EvokeDx provides a library of visual electrophysiology test strategies and other supportive tests organized by category (Figure 1):

- icVEP - isolated-check VEP
- Other VEP - ISCEV standard and novel tests
- ERG - ISCEV standard and novel tests
- Visual Acuity – ETDRS and Pediatric

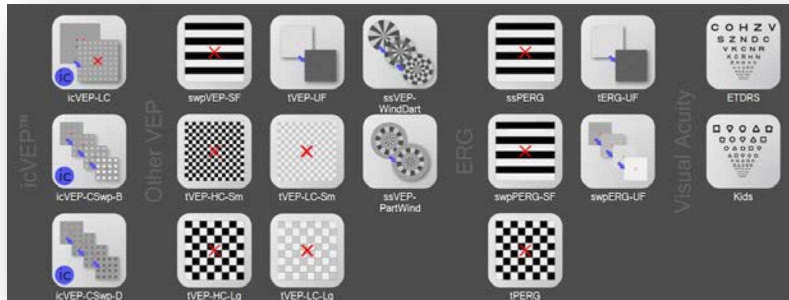


Figure 1 EvokeDx Test Library and Categories

icVEP™

EvokeDx uniquely features icVEP, a patented test strategy based upon studies designed to emphasize contributions to the VEP selectively from the ON or OFF subdivisions of the magnocellular neural pathways[1,2,17]. This work demonstrated differences in the ON and OFF pathways that were previously thought to be 'mirror-image' systems, which were further confirmed by histological staining of the different cell types in human retina3 and by single-cell recordings from the primary visual cortex of monkeys[4].

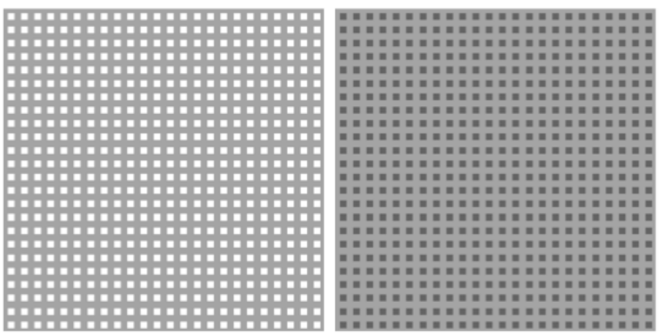


Figure 2 - icVEP Bright & Dark Check Patterns

Luminance of the checks varies sinusoidally in time such that the pattern smoothly appears and then disappears. The low contrast bright-check pattern, is thought to emphasize the M-ON pathway.

icVEP tests are designed to assess low contrast processing in the visual system, which are deficient in various disorders, including glaucoma[5,18]. This icVEP research demonstrated high classification accuracy for early-stage glaucoma in a Phase I NIH-funded study[6] (A'=94%) and in a multisite Phase II NIH-funded study[7] (A'=89.2%).

A contrast-sweep version of this icVEP technique[1] was applied to the study of schizophrenia and autism which discovered selective deficits in visual processing[10,11,13,16]. Selective low-contrast deficits were found using this technique in a study of patients with retinitis pigmentosa as well[8].

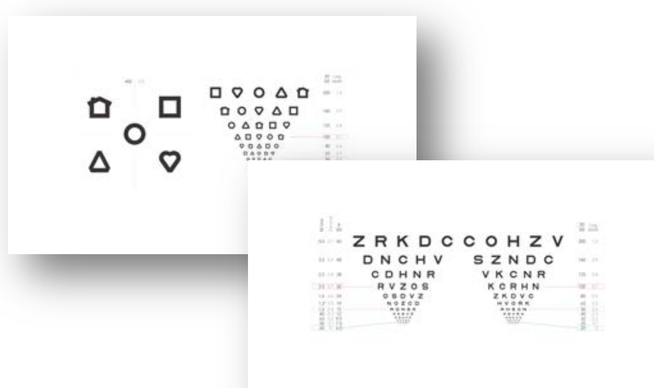
Other VEP and ERG

VEP tests explore neural function at the level of the visual cortex. Comparisons between the retinal and cortical responses help facilitate differential diagnosis of visual dysfunction.

ERG's elicited by patterned stimuli (PERGs) reflect the activity of the inner retina (primarily retinal ganglion cells) whereas ERGs resultant from luminance modulation of a uniform field taps activity of the outer retina (primarily ON bipolar cells). It follows that ERG tests assess various types of visual function responses prior to modification neurons in the brain.

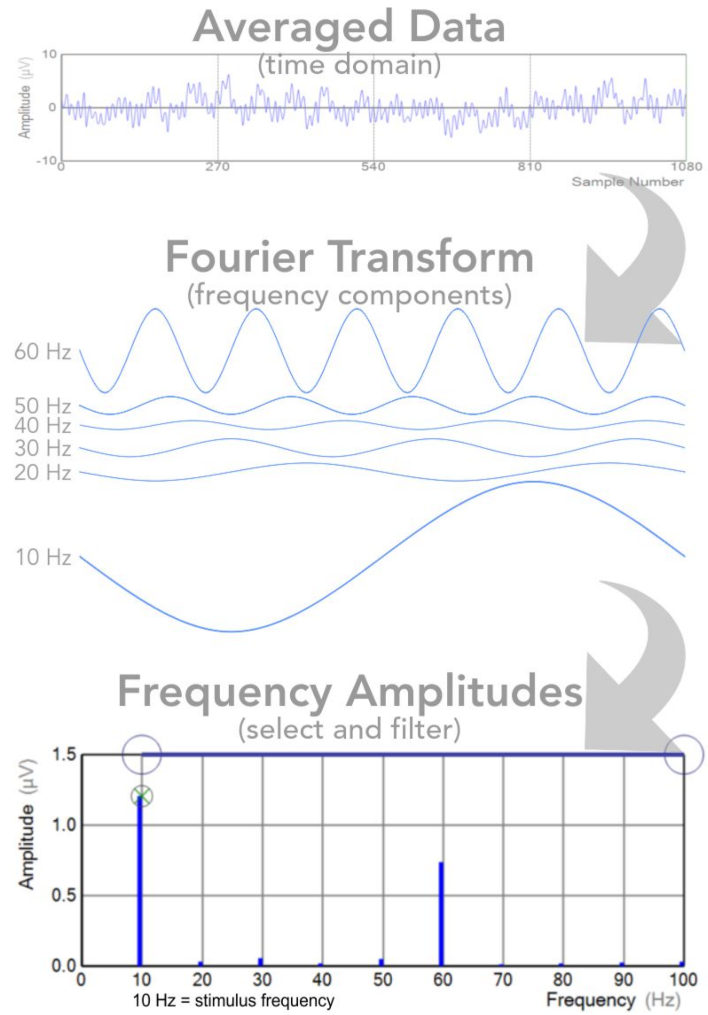
Visual Acuity

Visual acuity charts (Sloan ETDRS and pediatric optotypes) are available to conveniently verify that the patient has adequate visual acuity (~20/30), including any needed refraction or near add, for high spatial frequency tests (e.g. icVEP and tVEP small-check stimuli). The acuity charts are precision displayed with optotypes calibrated for the VEP/ERG testing distance of 65 cm on the OLED patient stimulus monitor. An enlarged preview of the same is also shown on the operator's monitor for patient response verification.



