

Integrated Neural Photo-stimulation and microperimetric fixation analysis.

Clinical experience of the Low Vision Research Centre of Milan

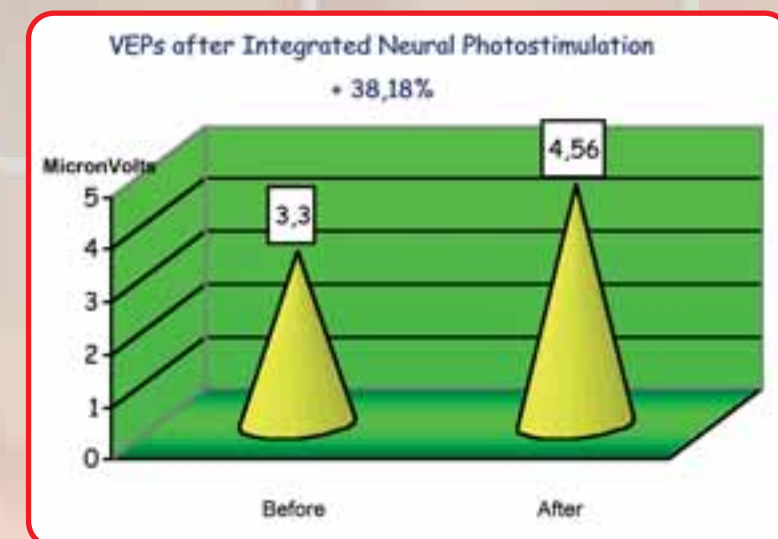
ARVO 2006 - Fort Lauderdale - USA

Paolo Limoli MD^{o*}, Enzo Vingolo PhD^{^*}, Laura D'Amato MD^o, Enrico Giacomotti MD^o, Roberta Solari^o, Patrizia Costanzo*, Antonella Ribecca*, Riccardo Di Corato^o, Elena Gilardi^o

^oLow Vision Research Centre - Milan, [^]La Sapienza University - Rome, *Eye.com - Palermo paololimoli@libero.it

Purpose:

Neural photo-stimulation improves VEPs, Visus and reading coefficient. We have hypothesized that photo-stimulation as the principal mechanism improves the quality of fixation, and in a chain reaction beginning with the foveal detection, all the other visual parameters.



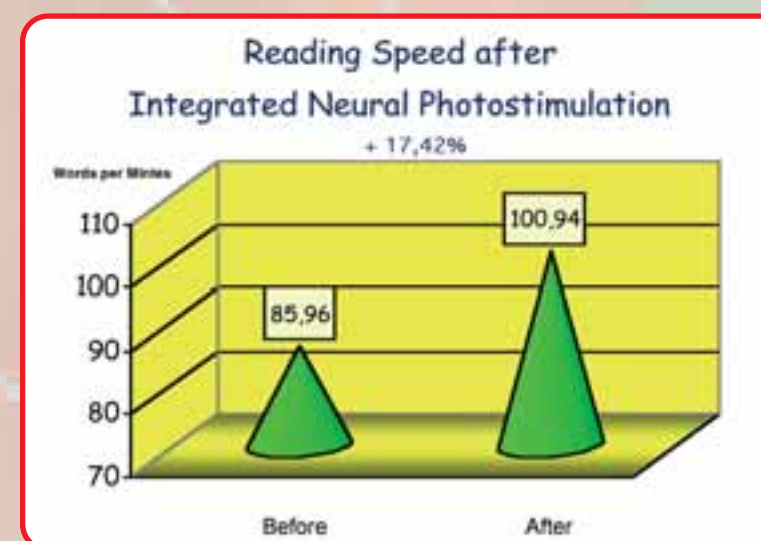
PICT. 1: VEPs has an indicative improvement after Integrated Neural Photostimulation ($p = 0,0000007281$ - St. Dev. = 3,04862).

Patients and methods:

In order to do this study we have developed a new method of stimulation called Integrated Neural Photo-stimulation (INP), which incorporates three methods: Visual Pathfinder, I.B.I.S. and Sound Biofeedback.

At the beginning (T₀) and at the end (T₁) of each cycle we analyse the fixation percentage within foveal two central degrees, stability score, BCVA, near visual acuity in pts, VEPs, reading speed and reading coefficient.

We examined examples (Group A) composed of 67 eyes (34 adults average age 66 years, ranging from 15 to 90 years). This group has the following characteristics: average fixation percentage within two central degrees foveal 43,17% (max



PICT. 2: The change of reading speed after Integrated Neural Photostimulation shows an indicative improvement ($p = 0,0000000580$ - St. Dev. = 47,2983).

