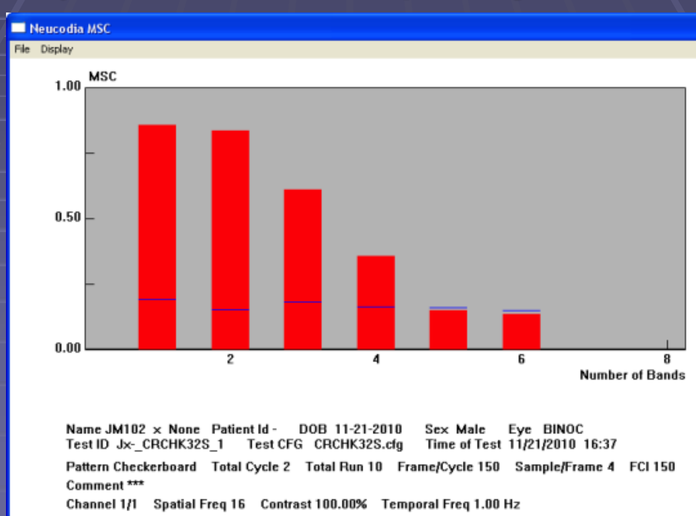




Transient VEP – 2-s duration
Contrast-Reversing Checkerboard
7-yr-old **Spectrum**



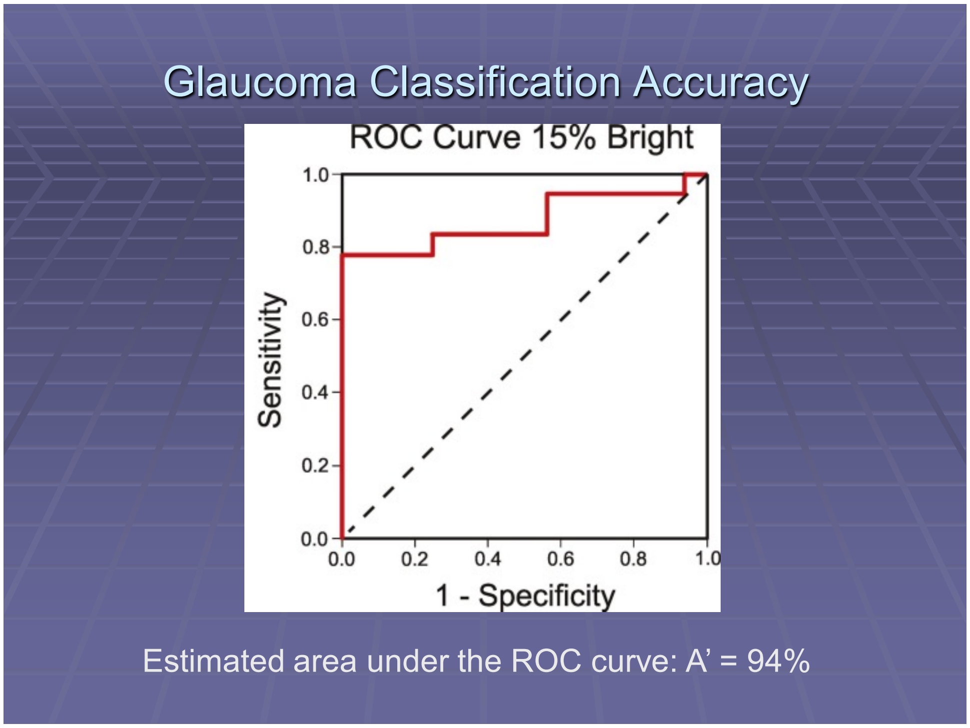
Transient VEP – 2-s duration
Contrast-Reversing Checkerboard
7-yr-old MSC **Frequency Bands**