Analytics

Data Evaluation with Fourier Transform Tools
All EvokeDx VEP and ERG signals are recorded synchronously as time-stamped amplitudes using very short interval test "runs" of a few seconds. The patient's attention, cooperation, and comfort is enhanced by administering these very short tests compared to conventional extended tests that take one minute or longer with no breaks with earlier VEP/ERG technologies. Ten short runs are averaged (after validation with artifact rejection and outlier analysis), and the response waveform is represented in a time-domain plot.

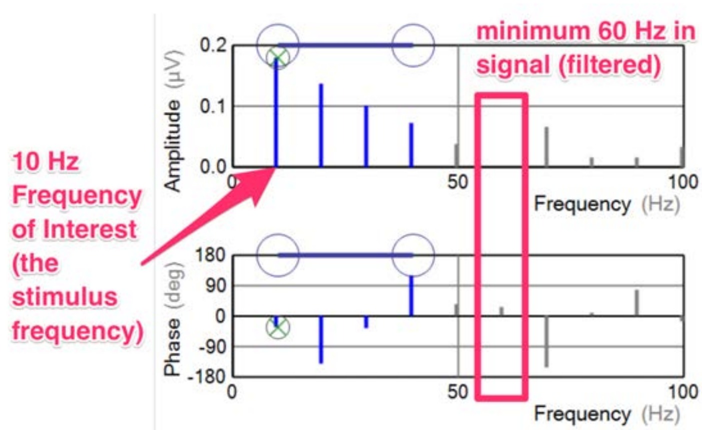


EvokeDx analytics are key to new insights into visual electrophysiology results. *Fourier analysis* is used to decompose the complex and repetitive time-based waveform into a set of sinusoidal functions, *frequency components,* each one specified by a single frequency (in Hz), and quantified by an amplitude and phase value. The lowest frequency is the *fundamental frequency* or *first harmonic (equal to the stimulus frequency)*, with multiples of this referred to as second, third … harmonics. Fourier analysis, well known in other physical and biological fields (e.g. data assessment in OCT), allows a rich, statistical assessment of the composition of the entire response rather than just picking out one or two points in time (e.g. N75, P100) and trying to draw a conclusion based upon some latency or amplitude value. Fourier analysis opens the door to a series of advanced analytics unavailable with time-domain data analysis.

Key Analytics and Metrics

Filters

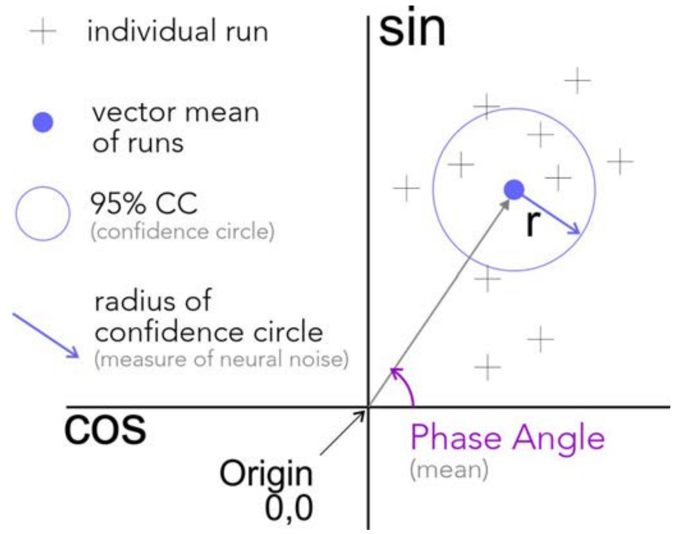
After applying a discrete Fourier transform, the VEP waveform is decomposed into its constituent frequency components, allowing certain components to be selectively removed from the frequency spectrum, followed by a reconstruction into a modified time-domain waveform. A Fourier filtering technique, by default, is used to assess and remove excessive environmental noise (e.g. EMF's at 60 Hz or 50 Hz) that can be picked up by the sensors prior to amplification - commonly due to a loose connection between the sensor and the scalp. It is recommended, if a large amount of 60-Hz noise is detected, that the source of the recording problem should be identified and corrected: for example, by reapplying the loose sensor to the head or by turning off and unplugging other electronic equipment in the area that is responsible for the EMFs.



T^2_{CIRC}

This multivariate statistic is calculated on the sine and cosine coefficients of a VEP frequency component to estimate the variability (noise) in the set of responses at the test's Frequency Component of Interest (FCI).

Each individual run's response component is plotted, with the vector-mean (dot), and a noise circle (radius r) indicating the 95% confidence circle (CC). If the noise circle includes the origin, the response is not significant.



SNR (Signal to Noise Ratio)

SNR is the strength of the recorded signal at the frequency of interest relative to the level of noise at the same frequency.

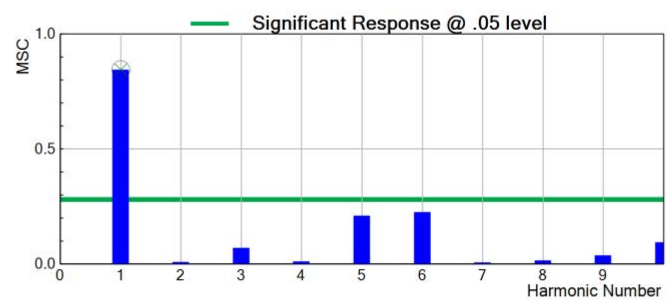
A SNR value below 1 indicates that the noise circle overlaps the origin of the sine-cosine plot and that the response is not significant at the .05 level. A SNR value above 1 indicates a significant response. This ratio serves to adjust for overall gain differences in recorded EEG signals across individuals that can result from non-neural factors such as the amount of cerebrospinal fluid between the skull and the brain.

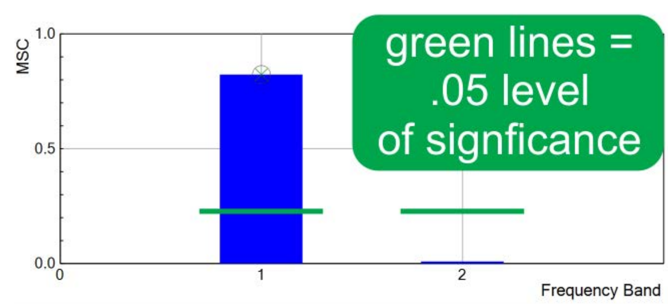
F_{STAT}

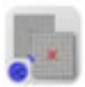
F_{STAT} assesses if two sweep VEP/ERG functions are statistically different or not. For example, the F_{STAT} may be used to determine if fellow eye monocular responses are matched or differ sufficiently to raise concerns about a unilateral condition such as amblyopia. An observed F value obtained from the comparison of two functions being tested is compared to a critical F value set by a specified significance level (e.g., .05). F_{STAT} shares the same type of bar graph (red-yellow-green) as SNR.

Coherence (MSC)

To quantify the level of signal power in the response compared to the total power (signal + noise), a *coherence* measure is used. Magnitude squared coherence (MSC) is calculated for a frequency component of interest and then compared to a critical value to determine if a significant response exists at that frequency. Average MSC values for *bands of frequency components* are also calculated that have been found to reflect distinct neural mechanisms.