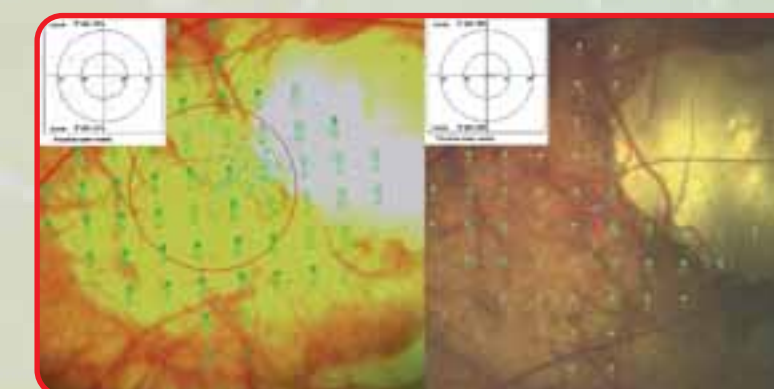


PICT. 3: The Visual Pathfinder (VP) (A) suggest to the patient's eye a stimulus with an optical pattern at variable space frequency, as three electrodes recording relative Visual Evoked Potentials (VEPs). The I.B.I.S. (Improved Biofeedback Integrated System) (B, C) is an instrument which combines the flicker stimulation and sound feedback that the patient learns to maintain steady and high-pitched. The Sound Biofeedback is made by Microperimetry MP1 (D, E). The sound is continuous only if patient maintains the fixation on the chosen point. The repeated presentation such as on-off of the optical patterns improve visual performance in low vision and amblyopic patients as well as in anyone who needs to improve his visual acuity. The patients undergo a rehabilitative cycle of ten sessions if it is their first time, and a cycle of five sessions if the patient has previously undergone a neural photo-stimulative cycle. The stimulation begins with the VP (A) (10 minutes per eye) and contemporary VEPs recording, followed by stimulation with the IBIS (B, C) (5-7 minutes per eye) and ends with Sound Biofeedback by MP1 (D, E) (1 minute per eye). In our work we have considered at the end (T₁) of each cycle, the changes of the quality of vision (BCVA, pts, fixations percentage), about two groups: the group A of 67 eyes treated with Integrated Neural Photostimulation (A, B, C, D, E) and the group B of 22 eyes treated with only Biofeedback Visual Pathfinder (A).

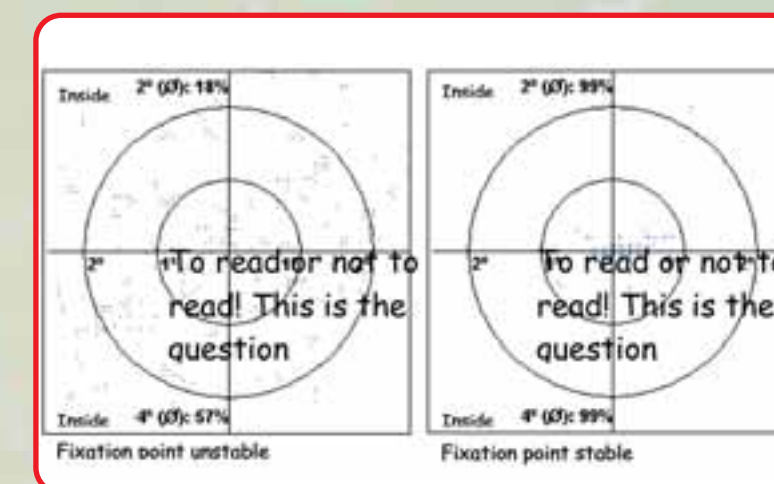
97% and min 0%), with stability score of 1,16 (stable 0, relatively unstable 1, unstable 2); average BCVA 0,31 (max 1,0 and min 0,01); average near BCVA 29,27

pts (max 6 pts and min 74 pts), average VEPs 3,3 micronvolts (max 11,24 min 0,10); average reading speed 85,96 words per min. (max 184 min. 20); average reading coefficient 83,18 (max 184 min 18).

