Neurofisiologia ed Elettrofisiologica del sistema visivo

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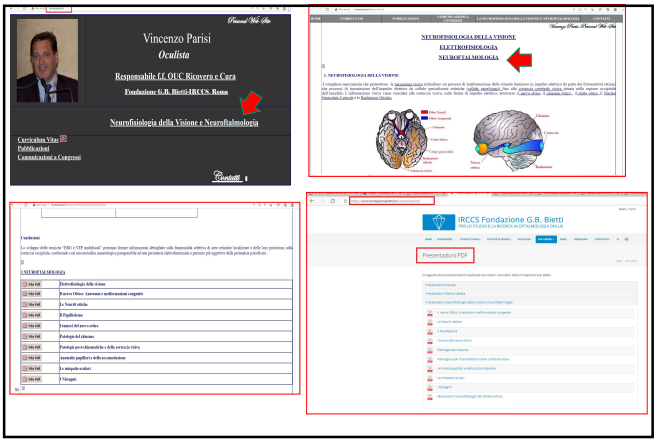

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forma, colore, dimensioni, contrasto, posizione nello spazio,…

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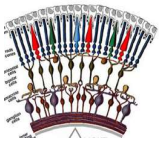
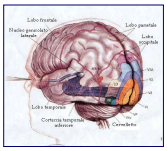
La Visione

La visione è la manifestazione di raffinati e complessi eventi neurosensoriali legati a fenomeni di traduzione dello stimolo luminoso in impulso nervoso …..



...e della trasmissione dell'impulso nervoso lungo le vie visive, cioè dalle cellule ganglionari retiniche fino alla corteccia cerebrale occipitale.



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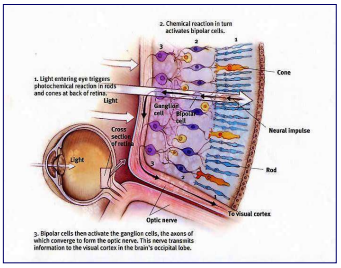
La retina



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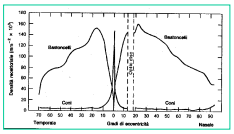
Cellule Fotorecettoriali:

Bastoncelli:

- rilevano stimoli di bassa intensità luminosa
- frequenza inferiore ai 12 Hz



Coni:

- mediano la visone dei colori
- alta risoluzione temporale (fino a 55 Hz)
- alta risoluzione spaziale (fino a 60 cicli/grado)

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Cellule Fotorecettoriali: trasduzione dell'impulso luminoso in impulso elettrico:

- al buio: apertura dei canali del Na+ e del K+ Ý corrente al buio Ý rilascio di neurotrasmettitori
- alla luce : assorbimento di un fotone da parte di un pigmento situato nei dischi esterni dei fotorecettori: la rodopsina Ý ciclo del retinale chiusura dei canali del Na+ e del K+ Ý fotocorrente Ý iperpolarizzazione della membrana cellulare

Ý riduzione del rilascio di neurotrasmettitori

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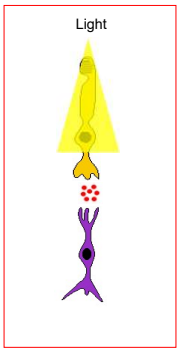

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La rodopsina:

- proteina : 348 aminoacidi
- la sintesi di tale proteina è regolata da geni presenti nel DNA.
- Anomale sequenze di nucleotidi dei geni → sostituzione di un aminoacido → mutazione della rodopsina
- La sostituzione del 23esimo aminoacido "prolina" → "istidina" (Pro 23 His)* → degenerazione del fotorecettore (perdita o assenza del segmento esterno)

→ Retinite Pigmentosa

* Dryja et al. Nature, N Eng J Med, 1990

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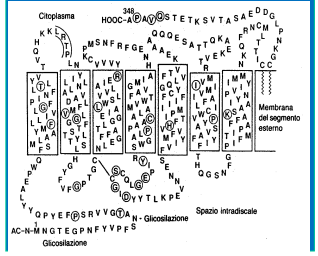
Struttura Rodopsina