Tests		Applications	Key Metrics	Refs
	icVEP-LC Isolated-check VEP (icVEP) Low Contrast	Assesses low contrast processing Primarily drives the magnocellular (large cell) pathway. Bright checks: M-ON *autism, glaucoma, Parkinson disease, retinitis pigmentosa, schizophrenia, TBI, visual development icVEP-LC is an approximate subset, 4rd step, of icVEP-CSwp-B (below)	**SNR:** > 1 (green = significant / measurable response) **T^2_{circ}:** 95% CC (confidence circle) does not include Origin (0,0) • = significant response • "+" = each run • Solid dot = mean of 10 runs • Phase angle - 4 quadrants represent phase (timing) of sinusoid • Responses in similar phase (tightly grouped together) **FCI:** 10 Hz (= stimulus frequency) (FCI = Frequency Component of Interest) Coherence (MSC) • 1st MSC frequency band above black line = significant response (p < .05), odd harmonics • 1st harmonic (10 Hz) in green zone = significant response (p < .05) **Waveform:** ~ sinusoidal (analog of the sinusoidal stimulus)	1,2, 6,7, 8,9, 10,11,12, 13,14,15, 16,17,18, 19
	icVEP-CSwp-B icVEP Contrast Sweep - Bright	Assesses low contrast processing Primarily drives the magnocellular (large cell) pathway. Bright checks: M-ON Dark checks: M-OFF *autism, glaucoma, Parkinson disease, retinitis pigmentosa, schizophrenia, TBI, visual development	**SNR:** <1 at the lowest modulating contrast levels, (typically first 1 or 2 steps), increasing >1 as the modulating contrast increases F_{STAT} • Comparison by step of SNR • F_{STAT} Overall, averaged function across the entire response • F_{STAT} Comparison of two overall functions (e.g. compare two fellow eye responses) **T^2_{circ}:** 95% CC does not include Origin (0,0) for significant response • Phase angle - responses in similar phase **FCI:** 10 Hz (= stimulus frequency) Coherence (MSC) – when SNR > 1 • 1st MSC frequency band (odd harmonics) • 1st harmonic (10 Hz) **Waveform:** ~ sinusoidal (analog of the sinusoidal stimulus) when SNR > 1	
	icVEP-CSwp-D icVEP Contrast Sweep - Dark			
	swpVEP-SF Sweep VEP – Spatial Frequency	Contrast-reversing horizontal gratings (high contrast) to assess spatial processing *amblyopia, yields and estimate of visual (grating) acuity, cortical visual impairment, cataract effects on acuity, macular function	**SNR:** > 1 reducing typically to < 1 at the highest spatial frequencies, typically last 1 or 2 steps **Amp : Phase** : estimating visual (grating) acuity in cycles/degree (star symbol) F_{STAT} • Measureable (green) **FCI**: 15 Hz (2nd harmonic of 7.5 Hz stimulus) **Coherence (MSC)** – significant when SNR >1 • 2nd MSC frequency band (even harmonics) • 2nd harmonic (15 Hz) (contrast-reversing patterns should yield significant 2nd harmonic)	20,21,22, 23,24,25
	ssPERG Steady-State Pattern ERG	Spatial processing in inner retina (retinal ganglion cells). Can evaluate both eyes simultaneously. *evaluate suspected unilateral defects, e.g., glaucoma ssPERG is a subset, 3rd step, of swpPERG-SF (below)	**SNR:** > 1 (green = significant / measurable response) **T^2_{circ}:** 95% CC does not include Origin (0,0) **FCI:** 15 Hz, (2nd Harmonic (7.5 Hz stimulus) Coherence (MSC): • 2nd MSC frequency band (even harmonics) • 2nd harmonic (15 Hz)	13,26, 27,28,29, 30,31,32, 33,34
	swpPERG-SF Sweep PERG - Spatial Frequency	Contrast-reversing horizontal gratings - has typically lower maximum spatial frequency response compared to swpVEP-SF *amblyopia, cortical visual impairment, macular degeneration, and optic neuropathy.	**SNR**: > 1 reducing typically to < 1 at the highest spatial frequencies **Amp - Phase**: estimating visual (grating) acuity in cycles / degree (star symbol), with typically lower values than swpVEP-SF F_{STAT} • Comparison by step of SNR • F_{STAT} overall, each eye response • F_{STAT} comparison of the overall function of each eye response across the sweep response function **FCI**: 15 Hz (2nd harmonic of 7.5 Hz stimulus) Coherence (MSC) – when SNR > 1 • 2nd MSC Frequency Band significant (even harmonics)	
	tVEP-HC-Sm Transient VEP High-Contrast Small Checkerboard	Conventional high contrast, contrast-reversing checkerboard pattern. *depression, MS, optic neuritis, Parkinson disease, excitatory and inhibitory postsynaptic potential	**FCIs**: even harmonics of 1Hz stimulus Coherence (MSC) • 2nd MSC frequency band is typically significant and most prominent (selected even harmonics 14-28 Hz) **Waveform Peaks**: N75, P100, N135	35,36,37, 38,39,40, 41,42,43, 44

* Published Work for Potential Uses

	tVEP-HC-Lg Transient VEP High-Contrast Large Checkerboard	activity, assessment of combined input to visual cortex from multiple parallel pathways, traumatic brain injury, visual development Large-check checkerboard less sensitive to refractive errors, and useful when high spatial frequency function is compromised (e.g. macular disease)		
	tVEP-LC-Sm Transient VEP Low-Contrast Small Checkerboard	Conventional low contrast, contrast-reversing checkerboard pattern. *autism, depression, multiple sclerosis, optic neuritis, Parkinson disease, schizophrenia, traumatic brain injury, visual development Large-check less sensitive to refractive errors and useful when high spatial frequency function is compromised (e.g. macular disease)	**FCIs**: even harmonics Coherence (MSC): • 1^{st} MSC frequency band significant and more prominent (selected 6-12 even harmonics) **Waveform Peaks: N75, P100, N135** Peaks are later with low contrast compared to high contrast	See tVEP-HC
	tVEP-LC-Lg Transient VEP Low Contrast Large Checkerboard			
	tPERG Transient PERG	Conventional high-contrast large-check checkerboard pattern. Large-check less sensitive to refractive errors and useful when high spatial frequency function is compromised (e.g. macular disease) *glaucoma, diabetic retinopathy	**FCIs**: Even harmonics Coherence (MSC): • 1^{st} MSC frequency band significant and more prominent **Waveform Peaks**: N35, P50, N95	35,36, 44,45
 Typically run together	ssVEP-WindDart Steady-State Windmill Dartboard	Lateral (inhibitory) interactions in visual processing evidenced by generation of 1^{st} harmonic and attenuation of 2^{nd} harmonic response *epilepsy, migraine, amblyopia (assesses GABA inhibitory circuits), TBI	**SNR:** > 1 (green = significant / measurable response) T^2_{circ}**:** 95% CC does not include Origin (0,0) **FCIs:** 1^{st} harmonic (4.29 Hz) and 2^{nd} harmonic (8.58 Hz) Coherence (MSC): • 1^{st} MSC frequency band (odd harmonics) significant and more prominent than 2^{nd} harmonic	46,47,48, 49,50,51, 52,53,54, 55,56,57, 58,59,60, 61
	ssVEP-PartWind Steady-State Partial Windmill	Baseline response for comparison to windmill-dartboard response. Typically prominent 2^{nd} harmonic response. *amblyopia, autism, epilepsy, migraine headaches, schizophrenia, TBI, visual development.	**SNR:** > 1 (green = significant / measurable response) T^2_{circ}**:** 95% CC does not include Origin (0,0) **FCI:** second harmonic (8.58 Hz) Coherence (MSC): • 2^{nd} MSC frequency band (even harmonics) significant and more prominent	
	tVEP-UF Transient Uniform Field VEP	Neural function of the outer retina using a broad "Uniform Field" stimulus with VEP or ERG. *assessment of visual function given optical problems (e.g., dense cataracts) or fixation difficulties.	**FCIs**: even and odd harmonics Coherence (MSC): • 1^{st} (even harmonics, more prominent) and 2^{nd} (odd harmonics) MSC frequency bands significant **Waveform Peaks**: N75, P100, N135	
	tERG-UF Transient Uniform Field ERG		**FCIs**: even and odd harmonics (1 Hz stimulus) Coherence (MSC): • 1^{st} (even harmonics, more prominent) and 2^{nd} (odd harmonics) MSC frequency bands significant Waveform Peaks: P100, N250	
	swpERG-UF Sweep Uniform Field Contrast ERG		**SNR:** <1 at the lowest luminance modulating (contrast) levels, (typically first steps #1 & #2)**, i**ncreasing > 1 as the luminance modulation increases F_{STAT} • Comparison by step of SNR • F_{STAT} Overall, each eye response • F_{STAT} Comparison of the Overall function of each eye response across the sweep response **FCI**: 1^{st} harmonic (6 Hz stimulus) Coherence (MSC): • 1^{nd} MSC frequency band significant (odd harmonics)	

