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NEUROFUNCTIONAL ACTIVATION OF HUMAN VISUAL CORTEX IN AMBLYOPIA INDUCED BY S/NRI TREATMENT AND SENSORY STIMULATION. *POTENTIAL APPLICATION FOR AN EYESIGHT IMPROVEMENT.*

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DISCLOSURE

« NO CONFLICT OF INTEREST TO DECLARE»

TOPICS

NEURAL PLASTICITY

AMBLYOPIA

EXPERIMENTAL RESULTS

CLINICAL APPLICATION/PROSPECTS

NEURAL PLASTICITY

functioning of brain …

…modifications - reorganizations

Structural

Dendrites morphology and density, Neurogenesis (birth of new neurons)

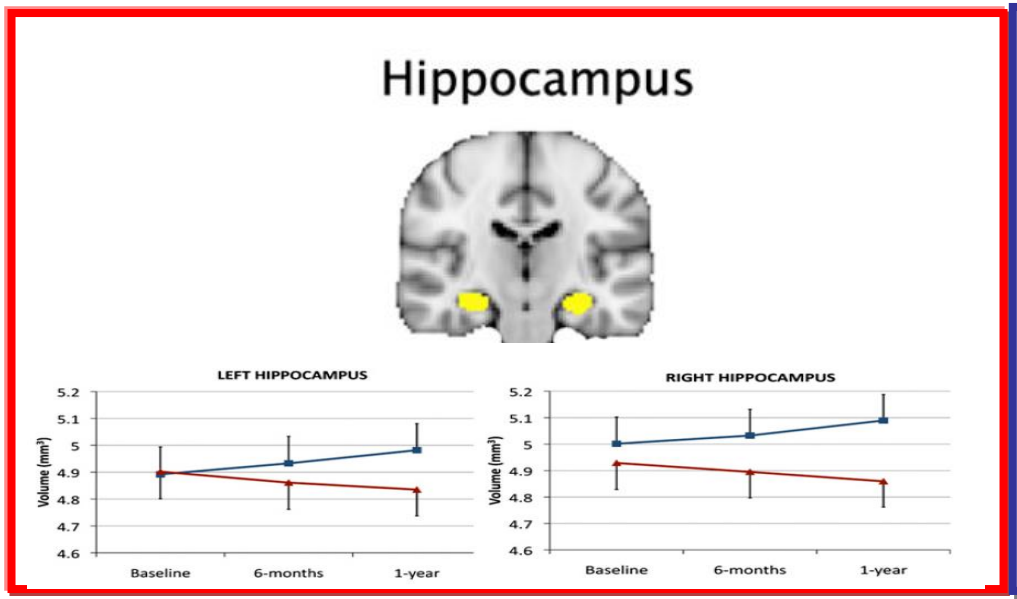
Functional

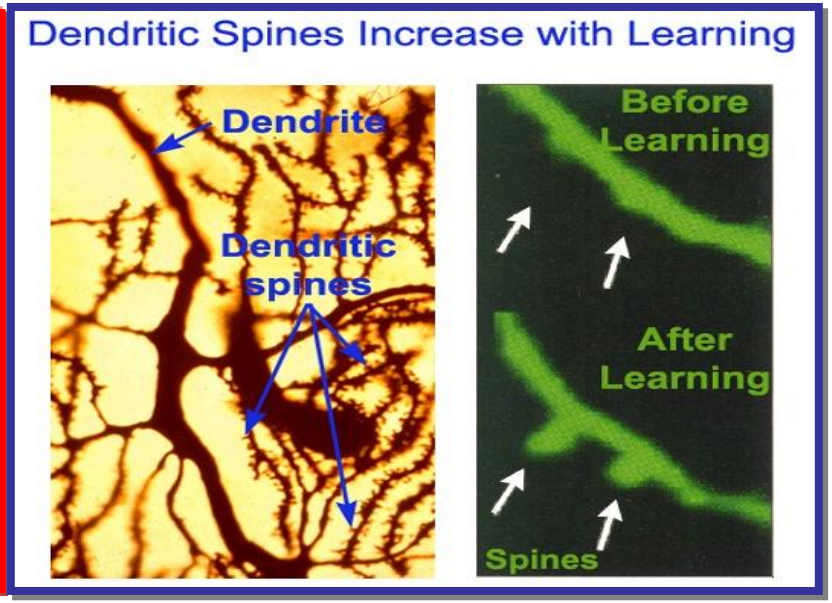
Changes of synapses and receptors, Signal transduction