Glaucoma Phase I NIH-Funded Study

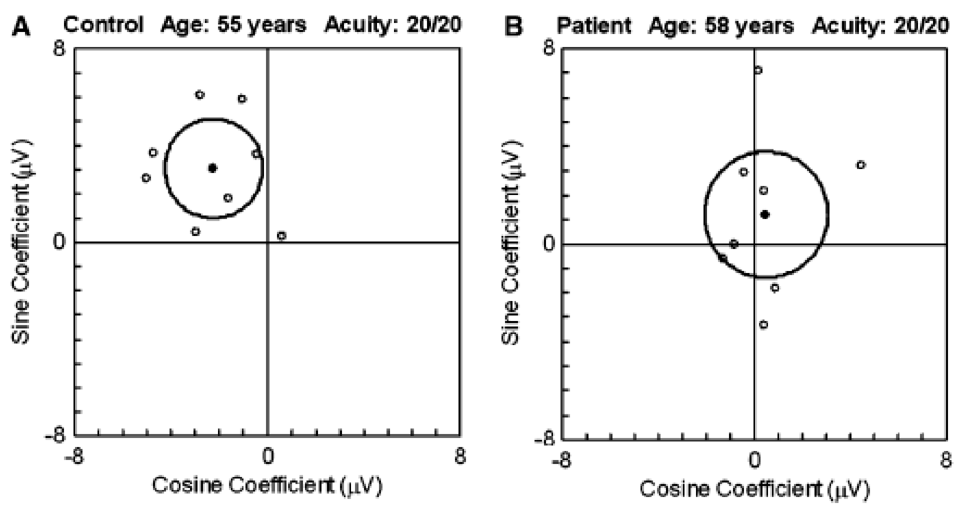
(Zemon et al., 2008): Early-Stage Glaucoma

Classification Accuracy (A') = 94%, Sensitivity = 78%, Specificity = 100%



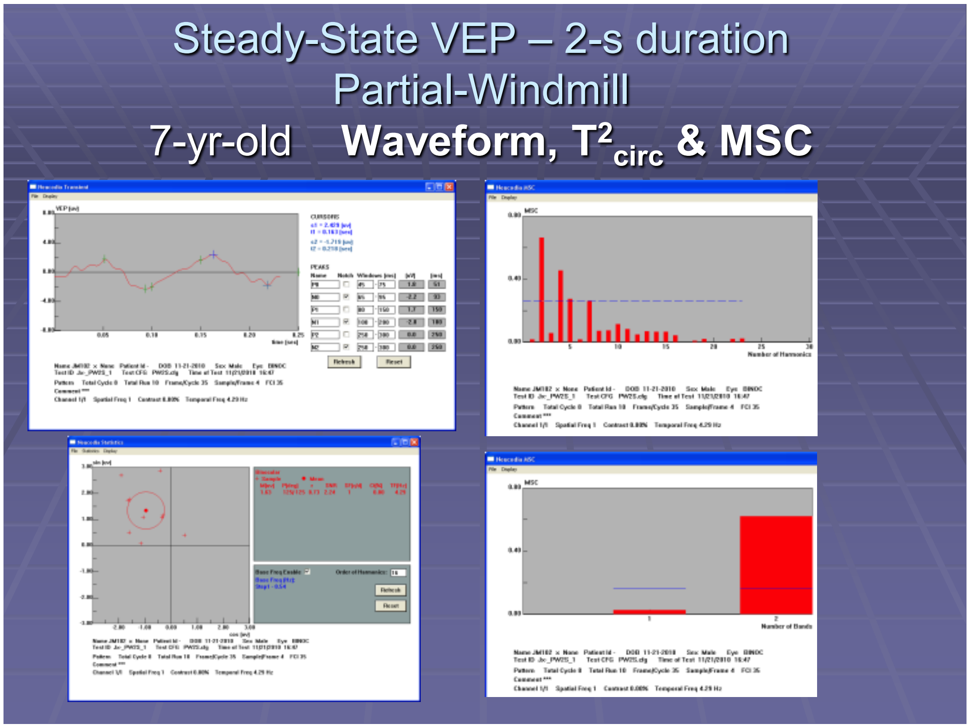
Example of a Significant Response (Control) and No Significant Response (glaucoma patient)