Mutazioni

Mutazione		Sequenza normale
Thr17met	C→T	GCG ACG GGT
Pro23His	C→A	AGC CCC TTC
Pro23Leu	C→T	AGC CCC TTC
Phe45Leu	T→C	ATG TTT CTG
Gly51Val	G→T	CTG GGC TTC
Thr58Arg	C→G	CTG ACG CTC
Del68-71	12 bp del	CTG CGC ACG CCT
Val87Asp	T→A	ATG GTC CTA
Gly89Asp	G→A	CTA GGT GGC
Gly106Trp	G→T	TTC GGG CCC
Leu125Arg	T→G	GCC CTG TGG
Arg135Leu	GG→TT	GAG CGG TAC
Arg135Trp	C→T	GAG CGG TAC
Cys167Arg	T→C	CGG TCG GCC
Pro171Leu	C→T	CCC CCA CTC
Tyr178Cys	A→G	AGG TAC ATC
Glu181Lys	G→A	CCC GAG GGC
Gly182Ser	G→A	GAG GGC CTG
Ser186Pro	T→C	TGC TCG TGT
Gly188Arg	G→A	TGT GGA ATC
Asp190Asn	G→A	ATC GAC TAC
Asp190Gly	A→G	ATC GAC TAC
His211Pro	A→C	GTC CAC TTC
Ile255Del	3 bp del	GTC ATC ATC ATG
Pro267Leu	C→T	GTG CCC TAC
Lys296Glu	A→G	GCC AAG AGC
Gln344Ter	C→T	AGC CAG GTG
Val345Met	G→A	CAG GTG GCC
Pro347Arg	C→G	GCC CCG GCC
Pro347Leu	C→T	GCC CCG GCC
Pro347Ser	C→T	GCC CCG GCC

Attualmente circa 100 mutazioni note

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La Retinite Pigmentosa

- Degenerazione retinica progressiva
- Malattia genetica:

- 19 % forma autosomica dominante (cromosomi 3, 6, 8)
- 19 % forma autosomica recessiva
- 8 % X-linked (braccio corto cromosoma X)
- 46 % forma isolata in un membro della famiglia*

- Differenti forme in relazione al tipo e alla localizzazione del fotorecettore colpito
- Associata a diverse patologie (Sindrome di…..)

* Bunker et al. , Am J Ophthalmol1984

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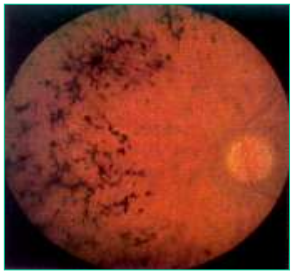
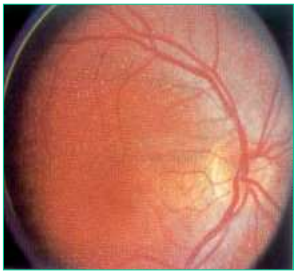
Retinite Pigmentosa — Fondo Albipuntato





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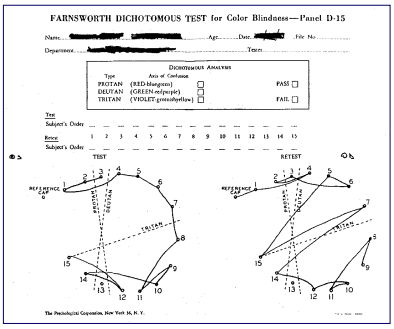
Senso Cromatico



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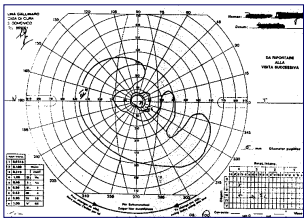
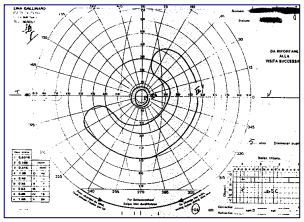
Campo Visivo





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Retinite Pigmentosa associata a:

- Malassorbimento lipidico, disturbi neuromuscolari con atassia, acatocitosi, ↓ livelli sierici di colesterolo e trigliceridi (Abetalipoproteinemia ereditaria, Sindrome di Bassen- Kornzwieg)
- Neuropatia periferica, atassia cerebrale, ↑ proteine liquido cerebrospianle e livelli sierici di acido fitanico (Malattia di Refsum)
- Sordità (Sindrome di Usher I e II)