Cellular/Molecular

Intracellular activity, Gene expression

The effective role of long-term antidepressant (ADs) administration in promote the ***neurogenesis and synaptogenesis*** in the adult hippocampus (1,2,3) as well as in increasing the expression of the ***Brain Derived Neurotrophic Factor*** (**BDNF**) and its primary receptor TrkB (4,5,6) has been clearly demonstrated so far





1) J.E.Malberg, A.J. Eish, E.J. Nestler, R.S. Duman***, - Journal of Neuroscience 20 – 2000;***

2) R.S. Duman***- Dialogues in Clinical Neuroscience- 6 (2) 2004***

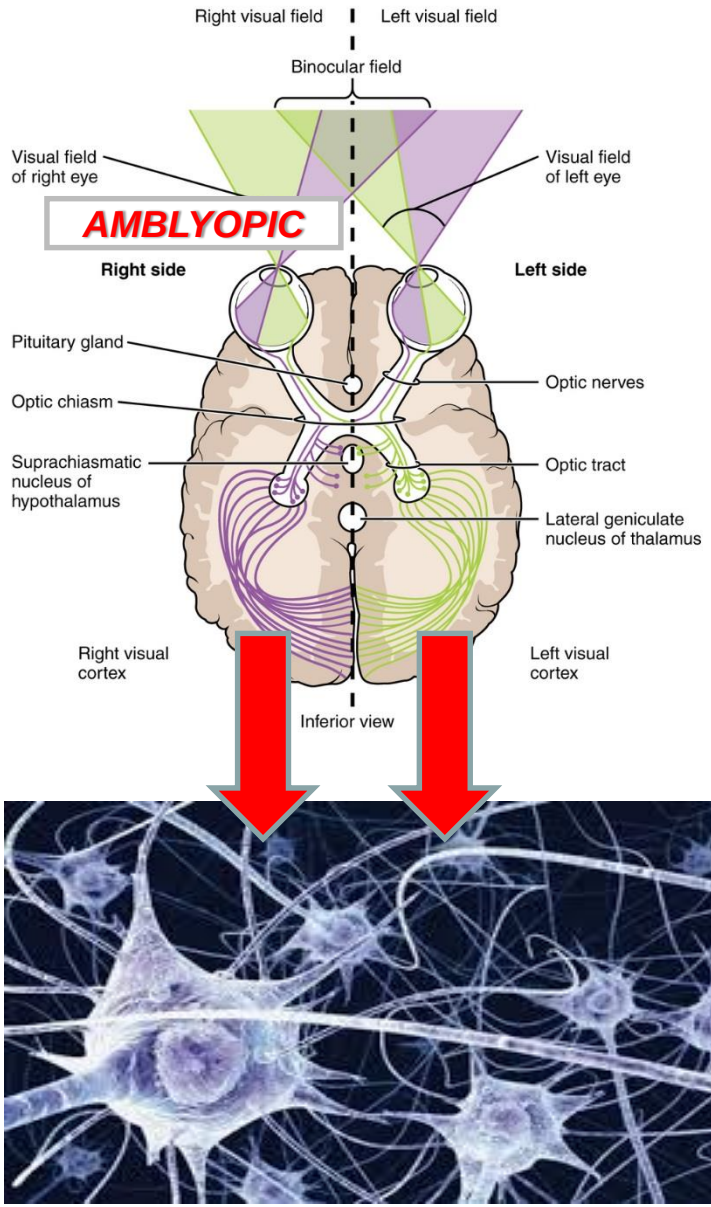
3) T. Hajszan, N.J. Mac Lusky, C. Leranth***, - Journal of Neuroscience 21 – 2005;***