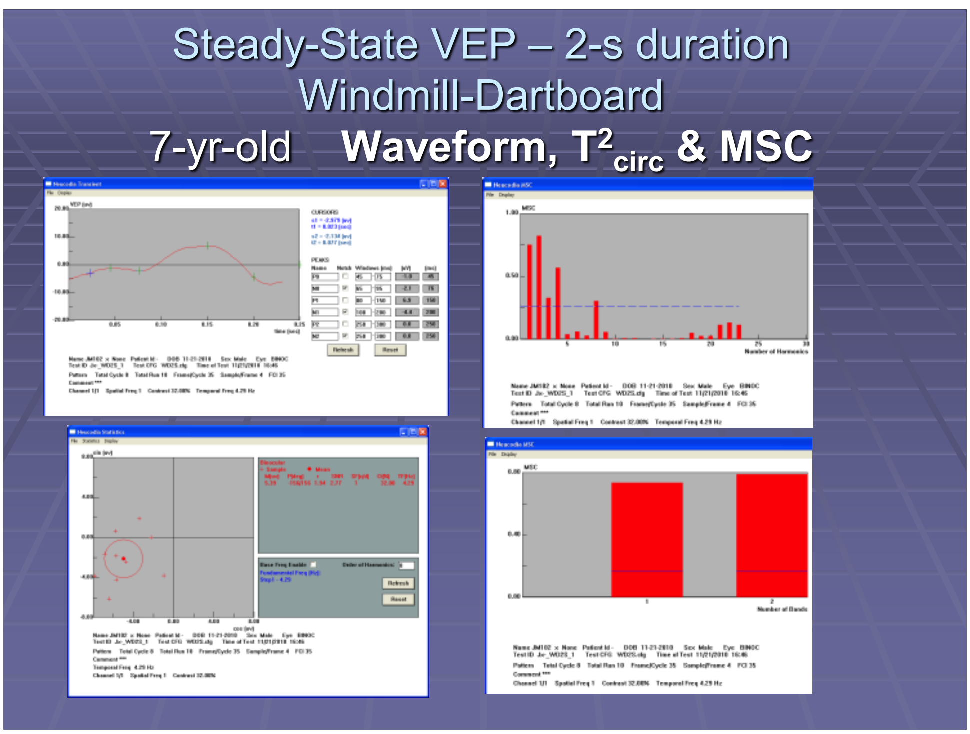
Fig. 3 Plot of sine versus cosine coefficient for the fundamental frequency component of the icVEP under the 15% bright-check condition for (a) one representative control (left half; SNR = 1.85) and (b) one glaucoma patient (right half; SNR = 0.50)



Glaucoma Phase II Multi-Site NIH-Funded Study (Zemon et al., 2011): Early-Stage Glaucoma Classification Accuracy (A') = 89.2%, Sensitivity = 84%, Specificity = 80.4%

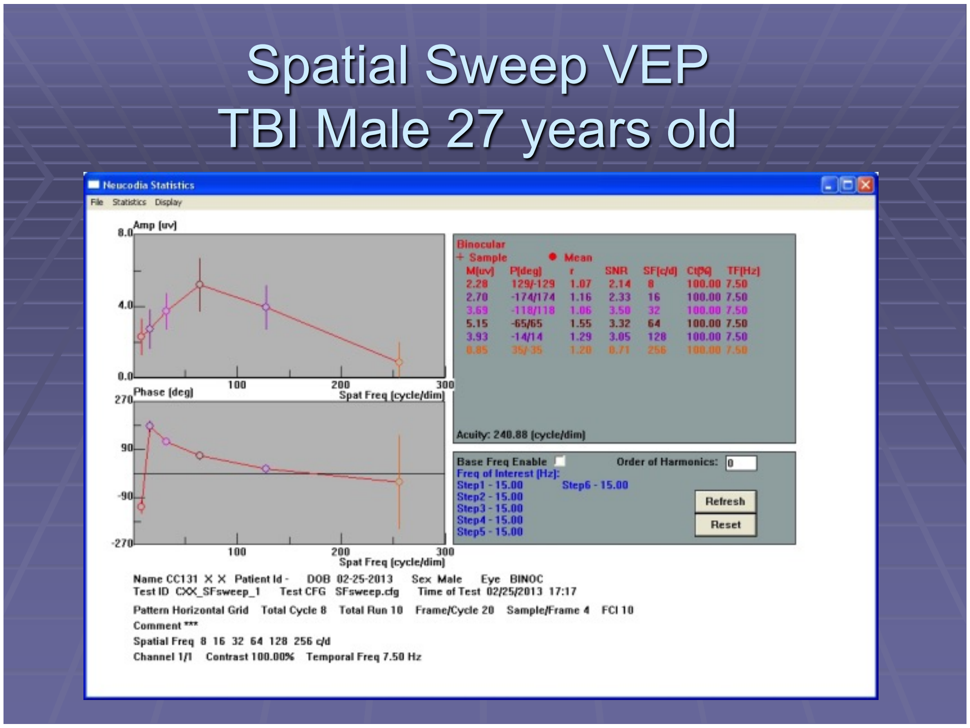
Radial Partial-Windmill and Windmill-Dartboard VEPs from a 7-yr-old Child

