

## Reverse-Engineering of Hyperopic Anisometropic Refractive Amblyopia

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### ABSTRACT

**Background.** Uncompensated hyperopic anisometropia is a strong amblyogenic factor. While the application of a lens prescription is essential in treatment, the selection of lens power is often more of an art than science.

**Case Report:** This case report illustrates the use of the visual evoked potential (VEP) as a direct and objective measure of cortical function to aid lens prescribing and monitoring the effects of optometric vision therapy.

**Conclusion:** The VEP can facilitate decision making processes for the clinician in titrating the anisometropic prescription toward isometropia while attaining and preserving symmetry in timing and amplitude of the signals to primary visual cortex between the two eyes.

**Keywords:** Anisometropia, developmental optometry, Hyperopia, Optometric Vision Therapy, Refractive Amblyopia, Visual Evoked Potential

### Introduction

Relatively low amounts of hyperopic anisometropia, generally held to be any amount above one diopter, are potentially amblyogenic.<sup>1</sup> Manas postulated that children under four years of age tend to develop hyperopia as an adaptation to environmental

stress, whereas the response after age four is typically in the direction of myopia.<sup>2</sup> Sherman reported a case of hyperopic anisometropic refractive amblyopia, termed *Adaptive Refractive Error Syndrome*, in which he was able to reduce the refractive status in the more hyperopic eye through under-correction from +3.50 to plano over a two year period.<sup>3</sup> He subsequently reported on another case in which the patient had moderate hyperopia through the right eye and high hyperopia through the left eye, for whom he was able to reduce though not eliminate the prescription required and minimize the amblyopia.<sup>4</sup>

The motivation for developing a different approach to refractive amblyopia is that children are often non-compliant with traditional approaches to amblyopia involving occlusion and wearing the full spectacle prescription as found on refraction. The PEDIG (Pediatric Eye Disease Investigator) studies have found that wearing the appropriate spectacle lens prescription is the most critical factor for improvement in refractive amblyopia in the absence of strabismus.<sup>5</sup>

How to determine the appropriate lens prescription for children with hyperopic refractive amblyopia remains as much an art as a science. In most instances, parents are surprised to learn that their child has refractive amblyopia, owing to the absence of any overt sign as ocular misalignment in strabismic amblyopia or diplopia. On the surface the child appears to function normally. When parents are advised that their child has hyperopic refractive amblyopia sufficient to require a spectacle lens or contact lens prescription, it often comes as a surprise.

When a lens prescription is given, the traditional approach in these cases has been to give the patient the full lens power as determined by refraction.<sup>6</sup> At the outset of therapy the parent is usually advised that the goal of therapy is to maximize the acuity and function through the amblyopic eye including binocular function. Traditionally the goal of treatment has not

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included the pursuit of reducing or eliminating the lens prescription, but to optimize function through the original prescription. However, we know that despite this disclaimer, parents tend to judge success in part by the need for the child to be dependent upon wearing the glasses. For some time now we have taken the approach of being conservative about the initial plus lens power given and have worked towards reducing lens power as vision function improves through active optometric vision therapy. We refer to this process as reverse-engineering of hyperopic anisometric refractive amblyopia. We used the findings from the visual evoked potential as an objective tool to assist us in determining how much and when to decrease the lens power our patients required.

### **The Visual Evoked Potential (VEP) in Amblyopia**

VEPs are visually evoked electrophysiological signals extracted from the electroencephalographic activity in the visual cortex recorded from the overlying scalp. As the visual cortex or V1 is activated primarily by the central visual field, VEPs depend upon the functional integrity of central vision at any level of the visual pathway including the eye, retina, the optic nerve, optic radiations, and occipital cortex.<sup>7</sup> Refractive amblyopia is a constellation of visual deficits in the central visual field with reduced visual acuity being just the tip of the cortical iceberg.<sup>8</sup>

To record VEPs clinically, we utilized the Diopsys™ NOVA-TR system to aid our objective documentation of the patient's response to amblyopia therapy. Measurements are taken at a fixation distance of one meter using a pattern-reversal waveform generated by a high contrast black and white checkerboard pattern. Our protocol is to obtain recordings for OD, OS and OU at three different check sizes, 16 (the largest), 32 (medium), and 64 (the smallest).

