A Randomized Controlled Trial Evaluating the Efficacy of Neural Vision Correction (NVC™) in Enhancing Unaided Visual Acuity in Low Myopes

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-----------------Introduction------------------

NeuroVision™ NVC vision correction technology is a non-invasive, patient-specific treatment based on visual stimulation and facilitation of neural connections responsible for vision. The technology involves the use of an internet-based computer generated visual training exercise regime using sets of patient specific stimuli based on Gabor patches, to sharpen contrast sensitivity and visual acuity.

Following the conclusion of a non-comparative interventional study which demonstrated the efficacy and safety of NVC technology in improving unaided visual acuity and contrast sensitivity in 20 patients with low myopia, we embarked on a randomized controlled trial to evaluated the efficacy of NVC technology in enhancing the unaided visual acuity (UAVA) in low myopic patients (LMP).

We present here the results of a planned interim analysis that was done at treatment completion of 75% of the study subjects. This study was conducted in active Military servicemen in the Singapore Armed Forces.

-----------------Scientific Background------------------

Cortical neurons in the visual cortex function as highly specialized image analyzers or filters, responding only to specific parameters of a visual image, such as orientation and spatial frequency, and visual processing involves the integrated activity of many neurons, with inter-neural interactions effecting both excitation and inhibition[1]. Visual contrast activates neurons involved in vision processing, and neural interactions determine the sensitivity for visual contrast at each spatial frequency, and the combination of neural activities set Contrast Sensitivity Function (CSF)[1,2]. The relationship between neuronal responses and perception are mainly determined by the signal-to-noise ratio (S/N ratio) of neuronal activity, and the brain pools responses across many neurons to average out noisy activity of single cells, thus improving S/N ratio, leading to improved visual performance and acuity[3].

Studies have shown that the noise of individual neurons can be brought under experimental control by appropriate choice of stimulus conditions, and CSF can be increased dramatically through control of stimulus parameters[4-8]. This precise control of stimulus conditions leading to increased neuronal efficiency is fundamental in initiating the neural modifications that are the basis for brain plasticity[9,10]. Brain plasticity (the ability to adapt to changed conditions in acquiring new skills) has been demonstrated in many basic tasks, with evidence pointing to physical modifications in the adult cortex during repetitive performance[11-12].

NeuroVision's technology probes specific neuronal interactions, using a set of patient-specific stimuli that improve neuronal efficiency[6,13] and induce improvement of CSF due to a reduction of noise and increase in signal strength. As visual perception quality depends both on the input received through the eye and the processing in the visual cortex, NeuroVision's technology compensates for blurred (myopic) inputs, coming from the retina, by enhancing neural processing.

------------------Technology Implementation -------------------

The building block of these visual stimulations is the Gabor patch (Figure 1), which efficiently activates and matches the shape of receptive field in the Visual Cortex.

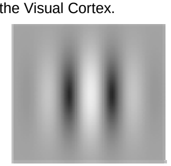

Figure 1: The Gabor Patch

The fundamental stimulation-control technique is called "Lateral Masking", where collinearly oriented flanking Gabors are displayed in addition to the target Gabor image. The patient is exposed to two short displays in succession, in a random order; the patient identifies which display contains the target Gabor image (Figure 2). Audio feedback is provided with an incorrect response. The task is repeated and a staircase is applied until the patient reaches their visual threshold level.

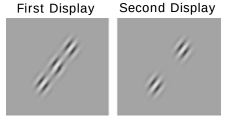

Figure 2:

Lateral Masking images

-----------------The NeuroVision System------------------

The NeuroVision System is a software-based, interactive system tailored and continuously adaptive to the individual visual abilities. In the first stage, the subject is exposed to a set of visual perception tasks, aimed to analyze and identify each subject's neural inefficiencies or deficiencies. Based on this analysis, a treatment plan is initialized, and subject specificity is achieved by administering patient-specific stimuli in a controlled environment.

Each session is designed to train, directly and selectively, those functions in the visual cortex, which were diagnosed to be further enhanced. At each session an algorithm analyzes the patient's responses and accordingly adjusts the level of visual difficulty to the range most effective for further improvement. Between sessions, the progress of the patient is taken into account by the algorithm for the next session generation. Thus, for each subject an individual training schedule is designed based on the initial state of visual performance, severity of dysfunction and progress in course of treatment. The treatment is applied in successive 30-minute sessions, administered 2-3 times a week, a total of approximately 30 sessions. Every 5 sessions, subject's visual acuity is tested in order to continuously monitor subject's progress. The average entire treatment duration is around 3 months.

-----------------Methods---------------

- 67 adults aged 17-55, with Low Myopia, having **cycloplegic** spherical equivalent (SE) in the range of -0.5DS to –1.5DS and astigmatism in the range of 0.0DC to -0.75DC were recruited.
- Baseline Unaided Visual Acuity (UAVA) in both eyes was 0.2 logMar (20/32) or worse.
- The subjects were randomly divided into 2 groups:
  54 LMP were allocated in the treatment group - completed real NVC treatment
  13 LMP were allocated to the control group - completed sham treatment (placebo)
- The study was double masked
- UAVA was tested at Baseline and at the End of Treatment using ETDRS charts
- A **significant improvement** in UAVA was defined as improvement in UAVA of 0.2 logMar (2 lines) or more.
- All analyzed subjects completed NeuroVision or sham treatment without any major incompliance with the treatment schedule and protocol.