Additional references: 62,63,64,65,66,67,68,69,70,71,72,73

[*] Published Work for Potential Uses

Visual Structure/Function, Concomitant Disorders, & EvokeDx Tests

Neural function in the visual system is often segmented into anatomical structures such as the **outer retina**, **inner retina**, and **central visual pathways** in the brain (e.g., the relay station in the thalamus, dorsal lateral geniculate nucleus [LGN], and its projection to primary visual cortex, V1). Subsequent processing takes place in visual association areas of the cerebral cortex (e.g., V2, V3, V4, V5). Visual information is sent via parallel neural pathways through each of these structures with crosstalk occurring primarily at the more central sites. The electrophysiological tests and accompanying response measures provided in EvokeDx are designed (based on the wealth of knowledge accrued from extensive neurophysiological studies) to tap the various types of neural function that occur at each of these levels of visual processing. Disorders of the visual system affect particular cell types and mechanisms along these pathways, and therefore, certain tests may be selected for a given patient predicated on the expected site or sites of dysfunction related to the disease process. Note that dysfunction at an early level (e.g., photoreceptors or retinal bipolar cells) can be reflected in responses tapped at higher levels (cortical activity recorded on the scalp over the occipital lobe, VEP) as well as with recordings near the primary site (ERG measured below the lower eyelid). Also, the integrity of the physiological optics affects the neural responses elicited by the stimuli.

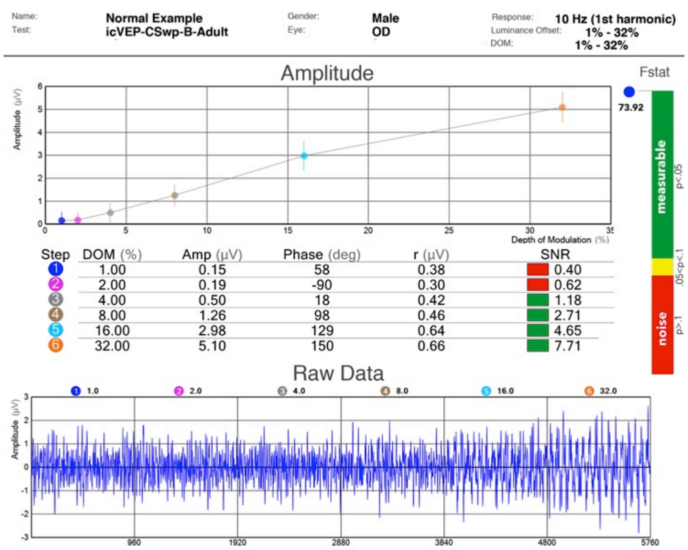
The table below illustrates categories of visual structure and function of disorders independently researched and reported to compromise each neural response, and EvokeDx tests, as examples only, that may be useful in examining each kind of activity generated (references cited* above by test topic). Note that disorders are listed in a particular category of structure/function, but certain disorders might act on multiple levels, e.g., glaucoma has been shown to affect neurons within the brain as well as retinal neurons.

Visual Structure | Function	Disorder Examples	EvokeDx Tests															
		icVEP -LC	icVEP CSwp -B	icVEP CSwp -D	swp VEP -SF	ss PERG	swp PERG -SF	tVEP -HC -Sm	tVEP -HC -Lg	tVEP -LC -Sm	tVEP -LC -Lg	t PERG	ssVEP Wind Dart	ssVEP -Part Wind	tVEP -UF	tERG -UF	swp ERG -UF
Physiological optics *(imaging the stimulus)*	refractive error				✓		✓		✓						✓	✓	✓
	cataracts				✓		✓		✓						✓	✓	✓
Outer retina *(visual transduction and encoding, formation of parallel pathways)*	macular degeneration	✓	✓	✓	✓		✓	✓	✓			✓	✓	✓			
	retinitis pigmentosa	✓	✓	✓					✓							✓	✓
	night blindness (congenital stationary)				✓		✓	✓	✓						✓	✓	✓
Inner retina *(conversion of graded electrical signals into trains of action potentials for transmission to brain)*	glaucoma	✓	✓	✓		✓	✓	✓	✓	✓	✓						
	diabetic retinopathy	✓	✓	✓	✓		✓	✓	✓			✓				✓	✓
	optic neuropathy /neuritis		✓	✓	✓		✓	✓	✓				✓	✓			
Central visual pathways *(formation of complex visual receptive fields for orientational and directional selectivity, binocularity / stereopsis, motion perception, brightness / darkness perception, color perception, interactions among parallel streams)*	amblyopia		✓	✓	✓		✓	✓	✓				✓	✓			
	autism	✓	✓	✓	✓			✓	✓				✓	✓			
	cortical visual impairment		✓	✓	✓			✓	✓				✓	✓			
	depression				✓	✓	✓	✓	✓			✓				✓	✓
	epilepsy							✓	✓				✓	✓			
	migraine headaches							✓	✓				✓	✓			
	multiple sclerosis				✓		✓	✓	✓	✓	✓		✓	✓			
	Parkinson disease		✓	✓	✓		✓	✓	✓			✓				✓	✓
	schizophrenia	✓	✓	✓				✓		✓			✓	✓			
	traumatic brain injury	✓	✓	✓	✓		✓	✓	✓				✓	✓			

* Published Work for Potential Uses, see "Tests – Key Metrics – Applications" table for applicable references

Analysis Examples

SNR (Signal to Noise Ratio) Relative to Sweep of DOM Contrast



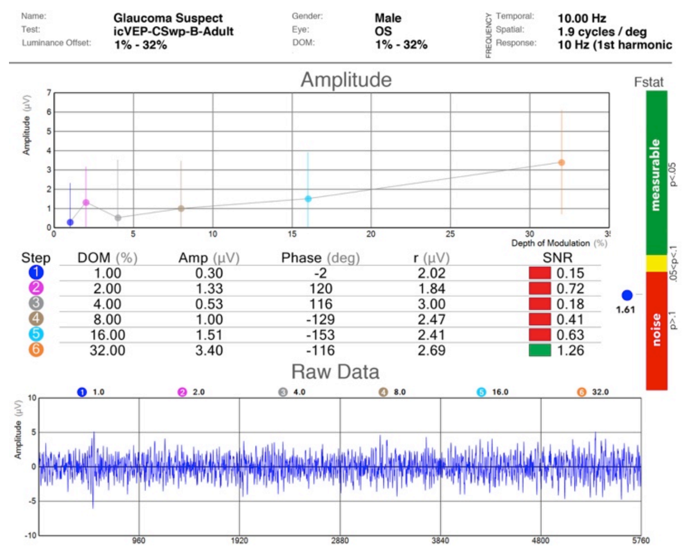


Figure 3 Illustration of a typical, VEP contrast response function obtained with the isolated-check VEP sweep stimulus. The stimulus depth of modulation (DOM) increases in successive steps, doubling in value, each step, from +/- 1% on the first step to +/- 32% on the final sixth step (+ DOM for bright checks and – DOM for dark checks). In the icVEP Sweep, typically, normal observers will not exhibit a significant response to the first two steps and as such will have SNR below 1, described as responses that are "in the noise". (Peak contrast is double the DOM value.) As DOM increases, typically responses at Steps 3-6 are "out of the noise" generally in a compressive non-linear manner with SNR values increasing. To the right of the Amp:Phase graph, the red-yellow-green bar, illustrates that the overall response (F_{STAT}) across all contrast conditions is significant.