VEP results are linked to two key features of the wave form. The first is a large dip that should occur at approximately 75 milliseconds (ms) from the onset of the wave, known as N75. This is followed by a rise to the peak which typically occurs at 100ms and is known as the P100. These two features are used to mark the two key properties of the VEP, the latency and amplitude. The time from the stimulus onset to the beginning of the response is referred to as the latency. The height difference between the N75 and P100 is known as the delta amplitude.

In theory, strabismic amblyopia would be expected to affect latency differences between the waveform of the right and left eyes individually, and both eyes together. This is because of suppression processes that are more active in strabismic amblyopia, and that disrupt neural transmission time. In refractive amblyopia suppression processes occur primarily due to the blur induced by refractive differences that should be reflected in amplitude more so than latency.

### **Case Report**

Jade had just turned 4 years old when she first came to our office. She was seen for a second opinion following a pediatric ophthalmologic visit that occurred one month earlier. Her parents were given a prescription for eyeglasses and were told that she has anisometric hyperopic astigmatism. Jade's parents felt that the prescription was too strong considering that she had no symptoms. Her birth and developmental histories were unremarkable.

Pertinent initial examination findings include unaided visual acuities (UVA) of 20/25-2 in the right eye (OD) and 20/30-2 in the left eye (OS). The objective refraction was conducted using the Grand Seiko open view auto refractor that measures refractive state in a binocular setting at distance and at near. The unit conducts five readings and provides the time averaged responses which were as follows:

Distance (6m) OD: +1.50-0.50x168

OS: +2.50-0.50x009

Near (33cm) OD: -1.50-0.75x157

OS: -0.50-0.75x006

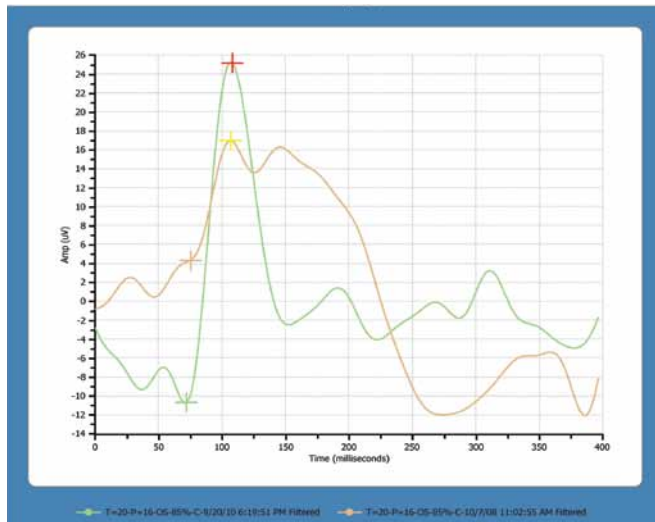
Subjective refraction did not yield any improvement over unaided acuity. Jade had normal fusion on the Worth 4 Dot target at distance and measured 250 seconds of arc on Randot Stereopsis at near. Cover test results were orthophoria at distance and near. Cycloplegic retinoscopy (1% Cyclopentolate) yielded OD: +4.75-1.00x180 and OS: +5.50-1.00x180. Ocular health was unremarkable in both eyes.

Jade's diagnosis was bilateral hyperopic astigmatism with refractive amblyopia of the left eye slightly greater than the right eye. In Jade's case we initially prescribed the following for full-time wear: OD: +1.25-0.75x180 and OS: +2.00-0.75x180.

Because amblyopia is defined as a developmental disorder that results in physiological alterations in the visual cortex and impairs form vision,<sup>9</sup> we instituted a program of office-based optometric vision therapy

**Table 1:** Comparing the delta amplitude for OS, pre and post vision therapy (VT). The VEP performed pre-VT was with +1.25-0.75x180, OD and +2.00-0.75x180, OS. The VEP performed post-VT was done without correction on.