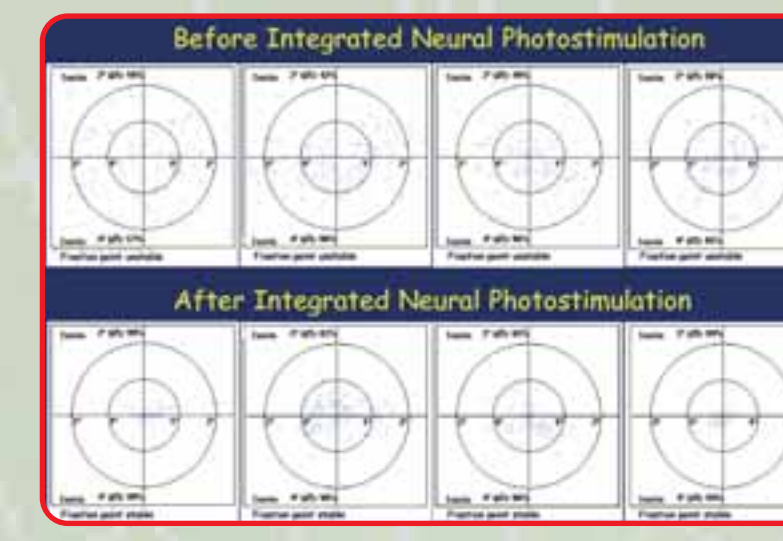
We compared the examples Group A with the variations obtained with the analogous Group B, of 22 eyes (17 adults average age 64,4 years, ranging from 17 to 90 years), who had previously undergone neural photo-stimulation done only with the Visual Pathfinder.



PICT. 4: Microperimetry of a 75 year old man with central myopic macular degeneration and amblyopia in his only eye and loss of the paracentral vision, before and after Integrated Neural Photostimulation. The fixation point is central but unstable (inside 2° 18%) and the BCVA is low (0,45 and 11 pts). After visual training the fixation point becomes stable (inside 2° 99%) and the BCVA is better (0,7 6 pts).



PICT. 5: Especially an unstable fixation point distorts the reading physiology: the searching movements of the eye are too frequent and the regression on the reading line is necessary. After visual training the fixation point becomes stable: the eye can flow along the reading line. This patient goes from 70 words per minute to 107 words per minute. The better collimation of fixation inside two central degrees, causes an improvement of foveal detection which determines an improvement of visual acuity and the reading performance.



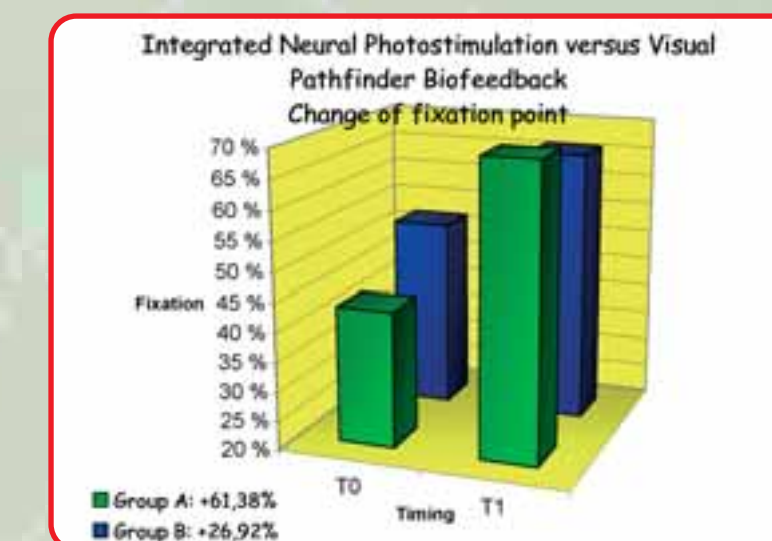
PICT. 6: The stability of fixation point increase almost always with the visual training. But this increase can be modeled and improved depending on the photostimulative method used. Our research shows that Integrated Neural Photostimulation is very interesting in improving the quality of the fixation point.

This second group has the following characteristics: average fixation percentage within two central degrees foveal 52,00% (max 97% and min 3%), with stability score of 0,90; average BCVA 0,38 (max 1,0 and min 0,01); average near BCVA 22,20 pts (max 6 pts and min 70 pts). VEPs, reading speed and reading coefficient were not examined in this group.