Figure 4 In contrast to a typical response function, as shown in Figure 3, the data from a glaucoma suspect patient demonstrates a non-significant response to the first 5 steps of the test (SNRs all less than 1, ranging from 0.15 to 0.63). The F_{STAT} (red-yellow-green bar), indicates whether the overall response across the six conditions achieves statistical significance or not - in this example he overall response is non-significant (it appears in the lower red zone). This patient only exhibits a significant response to the final sixth step (highest DOM of +/- 32%, contrast of 64%) and is only just out of the noise slightly above an SNR of 1 (just in the green). The individual steps in the Amplitude Vs DOM graph show a flat response and do not "climb out the noise" as in the case of the normal observer.

T^2CIRC SINE : COSINE

T^2_{CIRC} is a relatively new statistic (Victor and Mast, 1991[74]) used to evaluate evoked potentials by determining if the Fourier component of interest is significant. As an example for the icVEP tests, the response frequency of interest is 10Hz, which is the frequency at which the stimulus is sinusoidally modulated. T^2_{CIRC} utilizes all the information available in that frequency response (amplitude and phase values), which is not the case with other statistical measures (e.g., Rayleigh criterion) employed in other analysis methods and is therefore a more robust way of detecting and quantifying steady state VEP responses. Signal reliability is evaluated by the T^2_{CIRC} statistic, which analyzes the two-dimensional Fourier vectors and indicates whether the average vector is significantly different than the NULL vector. The fundamental output of the Fourier transform is to convert time-domain data to the frequency domain. T^2_{CIRC} also calculates the radius of the noise circle "r" which defines the 95% Confidence Circle (CC).

The T^2_{CIRC} Sine:Cosine graph plots the responses from individual "runs" ("+" symbols) along with their vector mean ("•"). More significance responses are more tightly clustered together away from the origin (0,0) (requires similar amplitudes and phase angles). Surrounding the mean response is the 95% CC and if it encompasses the origin (0,0), the response is **non-significant**. If the 95% CC does not encompass the origin, it represents a **significant response**, with larger distances from the origin being more significant.

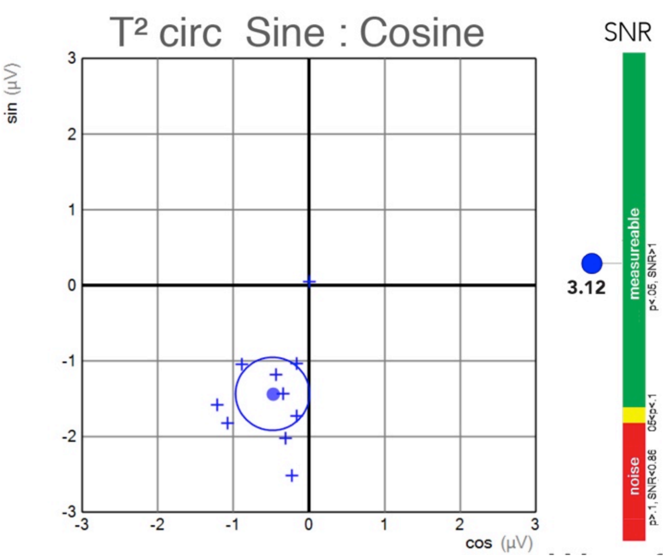


Figure 5 illustrates a significant response to the icVEP stimulus. Responses from all 10 runs (+) are all located in the lower left quadrant of the graph, in general proximity with the corresponding 95% CC not inclusive of (in fact far away from) the origin. The small blue dot (in the center of the 95% CC) represents the mean of the 10 individual runs. The SNR bar (red-yellow-green) shows a significant SNR (measureable response) of 3.12.

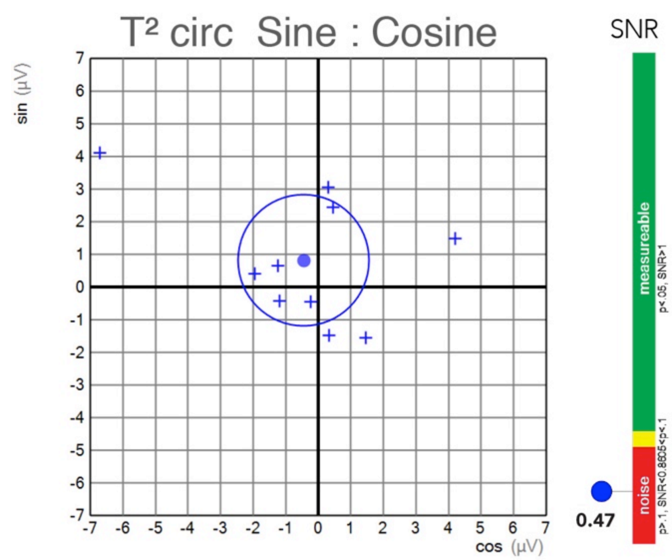
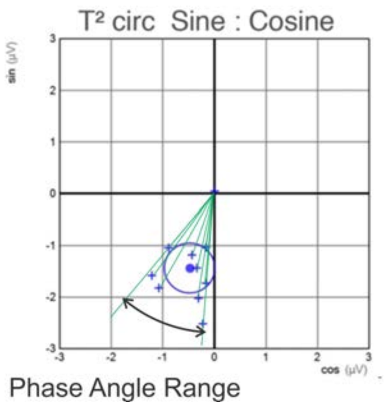
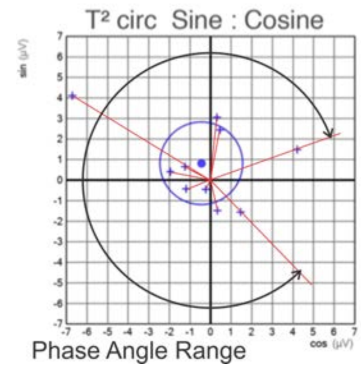


Figure 6 illustrates a non-significant VEP response to the same stimulus as in Figure 5. The responses to the 10 runs are more scattered about (large differences in amplitude) in all 4 quadrants (large changes in phase angle). The 95% CC includes the origin of the Sine:Cosine graph and therefore is a non-significant response. In addition, the SNR is low, 0.47 and in the noise (red) section of the SNR bar.

Phase Angle



Phase Angle represents timing of the measured response, defined for the Frequency Component of Interest (FCI). A tightly grouped series, of responses (depicted left) in one or two quadrants, shows a relatively consistent set of responses (over the 10 runs). A large spread of responses (right) occupying 3 or 4 quadrants indicates poor consistency from run to run, indicative of noise rather than a real response.