	Pre-VT	Post-VT
1-Check Size 16	12.6 uV	35.8 uV
2-Check Size 32	20.4 uV	26.2 uV
3-Check Size 64	16.4 uV	21.6 uV

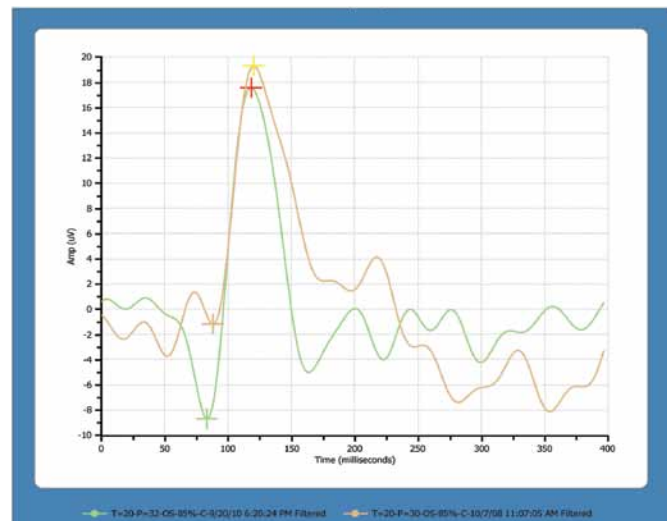


**Figure 1:** Pre and Post Therapy VEP waveform for OS at check size 16. Brown waveform is pre-VT and green waveform is post-VT. Pre-VT is with Rx and post-VT is without Rx.

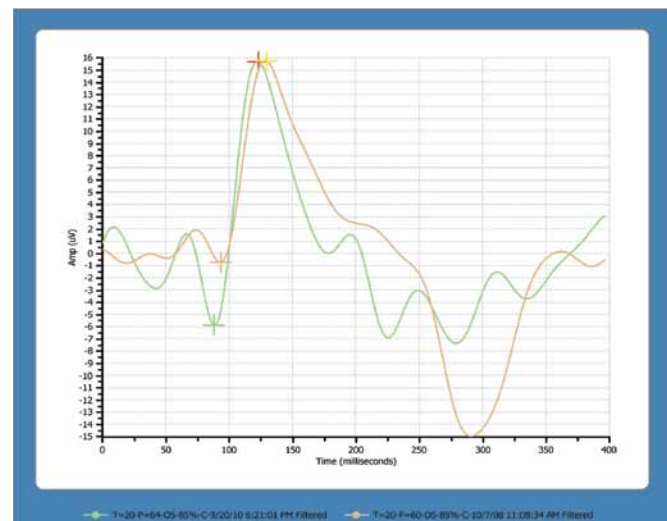
to improve her functional vision skills related to the amblyopia and to help improve her binocular skills. Pursuing a goal of decreasing the power difference between the two eyes, we reduced her prescription in the left eye to match the right at +1.25-0.75x180, and advised her to wear them full time. We subsequently reduced her spectacle lens powers in both eyes to +0.75-0.50x180 and instructed Jade to use her glasses for all sustained visual tasks such as school work.

Upon completing office-based optometric vision therapy Jade's visual acuity had improved to OD: 20/20 and OS: 20/25+2 with unaided acuity the same as aided acuity for both OD and OS. The conventional explanation for her improvement despite her high amount of latent hyperopia is that Jade had learned to accommodate more precisely through her left eye as a result of vision therapy.

When Jade returned for follow-up her parents' goal remained for her to function well and be free of amblyopia without wearing spectacles. We reduced her prescription to Plano in the right eye, but maintained the habitual power for her left eye since her visual acuity



**Figure 2:** Pre and Post Therapy VEP waveform for OS at check size 32. Brown waveform is pre-VT and green waveform is post-VT. Pre-VT is with Rx and post-VT is without Rx.