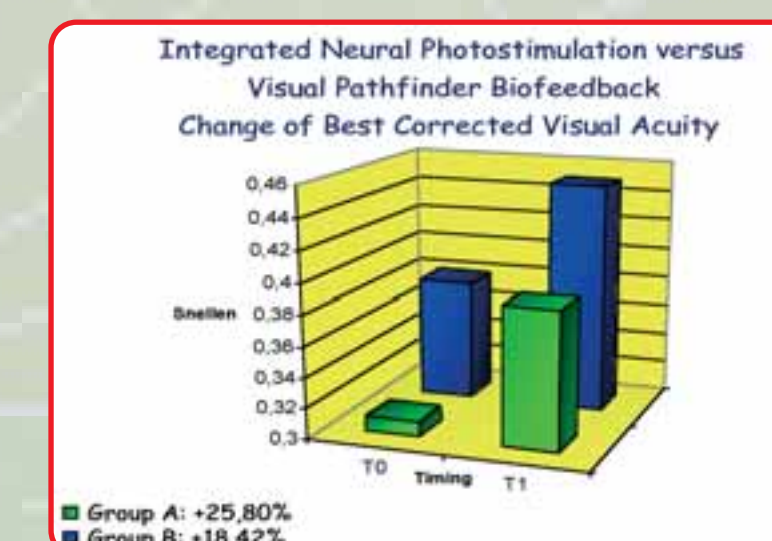
We subsequently compared the increase in the fixation percentage within two central degrees, the BCVA and the near visual acuity, for close up done with the integrated neural photo-stimulation (Group A) and after neural photo-stimulation done only with the Visual Pathfinder (Group B).

Results:

- 1) The fixation percentage changes: Group A, from 43,17 (T₀) to 69,62% (T₁), increase 26,50, percentage change 61,38% ($R = 0,0000000129$ - Dev.St 31,320474), increase of stability score 0,54 (47%) ($R = 0,0000000437$ - Dev. 0,7469245). Group B, from 52 (T₀) to 66% (T₁), in-



PICT. 7: In this research on 67 eyes treated with Integrated Neural Photostimulation and 22 eyes treated only with the Visual Pathfinder Biofeedback, the increase of stability of the fixation point seems to be better in the first group. Group A: + 61,38% ($p = 0,0000000129$ - St. Dev. = 31,320474), Group B + 26,92 % ($p = 0,019677866$ - St. Dev. = 33,76488605).



PICT. 8: In this research the increase of BCVA seems to be better in the first group, treated with Integrated Neural Photostimulation. Group A: + 25,80% ($p = 0,0000427252$ - St. Dev. = 0,3004309), Group B 18,42% ($p = 0,039093802$ - St. Dev. = 0,344299151).

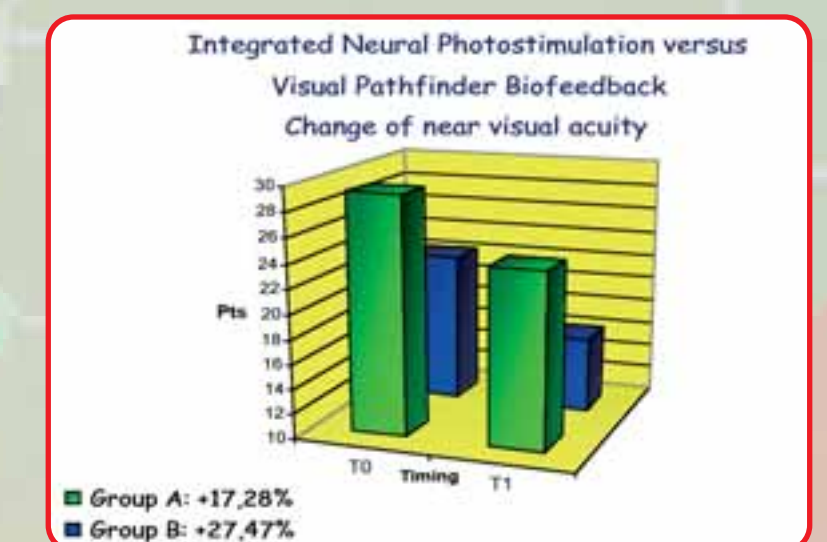
crease 14, (26,92 %) ($R = 0,019677866$ - Dev.St. 33,76488605), increase of stability score 0,17 (19%) ($R = 0,05488796$ - Dev. 0,8).

- 2) The BCVA changes: Group A, from 0,31 to 0,39, increase 0,08 (25,80%) ($R = 0,0000427252$ - Dev.St. = 0,3004309). Group B, from 0,38 to 0,45, increase 0,07 (18,42%) ($R = 0,039093802$ - Dev.St. 0,344299151).