MSC (Magnitude-Squared Coherence)

Coherence with the MSC statistic is used to estimate signal power relative to signal + noise power in a VEP frequency response and is related to the T^2_{CIRC} statistic. EvokeDx uses MSC to measure the strength of the VEP response in the frequency domain for each harmonic frequency component and for bands of frequency components. To a symmetrical, contrast-reversing pattern, odd harmonics should show no significant response, but even harmonics (e.g., a frequency band containing) with the 2nd and 4th harmonic) tend to represent significant responses at or above the .05 level. The black bar is the critical value for significance.

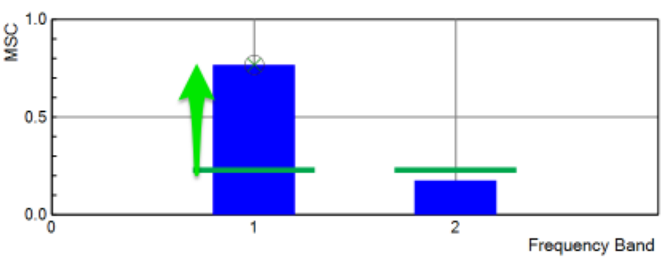


Figure 7 illustrates a significant MSC response in the first frequency band as illustrated by the blue bar extending well above the critical MSC value for .05 significance (green line) at .767, and a non-significant response in the second frequency band (below the green line).

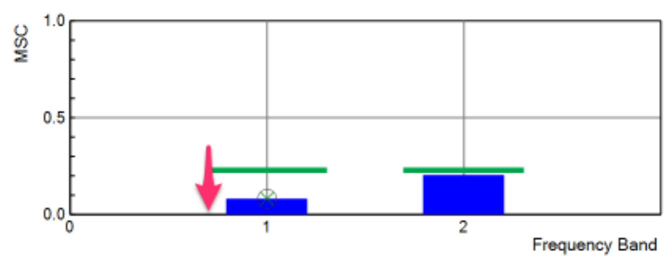


Figure 8 illustrates non-significant responses for both first and second frequency bands, as they are below the critical MSC value at the .05 level significance.

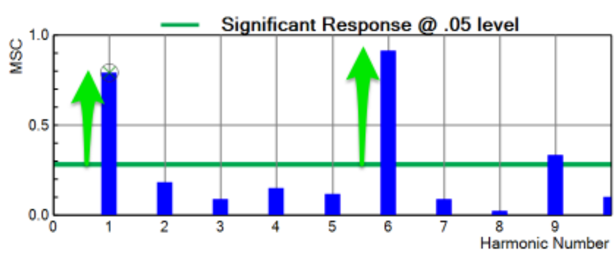


Figure 9 illustrates ten, discrete frequency (harmonic) components obtained by a discrete Fourier transform on the collected time-based data, with the first harmonic as a significant MSC response well above the .05 significance level (above the green line) at .794. The other harmonic components are well below the .05 level and are therefore non-significant. Note that the sixth harmonic is the 60 Hz (6 X 10Hz), likely to include line (electrical power) noise.

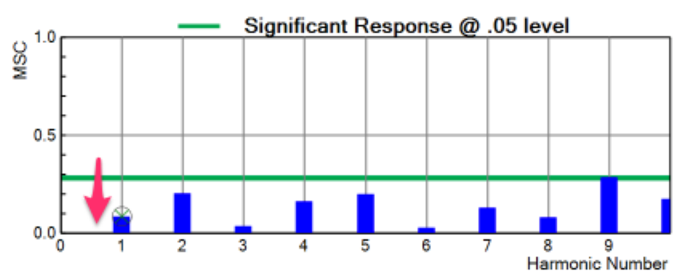


Figure 10 illustrates non-significant responses where each of the frequency components extracted from the time-domain measured responses are well below the significant level $p<.05$, (marginally with the ninth harmonic).

Waveforms

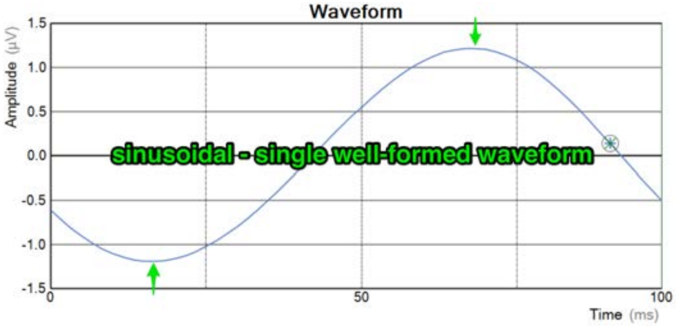


Figure 11 The waveform is Fourier reconstructed from the selected frequency components. This illustration is of an icVEP-LC test response on a healthy observer and it demonstrates a **sinusoidal response** recording that is a strong analog of the sinusoidal stimulus and represents an **excellent icVEP response**. When this type of stimulus pattern that is presented sinusoidally, a perfect response (which does not occur in nature) would also be sinusoidal, reflecting a Coherence (MSC) value of 1.0.

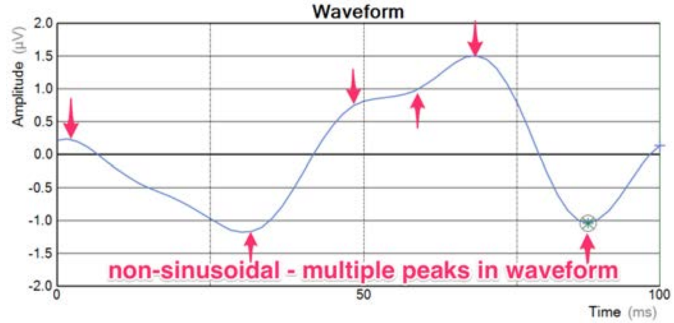
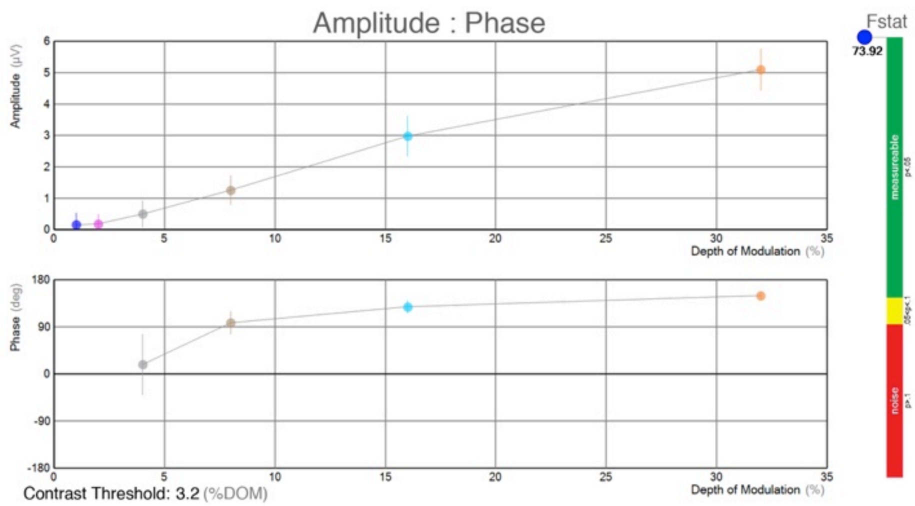


Figure 12 Using the same icVEP-LC test conducted on a glaucoma suspect, the Fourier reconstructed waveform is clearly **not a sinusoidal pattern** with multiple peaks and periods – a **non-significant response**.