**Figure 3:** Pre and Post Therapy VEP waveform for OS at check size 64. Brown waveform is pre-VT and green waveform is post-VT. Pre-VT is with Rx and post-VT is without Rx.

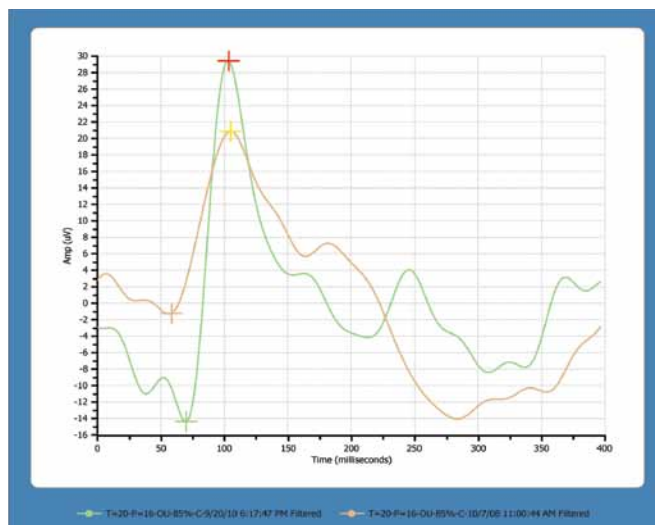
through that eye was still not 20/20. Several months later upon her most recent evaluation, Jade's unaided VA continued to be OD 20/20 and OS 20/25+2. The subjective refraction was OD Plano and OS +1.00-0.50x180 OS with no change in acuity. She continued to measure orthophoria on the cover test at distance and near. Her binocular step vergence ranges were BO >40 prism diopters and BI x/18/12. Jade continued to have reliable fusion on Worth 4 Dot testing at all distances and attained full Randot Stereopsis.

## Discussion

Visual Evoked Potential (VEP) testing was done initially to obtain objective baseline data and again about 2 years later to document post-therapy status.

**Table 2:** Comparing the delta amplitude for OU, pre and post vision therapy (VT). The VEP performed pre-VT was with +1.25-0.75x180, OD and +2.00-0.75x180, OS. The VEP performed post- VT was done without correction on.

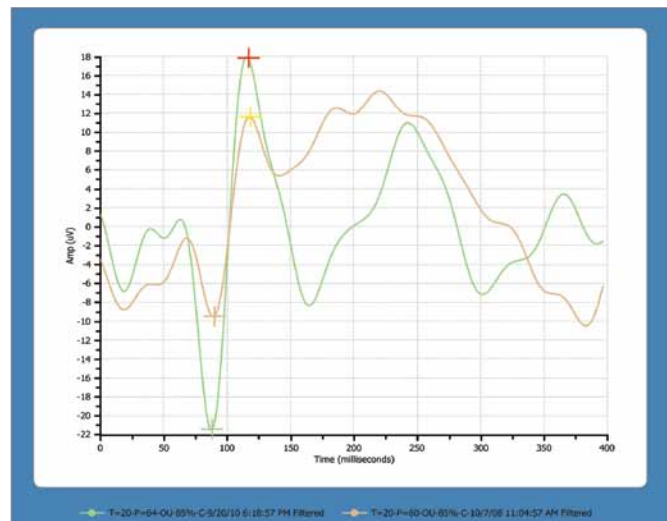
	Pre-VT	Post-VT
4-Check Size 16	22.0 uV	43.7 uV
5-Check Size 32	21.5 uV	47.3 uV
6-Check Size 64	21.0 uV	39.2 uV