----------------- Results- --------------

- Mean improvement in UAVA was 1.78 logMar lines in the treatment group and 0.23 logMar lines in the control group.
- 35 subjects (64.8%) in the treatment group achieved an improvement of 2 logMar lines or more (Significant Improvement) in at least one of their eyes.
  Only 1 subject (7.7%) in the control group achieved a Significant Improvement in at least one of their eyes
  ($p < 0.0005$, Fisher's Exact Test, OR = 22.105, 95% CI 2.666 to 183.256)
- 16 subjects (29.6%) in the treatment group achieved a Significant Improvement in both of their eyes.
  No subjects (0.0%) in the control group achieved a Significant Improvement in both of their eyes ($p = 0.028$)
- Mean Baseline Cycloplegic refraction was -1.29D.
- Mean refractive error remained unchanged.
- No adverse events were reported.

-------------------- Results Cont'd--------------------

Table 1. Summary of baseline VA, end of treatment VA, and improvement of VA

	Control Group (n = 13)	Treatment Group (n = 54)
Right eye baseline unaided VA (logMar)		
Mean (SD)	0.36 (0.10)	0.42 (0.15)
Median (range)	0.40 (0.20 – 0.46)	0.40 (0.20 – 0.80)
Left eye baseline unaided VA (logMar)		
Mean (SD)	0.34 (0.12)	0.41 (0.15)
Median (range)	0.32 (0.20 – 0.62)	0.38 (0.20 – 0.72)
Right eye end of treatment VA (logMar)		
Mean (SD)	0.31 (0.15)	0.24 (0.15)
Median (range)	0.28 (0.14 – 0.70)	0.24 (-0.30 – 0.48)
Left eye end of treatment VA (logMar)		
Mean (SD)	0.34 (0.17)	0.23 (0.17)
Median (range)	0.28 (0.14 – 0.62)	0.22 (-0.30 – 0.66)
Improvement of right eye VA (logMar)		
Mean (SD)	0.04 (0.13)	0.18 (0.15)
Median (range)	0.06 (-0.26 – 0.20)	0.17 (-0.14 – 0.60)
Improvement of left eye VA (logMar)		
Mean (SD)	0.003 (0.13)	0.17 (0.16)
Median (range)	0.04 (-0.30 – 0.14)	0.19 (-0.28 – 0.56)

Table 2. Summary of Statistical Analysis

	Control Group (n = 13)	Treatment Group (n = 54)	
Average Improvement in UAVA (ETDRS Lines)	0.23 Lines	1.78 Lines	
% Subjects who Improved 2 Lines or above in Both Eyes	0%	30%	p=0.028
% Subjects who Improved 2 Lines or above in at least One Eye	8%	65%	p<0.0005

-----------------Conclusions-----------------

NeuroVision treatment for patients with low myopia demonstrates an improvement in Unaided Visual Acuity that is statistically significant from subjects receiving a sham treatment.

-----------------References-----------------

1. Hubel, D. H. & Wiesel, T. N. Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol. (Lond.)* 160, 106-154 (1962).
2. Polat, U. Functional architecture of long-range perceptual interactions. *Spat Vis* 12, 143-62 (1999).
3. Geisler, W. S. & Albrecht, D. G. Visual cortex neurons in monkeys and cats: detection, discrimination, and identification. *Vis Neurosci* 14, 897-919 (1997).
4. Kasamatsu, T., Polat, U., Pettet, M. W. & Norcia, A. M. Colinear facilitation promotes reliability of single-cell responses in cat striate cortex. *Exp Brain Res* 138, 163-72. (2001).
5. Polat, U., Mizobe, K., Pettet, M. W., Kasamatsu, T. & Norcia, A. M. Collinear stimuli regulate visual responses depending on cell's contrast threshold. *Nature* 391, 580-4 (1998).
6. Polat, U. & Sagi, D. Spatial interactions in human vision: from near to far via experience- dependent cascades of connections. *Proc Natl Acad Sci U S A* 91, 1206-9 (1994).
7. Polat, U. & Sagi, D. Lateral interactions between spatial channels: suppression and facilitation revealed by lateral masking experiments. *Vision Res* 33, 993-9 (1993).
8. Polat, U. & Sagi, D. The architecture of perceptual spatial interactions. *Vision Res* 34, 73-8 (1994).
9. Dosher, B. A. & Lu, Z. L. Perceptual learning reflects external noise filtering and internal noise reduction through channel reweighting. *Proc Natl Acad Sci U S A* 95, 13988-93. (1998).
10. Dosher, B. A. & Lu, Z. L. Mechanisms of perceptual learning. *Vision Res* 39, 3197-221. (1999).
11. Sagi, D. & Tanne, D. Perceptual learning: learning to see. *Curr Opin Neurobiol* 4, 195-9 (1994).
12. Gilbert, C. D. Adult Cortical Dynamics. *Physiological Reviews* 78, 467-485 (1998).
13. Polat, U. & Sagi, D. in *Maturational Windows and Adult Cortical Plasticity* (eds. Julesz, B. & Kovâcs, I.) 1-15 (Addison-Wesley, 1995).
14. Polat, U., Ma-Naim, T. Belkin, M. Sagi, D. Improving vision in adult amblyopia by perceptual learning. PNAS 101, 6692-97 (2004).