4) M.Nibuya, S. Morinobu, R.S. Duman, ***- Journal of Neuroscience 15 – 1995;***

5) E. Castren, ***Curr. Opin. Pharmacological 4 – 2004;***

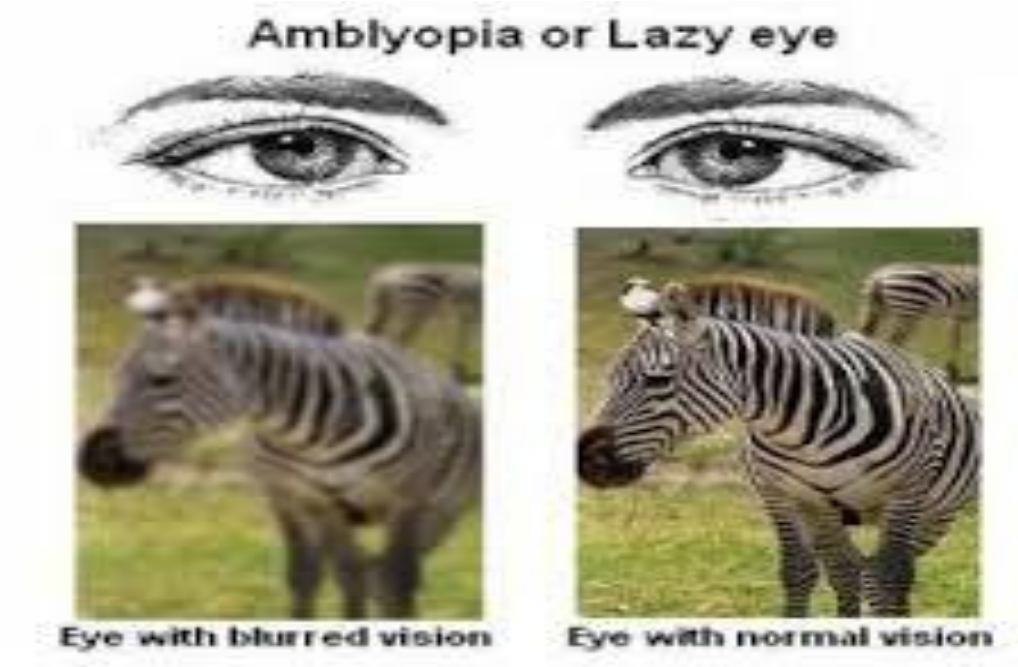
6) G. S. Tejada, M. Diaz-Guerra***, - Int. J. Molecular Science 18 (02) 2017***

AMBLYOPIA, otherwise known as "*lazy eye*", is a disorder of the visual system characterized by ***poor or indistinct vision***



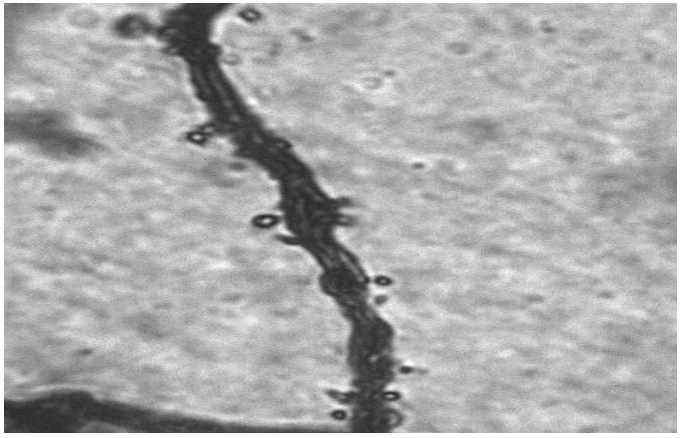
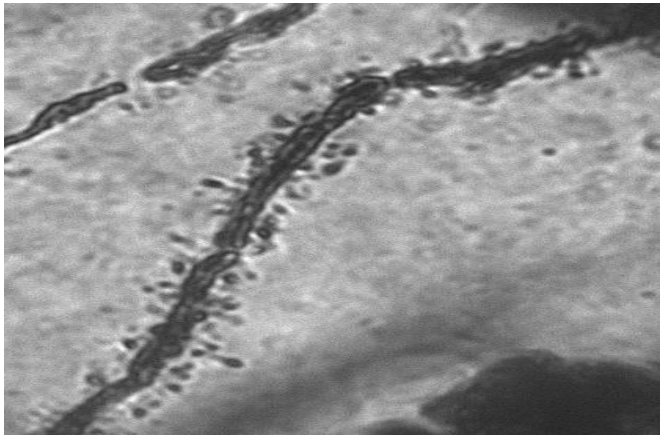
Developmental disease, due to the incomplete growth of the neuronal network in the visual cortex that receive the impulses from the amblyopic eye.

That is considered as an irreversible condition in adulthood !



A model of neuronal restored plasticity has been demonstrated in the ***visual cortex of amblyopic adults rodents*** treated with the Selective Serotonin Reuptake Inhibitor (SSRI) fluoxetine (5).