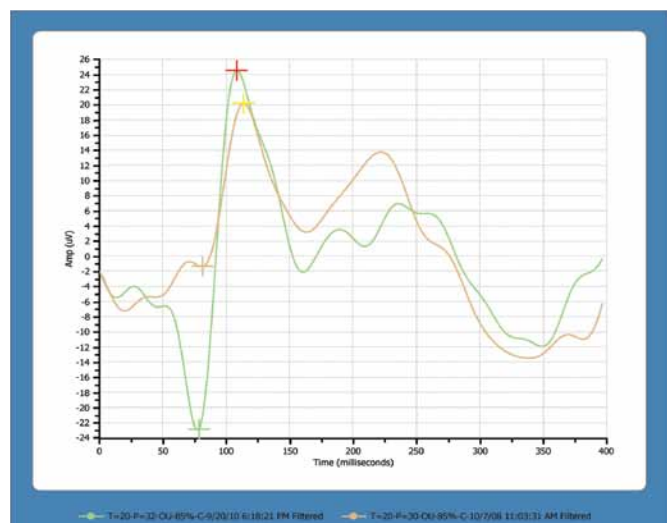
**Figure 4:** Pre and Post Therapy VEP waveform for OU at check size 16. Brown waveform is pre-VT and green waveform is post-VT. Pre-VT is with Rx and post-VT is without Rx.

Measurements were taken at a distance of one meter using a pattern-reversal waveform. Each recording lasted 20 seconds with her cooperation being excellent. Recordings were taken for OD, OS and OU at three different check sizes, 16 (largest), 32 (medium), and 64 (smallest). Jade’s individualized vision therapy program emphasized improving visual skills OS and OU, and those are the results from the VEP that we have included for comparison. All graphs are depicted under the filtered condition (which smoothes out the waveform).

Figures one through three compare the waveforms for OS pre and post therapy, the brown waveform representing the VEP prior to therapy and the green waveform representing the post-therapy results for the three different check sizes respectively. Figures four through six compare the waveforms for OU pre and post therapy, with the brown waveform again representing the VEP prior to therapy and the green waveform representing the post-therapy results for the three different check sizes respectively. VEP results



**Figure 5:** Pre and Post Therapy VEP waveform for OU at check size 32. Brown waveform is pre-VT and green waveform is post-VT. Pre-VT is with Rx and post-VT is without Rx.



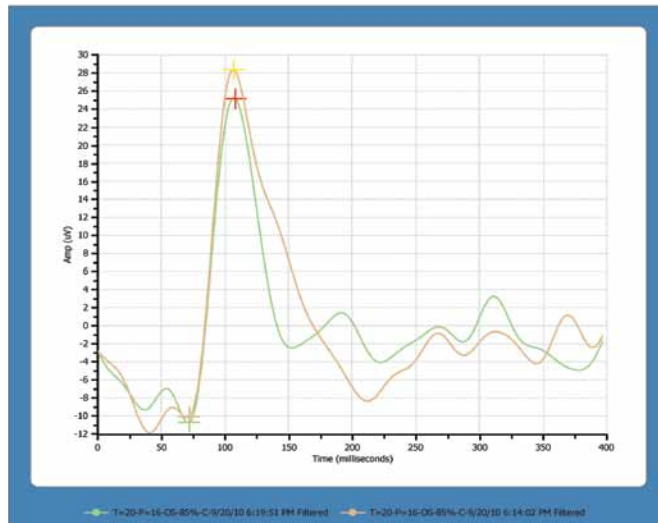
**Figure 6:** Pre and Post Therapy VEP waveform for OU at check size 64. Brown waveform is pre-VT and green waveform is post-VT. Pre-VT is with Rx and post-VT is without Rx.

give objective information that Jade has a much improved visual signal especially when comparing the binocular responses pre and post therapy (Figures 4 through 6 and Table 2). Under all conditions the amplitude has improved, the most significant being that the findings have an average increase in delta amplitude of 103% following vision therapy.

Figures seven through nine are the results of Jade’s VEP for OS only, with and without her prescription at check sizes 16, 32 and 64 respectively subsequent to vision therapy. The results through the glasses (+0.75-0.50x180) for the left eye at that time is represented by the brown waveform. The latency differences were not clinically significant. The amplitude difference is

**Table 3:** Comparing the delta amplitude for OS after completion of vision therapy with and without an Rx. The Rx is plano, OD and +0.75-0.50x180, OS.