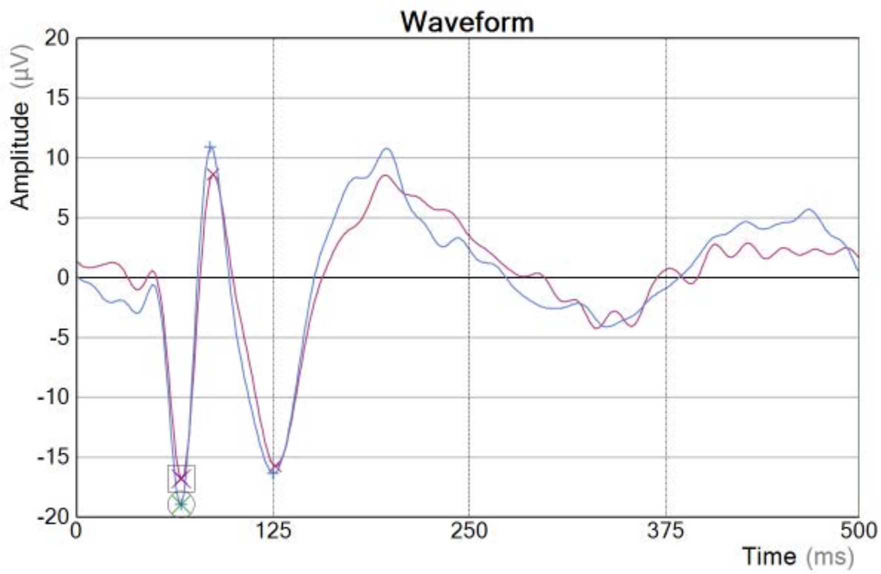


Step	DOM (%)	Amp (µV)	Phase (deg)	r (µV)	SNR
1	1.00	0.15	58	0.38	0.40
2	2.00	0.19	-90	0.30	0.62
3	4.00	0.50	18	0.42	1.18
4	8.00	1.26	98	0.46	2.71
5	16.00	2.98	129	0.64	4.65
6	32.00	5.10	150	0.66	7.71

Figure 13 Amplitude : Phase plot here illustrates the change in response to an increasing depth of modulation (from +/- 1 % to +/- 32%). This "sweep" test, starting at very low contrast, is useful to characterize the observer's low-contrast, high temporal frequency visual response, which is thought to reflect the M cells predominantly, and some researchers have suggested that this may be affected early on in the disease process. This sweep strategy is used for other test types (e.g. spatial frequency sweep). In this example, the observer's 3rd step at +/-4% DOM exits out of the noise with an SNR of 1.18 and is the first significant response in the sweep. The 4th through 6th steps show increasingly significant responses with SNRs increasing from 2.71 up to 7.71.

The Phase Angle is not plotted for the first two steps because the phase angle error bars exceed 180 degrees, i.e., there is no real phase angle. The errors bars can be viewed by simply selecting a particular step. The Error Bars (candlesticks), extending above and below each plotted amplitude and phase value, represent the 95% confidence interval around the mean response.

Waveforms and Peak Tables: Transient Responses



			N75	Δ	P100	Δ	N135
AMP (µV)	Test A (OD)	+	-18.92	29.82	10.89	27.23	-16.33
	Test B (OS)	×	-16.80	25.43	8.63	24.37	-15.74
		Δ		4.39		2.86	
Time (ms)	Test A (OD)	+	67		85		125
	Test B (OS)	×	67		87		127
		Δ	0		-2		-2

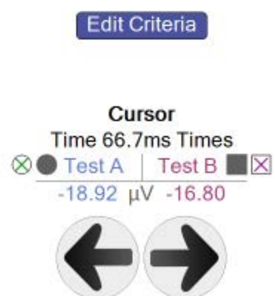


Figure 14 is a typical example of two monocular transient responses (tVEP-HC-Sm) compared. Cursor position is at the N75 location (sometimes called N0) and can be moved along the transient response lines by using the arrows below "Cursor". The N75, P100, and N135 peaks are correctly identified and are similar to the reference time values. The ranges which specify the peak definitions are accessed and can be edited by selecting the Edit Criteria button and entering alternate values. The delta (Δ symbol) shows the difference between peak amplitudes, difference of peak amplitude differences, and difference between peak times. Comparisons can be between two eyes, same eye over time, or two different cases.

Excessive 60 Hz Electrical Noise vs. Expected EEG Signal

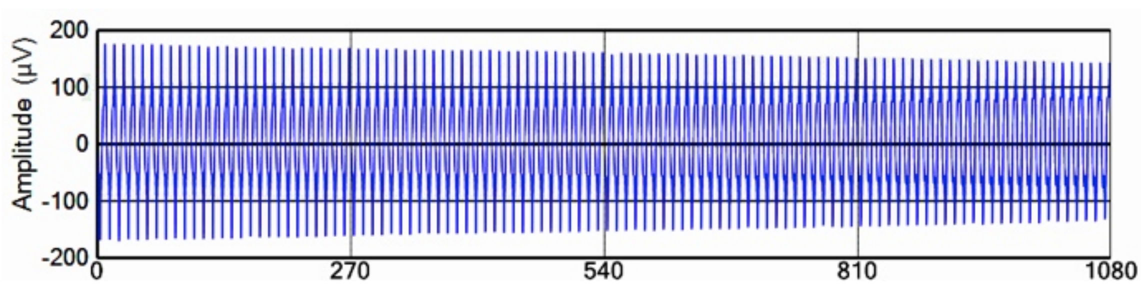


Figure 15 is an example of **unwanted 60 Hz noise** typically from electrodes that have no or inadequate apposition to the scalp or targeted skin areas. Without contact, the electrodes may act as antennas to sense electrical currents developed from wiring in the walls or other equipment in the room. The very high amplitude and highly uniform spacing (in this example almost +/- 200 µV) is unmistakable compared to a typical VEP waveform with amplitudes in the +/- 5 to 15 µV range (ERG approximately 0.5 to 1.5 µV), example shown as Figure 16.

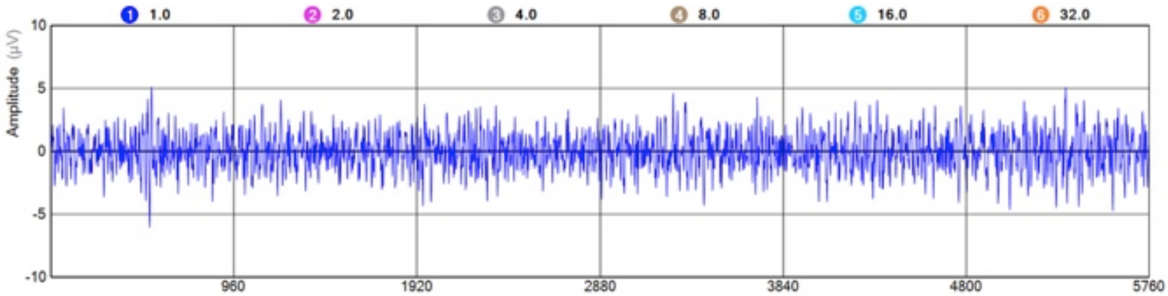


Figure 16 illustrates a **typical EEG pattern**. Note that there is a more irregular and lower amplitude signal than in the 60 Hz electrical noise example depicted in Figure 15.