5) *J.F.M.Vetencourt, A.Sale, A.Viegi, L.Baroncelli, O.F.O'Leary, E. Castren,* ***L. Maffei****,* ***- Science*** **18- 2008 ;**

the neurofunctional deficits of amblyopia in humans….

…. as a …

…. *reliable model to study the effects of specific, neurotrophic, interventions !!!*

Methods

Sample :

3 adult, male, amblyopic subjects (*1 bilateral with nystagmus*)

Stimulation:

- ***daily stimulation*** of the amblyopic eye (*alternate a day for bilateral*) for one/two hour/s (*watching TV*) for the whole period of observation;
- ***"antidepressant"*** S/NRI intake *(duloxetine 60 mg/die)*

Measures :

- Best Corrected Visual Acuity (BCVA) in the amblyopic eye at T0, T1 and T2 (respectively 0 – 6 - 12 months)

- **For one** subject, also the measurement of the ***Visual Evoked Potentials*** (VEPs), with pattern reversal of 15° and 60° (*checkerboards reversal per second*).

EXPERIMENTAL RESULTS

Measurements at T2 showed a functional increase of BCVA from :

- 4 to ***7/10*** (*case with VEPs registered):*

- 2 to ***5/10*** (*case with bilateral amblyopia and nystagmus*)

- 2 to ***5/10***

Results

***case with VEPs**:*

* **INCREASE** of N75-P100 – amplitude in ***μV*** from***:***

  -**0.42* to ***4.14 *(in 15° pattern of stimulation)*

  3.76 to ***5.33*** *(in 60° pattern of stimulation)*

* **DECREASE** of P100 **-** Latency Peak Time in ***msec*** *from:*

  117.77 to ***111.91*** *(in 15° pattern of stimulation)*

  112.5 to ***102.5*** *(in 60° pattern of stimulation)*

Discussion

- All the cases significantly improved their eyesight (BCVA), *with personal benefits*

- The VEPs results suggest that (*in the case studied*):

> the **initial low amplitude** in *μV* at T0 of N75- P100 *-0.42* (in 15°) and *3.76* (in 60°) indicates that the **neuronal activity was actually impaired**, due to the incomplete network, as it is expected in the corresponding visual cortex of the amblyopic eye;

> the **increased amplitude** in *μV* at T2 of N75-P100 to *4.14* (in 15°) and *5.33 μV* (in 60°) can be related to a **restored neuronal activity** while processing the electro-visual stimuli.

> the **decreased Latency Peak Time** of P100 from *117.77* (in 15°) and *112.5* (in 60°) *msec* at T0 to *111.91* (in 15°) *and 102.5* (in 60°) *msec* at T2 means that the **neuronal connections** within the cortical area are **more effective** in transmitting the impulses.

Conclusions

The clinical and the experimental results (*improvement of BCVA, increase of N75-P100 Amplitude in microvolts, the decrease of P100 Latency in milliseconds*), seem to confirm other findings and to demonstrate that also the human adult's neuronal cortex **can be activated or shaped**, after proper stimulation, **in order to support its natural and specific function**.

The elicited functional/structural adaptations observed in our cases might be explained through the **mechanism of neuroplasticity**, likely enhanced simultaneously by the **biomolecular effects** of the S-NRI Duloxetine (*production of **BDNF***) and the **active visual-sensory stimulation** (*watching TV*).

Prospects

As shown, since **adaptation** can occur also in cortical areas never properly developed before (*as the amblyopic one*), a **potential clinical application might be investigated in other neurological conditions**, where the neural network/functions has formerly been unexpressed or compromised (*congenital/degenerative diseases, stroke, traumatic/functional damages*).

Thank you !

QUESTIONS ?

NEURAL PLASTICITY

functioning of brain …

…modifications - reorganizations

Structural

Dendrites morphology and density, Neurogenesis (birth of new neurons)

Functional

Changes of synapses and receptors, Signal transduction

Cellular/Molecular

Intracellular activity, Gene expression

Neural plasticity is emerging as a fundamental and critical mechanism of neuronal function, which allows the brain to receive information and make the appropriate adaptive responses to subsequent related stimuli.

Elucidation of the molecular and cellular mechanisms underlying neural plasticity is a major goal of neuroscience research, and significant advances have been made in recent years.

These mechanisms include regulation of signal transduction and gene expression, and also structural alterations of neuronal spines and processes, and even the birth of new neurons in the adult brain