	Without Rx	With Rx
7-Check Size 16	35.8 uV	38.4 uV
8-Check Size 32	26.2 uV	34.6 uV
9-Check Size 64	21.6 uV	27.3 uV

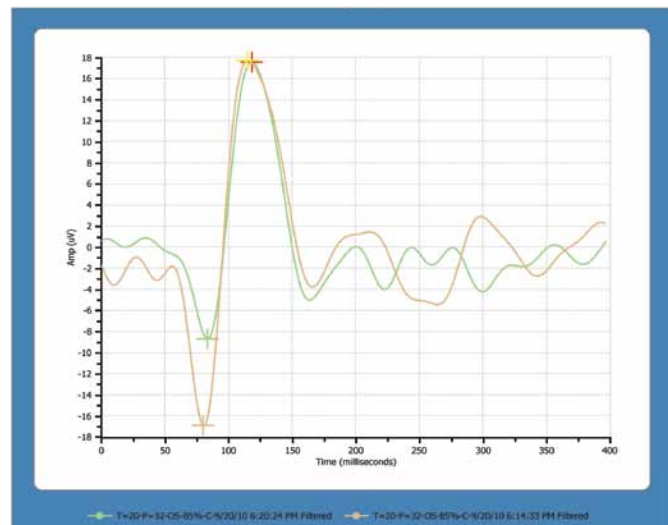


**Figure 7:** Post Therapy VEP waveform comparing OS with and without Rx at check size 16. The difference in the delta amplitude is clinically insignificant.

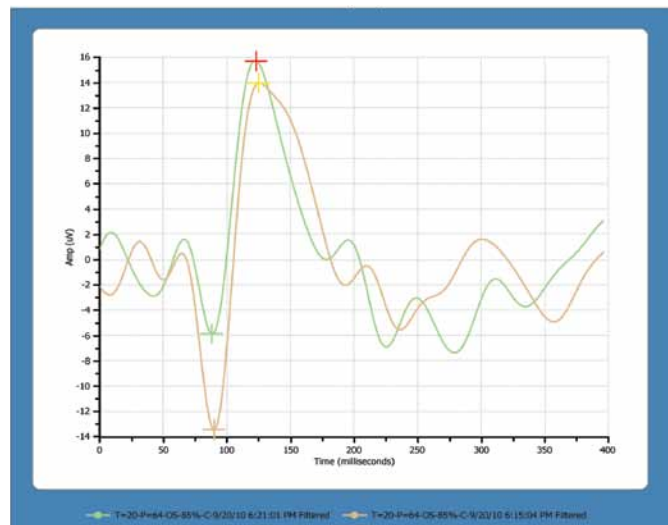
not significant at the largest check size, as the delta amplitude is very similar. The prescription makes a greater impact however at the smaller check sizes. For that reason it was determined that Jade should continue to use her glasses especially for sustained visual work but it would be less important for playing outside and watching movies or television.

## Conclusion

Visual evoked potentials recorded at different check sizes can be useful in documenting changes in cortical function prior to prescribing optometric vision therapy, and as a measure of progress during therapy or upon its completion. The use of VEP technology can also help guide us as to when it is safe to modify or discontinue a lens prescription without sacrificing visual quality from the retina to the cortex. Although best-corrected visual acuity remains the sine qua non of amblyopia, it is an inadequate measure of the timing and spatial characteristics that predispose the patient to this condition. Given the plasticity of the visual system, the VEP is a valuable adjunct in objectively monitoring the effects of a lens prescription



**Figure 8:** Post Therapy VEP waveform comparing OS with and without Rx at check size 32. Green waveform is without the Rx and the brown waveform is with the Rx.



**Figure 9:** Post Therapy VEP waveform comparing OS with and without Rx at check size 64. Green waveform is without the Rx and the brown waveform is with the Rx.

on monocular and binocular functions on a cortical basis. In Jade's case, her father was very interested in seeing her discontinue the use of a lens prescription as soon as possible. While he was focused primarily on cosmesis, the VEP served as an important visual aid in demonstrating effects of a lens prescription on brain function to the father. We continue to monitor Jade's visual status and will repeat the VEP testing on an annual basis.

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