VEP-estimated grating acuity (cycles/deg.) vs. Snellen acuity

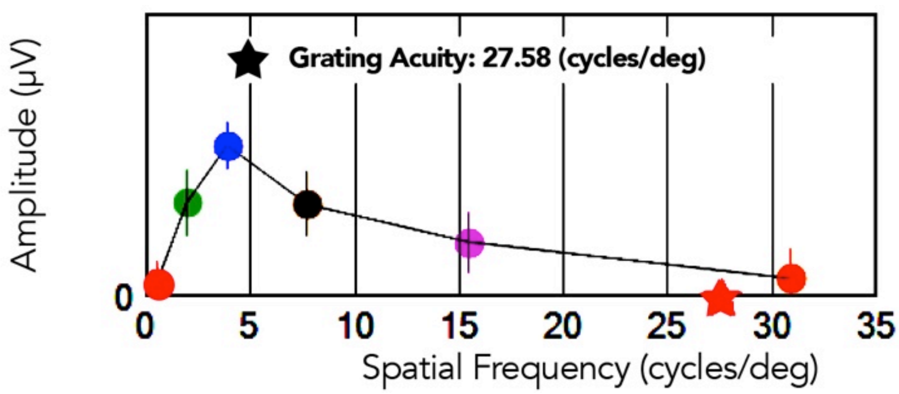
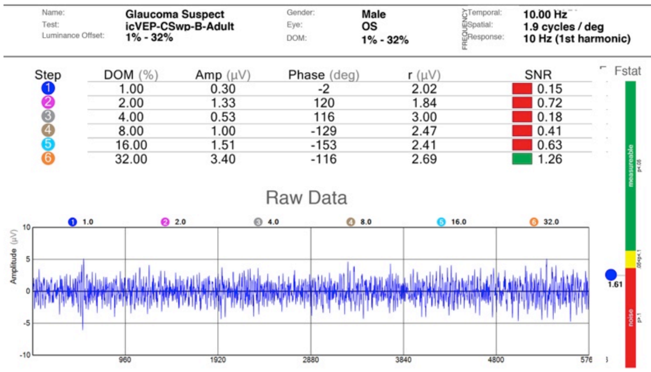


Figure 17 The swpVEP-SF test can be employed in cases where visual acuity is difficult to assess by standard measures and employs a series of square wave gratings which become finer and finer until the evoked potential eventually "disappears" and can be used to generate an **estimate of grating visual acuity**. In this patient the grating acuity estimal is 27.58 (cycles/deg), which approximates typical 20/20 vision (see **Figure 17)**.

Cycles / Degree	1.5	3	6	12	15	19	24	30
Snellen 20/xxx	/400	/200	/100	/50	/40	/32	/25	/20

Figure 18 Cycles / Degree grating acuity to Snellen acuity approximation

Sweep Test Examples



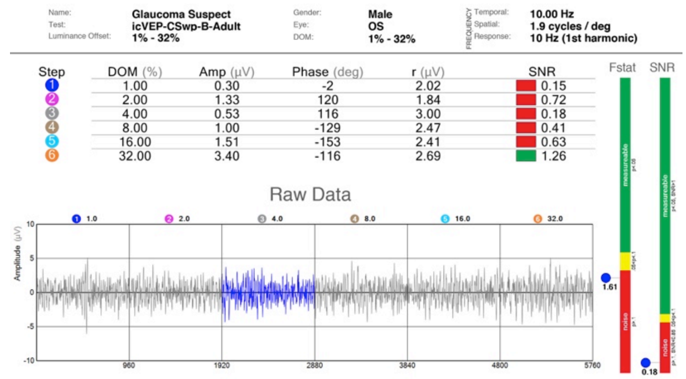


Figure 19 demonstrates all six steps of the icVEP-CSwp-Br-adult test in a glaucoma suspect. In this case the patient demonstrated poor/abnormal contrast responses throughout the first five steps with very low SNRs ranging from 0.15 to 0.63. Only the final 6th step demonstrates a barely significant response with an SNR of 1.26. The colored F_{STAT} bar demonstrates a non-significant response for the entire six-step sweep study with a F_{STAT} of 1.61, which corresponds to the red-noise section of the bar.

Figure 20 shows how to evaluate a single step of a multi-step sweep test. In this case, the third step at 4% DOM (highlighted in blue) is separately evaluated and has a low non-significant SNR of 0.18. (The step is selected by touching the 3rd step waveform on the screen). At this time, both F_{STAT} and SNR colored bars are displayed. The low SNR response of 0.18 corresponds only to the third step, whereas, the F_{STAT} of 1.61 applies to the entire six step sweep. Again, both SNR and F_{STAT} values are in the red-noise section of the bar and therefore are non-significant.

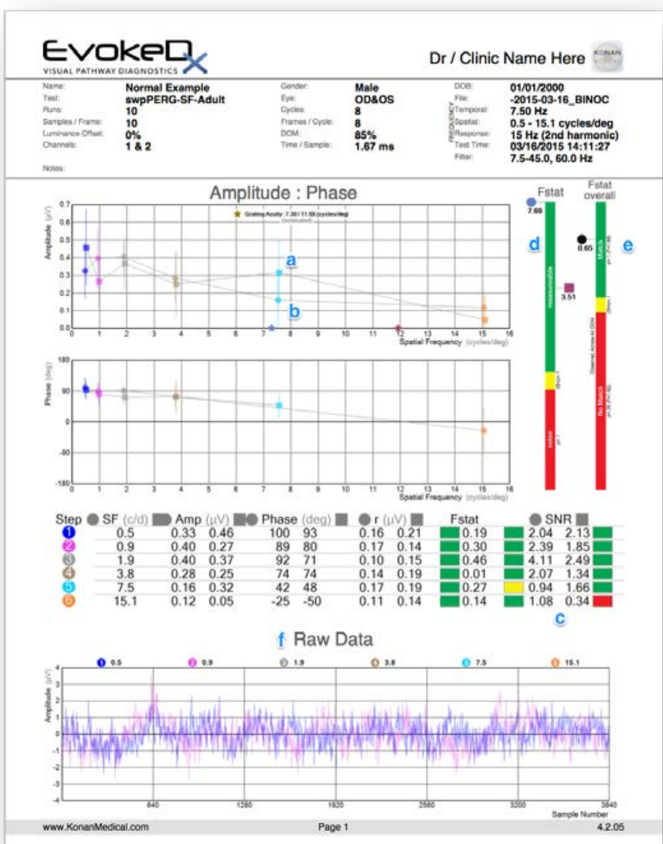


Figure 21 demonstrates a complete standard EvokeDx generated PDF report on a normal observer using the swpPERG-SF-Adult test which evaluates both eyes simultaneously using a 5-lead electrode cable, employing six steps with a temporal frequency of 7.5 Hz and analysis of the 2nd harmonic response at 15 Hz. (a) The right-eye (OD) data on the amplitude and phase graphs are denoted by circle symbols, and the (b) left-eye (OS) by square symbols, with colors corresponding to the color key of each step. The (c) SNR for fellow eyes at each step demonstrates similar and significant SNR responses except for the last two steps. The (d) F_{STAT} colored bar (red-yellow-green) demonstrates a significant response for the right eye overall response of 7.69, and left eye of 3.51, both in the green-measureable portion of the F_{STAT} bar. Also, the (e) Overall F_{STAT}, which compares the responses of the two eyes, is also in the match (green) portion of the bar at 0.65. The overall impression is that both eyes are essentially normal and identical.

The (f) Raw Data waveform (bottom graph) denotes the right eye amplitude in red and the left eye in blue, with each step representing decreasing spatial frequencies. Both the signal waveform as well as phase and amplitude results are fairly similar for fellow eyes as would expected in a healthy observer.

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