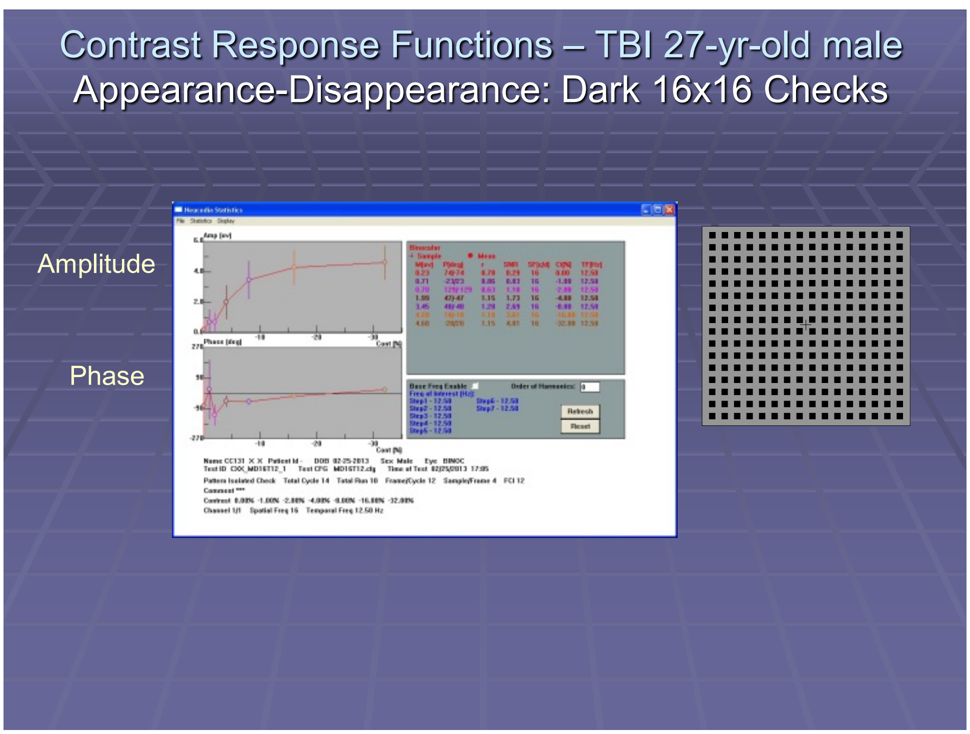


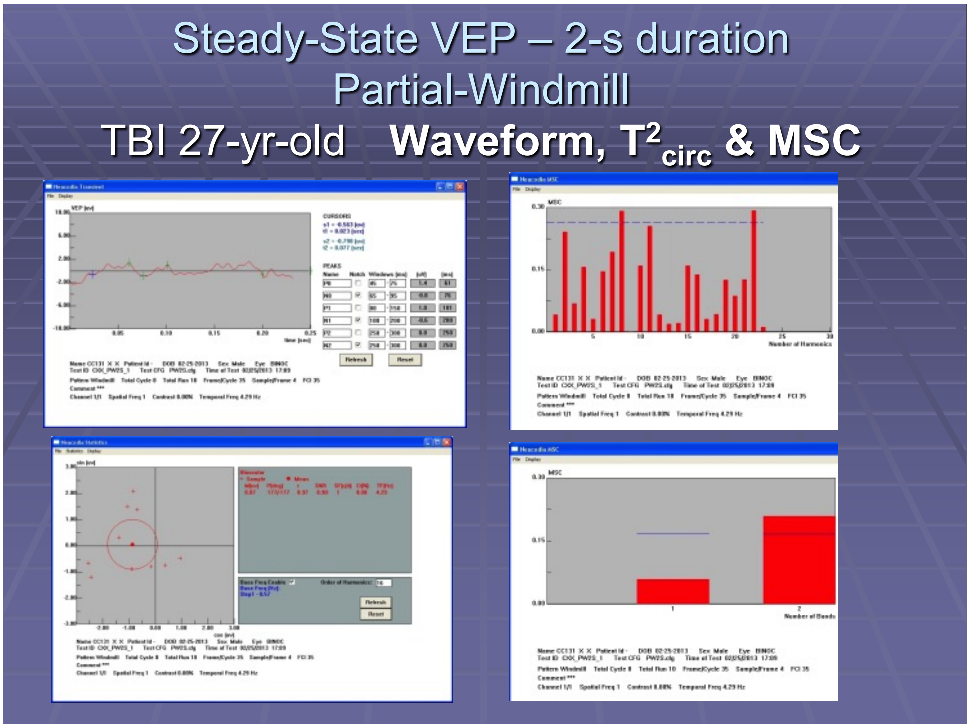


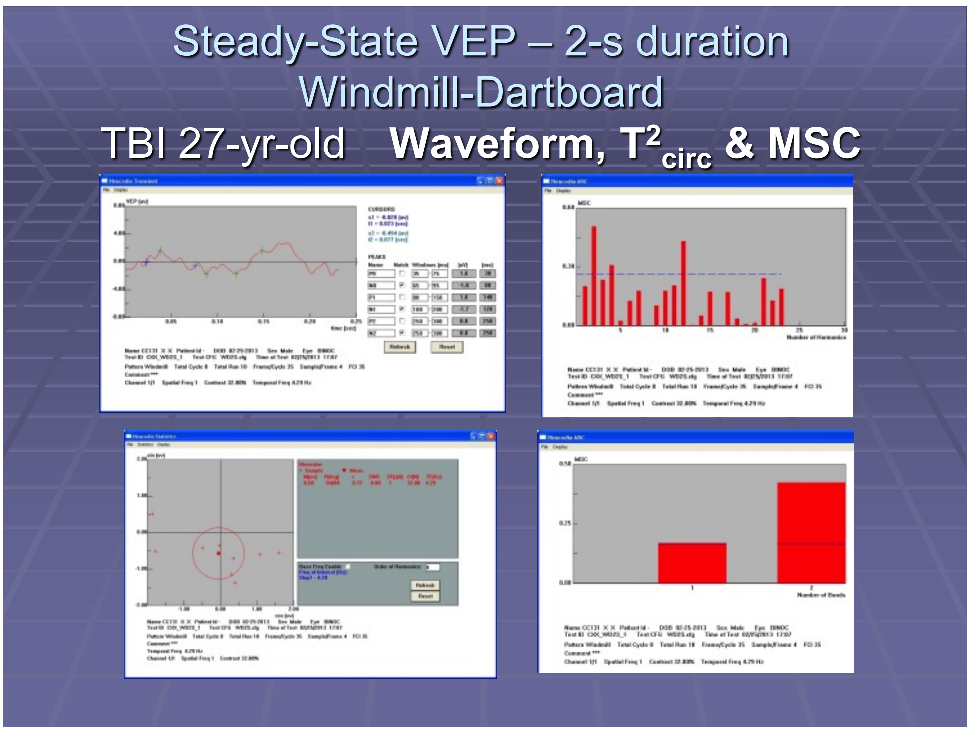
Example Data from a Veteran with a Traumatic Brain Injury

Normal spatial frequency sweep VEP and contrast response functions to isolated checks. Abnormal partial-windmill and windmill-dartboard VEPs.






Steady-State VEP – 2-s duration
Partial-Windmill
TBI 27-yr-old Waveform, T^2_{circ} & MSC


Steady-State VEP – 2-s duration
Windmill-Dartboard
TBI 27-yr-old Waveform, T^2_{circ} & MSC

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