- 3) The near visual acuity changes: Group A, from 29,27 pts to 24,21 pts, increase 5,06 pts (17,28%) ($R = 0,0000074095$ - Dev.St. = 29,047622). Group B, from 22,2 pts to 16,1 pts, increase 6,1 pts (27,47%) ($R = 0,002380547$ - Dev.St. 16,71085108).

Conclusion:

It confirms that the neural photo-stimulation, through a better collimation of fixation within two central degrees, results with an improvement of foveal detection which determines an improvement of visual acuity and reading. This increase can be regulated and improved depending on the photo-stimulative method used. At the moment, we feel that Integrated Neural Photostimulation causes a further increase of the fixation percentage and foveal detection, as such it has been analyzed with microperimetry and can be used successfully during visual rehabilitation.



PICT. 9: We have a better increase of near visual acuity in the second group. The percentage increase of the near visual acuity in Group A is inferior (but the absolute value is similar) because the sample treated with Integrated Neural Photostimulation presents a lower near visual acuity (29,27 pts, increase +17,28% $p = 0,0000074095$ St. Dev. = 29,047622) than the one of Group B treated with neural photostimulation done only with the Visual Pathfinder (22,2 pts, increase +27,47%, $p = 0,002380547$ - St. Dev. = 16,71085108).

References

Chen WR, Williamson A, Shepherd GM, Spencer DD, Kato K, Lee S. Long-term modifications of synaptic efficacy in the human inferior and middle temporal cortex. *Proc Natl Acad Sci USA* 1996;93(15):8011-5.

Martinez IL Jr, Derrick BE. Long term potentiation and learning. *Ann Rev Psychol* 1996;47:173-203

Kang H & Schuman E.M. Long-lasting neurotrophin-induced enhancement of synaptic transmission in the adult hippocampus *Science* 1995;267:1658-1662

Kristine Krug K., Thompson DI. University Laboratory of Physiology, Parks Road, Oxford OX1 3PT. Retinal activity is necessary for the rearrangement of the geniculate-cortical map in the Syrian hamster. *Journal of Physiology* (1997), 501.P, 96P

Limoli P, D'Amato L, Marino L, Giulotto A, Franzetti M, Carella A, Raspino S. Risultati preliminari sull'influenza della stimolazione maculare mediante Ambliam su occhi ipovedenti già sottoposti a riabilitazione visiva. *Ann Ottalmol Clin Ocul* 1993;Vol. CXIX, 4:309-317

Limoli PG, D'Amato L, Giulotto A. Plasticità neurosinaptica e biostimolazione ottica. *Atti 3° Congresso Nazionale "G.I.S.I.", Roma, 8/12/95* Minerva Oftalmologica, 1996:1471

Limoli PG, D'Amato L, Giuberti R. Neurosinaptica plasticità: teoria, pratica e promesse. *The international conference on low vision. Proceedings Vision 1996* Madrid, July 8-12, 1996

Limoli P, D'Amato L, Gilardi E, Solari R. Potenziamento a lungo termine e plasticità neurosinaptica. *Studio degli effetti della fotostimolazione neurale sul sistema neurovisivo. Il Subvedente, N.2, 9/1999:2-18*

Limoli PG, Vingolo EM, D'Amato L, Giacomotti E, Solari R, Costanzo P, Ribecca A, Venturi N. Effects of neural photostimulation on reading performances during visual rehabilitation. *ARVO 2004 - USA*

Limoli PG, Vingolo EM, D'Amato L, Giacomotti E, Solari R, Costanzo P, Ribecca A, Di Corato R. Microperimetry and fixation in the low vision patient. *ARVO 2005 - USA*

Lomo T. Trophic factors and postsynaptic activity in synapse formation. *Nature* 1983 Oct 13-19;305(5935):576.

Schlaggar B.L., Fox K. & O'Leary D.D.M. Postsynaptic control of plasticity in developing somatosensory cortex *Nature* 1993;364:623-626

Thorndike, E. *The Fundamentals of Learning*. New York: Teachers College Press. (1932).

Vidal-Sanz M et Coll. Axonal regeneration and synapse formation in the superior colliculus by retinal ganglion cells in the adult rat | *Neurosci* 1987;7:2894-2909

Vilegas-Peres M et Coll. Influences of peripheral nerve grafts on the survival and regrowth of axotomized retinal ganglion cells in adult rat | *Neurosci* 1988;8:265-280

Vingolo E, Limoli P, Ribecca A, Costanzo P. Visual Training in retinitis pigmentosa patients: neural plasticity and function recovery - *ARVO 2002*.