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Retinite Pigmentosa associata a:

- Ritardo mentale, polidattilia, obesità del tronco e degli arti, ipogonadismo (Sindrome di Laurance-Moon- Bardet-Biedl)
- Ptosi, oftalmoplegia esterna cronica (Sindrome di Kearns-Sayre)
- Deterioramento psicomotorio, atassia epilessia, decadimento mentale (Malattia di Batten nelle varie evoluzioni)
- Sindrome di Alstrom e Cockayne

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Decorso della RP

- Tipo di fotorecettori colpiti
- Età di insorgenza
- Compromissione funzionale
- Valutazione di eventuali sindromi e relativo interessamento di altri organi o apparati

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Cellule postrecettoriali:

Cellule amacrine, Muller, Interplessiformi:

- connettono più fotorecettori tra di loro e con le

Cellule bipolari:

- alcune classi sono attivate (depolarizzazione) dal maggior rilascio di neurotrasmettitore da parte dei fotorecettori (centro OFF)
- alcune classi sono attivate (depolarizzazione) dalla diminuzione di rilascio di neurotrasmettitore da parte dei fotorecettori (centro ON)

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Cellule postrecettoriali:

Cellule ganglionari:

- possono ricevere informazioni da 1 a 300 fotorecettori Ý campionamento retinico: 1/300 nella periferia retinica, 1/1 nella fovea Ý acuità visiva (massima nella fovea)
- Campi recettivi Centro ON Ý attivati dalla luce ed inibiti dal buio
- Campi recettivi Centro OFF Ý inibiti dalla luce ed attivati dal buio

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Cellule postrecettoriali: Cellule ganglionari:

nella periferia retinica :

- grande soma (G. magnocellulari) e assone di grosso calibro (alta velocità di conduzione)
- responsive a basse frequenze temporali e spaziali, alle variazioni di luminanza

nella macula:

- piccolo soma (G. Parvocellulari) e assone di piccolo calibro (ridotta velocità di conduzione)
- responsive ad alte frequenze temporali e spaziali, alle variazioni di contrasto cromatico

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Valutazione funzionale del sistema visivo

•Metodiche psicofisiche:

-Acuità visiva, Campimetria e Perimetria, Senso cromatico, Sensibilità al contrasto…

Queste metodiche psicofisiche essendo basate su risposte soggettive fornite dal paziente, non permettono di identificare in maniera selettiva quali strutture della via ottica siano funzionalmente compromesse

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Metodiche Elettrofunzionali

•Forniscono informazioni selettive sulla funzionalità delle differenti strutture delle vie ottiche

(differenti strati retinici, nervo ottico, vie ottiche postchiasmatiche)

•Costituiscono una metodica semeiologica obiettiva, non influenzata dalla risposta soggettiva del paziente

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EVIDENZE DALLA RICERCA

APPLICAZIONI CLINICHE

1) COME SI ESEGUE UN ESAME

2) COME SI INTERPRETA

3) COME SI INTEGRA CON LA SEMEIOTICA PSICOFISICA E MORFOLOGICA

4) CONSIDERAZIONI NEUROFISIOPATOLOGICHE

5) DIAGNOSI PRECOCE E FOLLOW-UP

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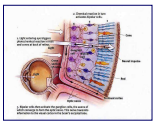
1) ESPLORAZIONE ELETTOFUNZIONALE DELLA RETINA:



ERG da Flash, ERG da Pattern

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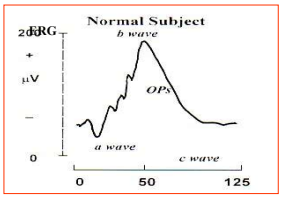
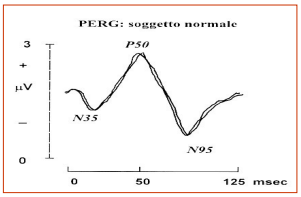
L'ELETTRORETINOGRAMMA (ERG)

- Risposta bioelettrica dell'intera retina ad uno stimolo visivo:
- Flash: lampo di luce stroboscopica
- Pattern: modello strutturato costituito da barre o scacchi che si alternano in modo cadenzato nel tempo





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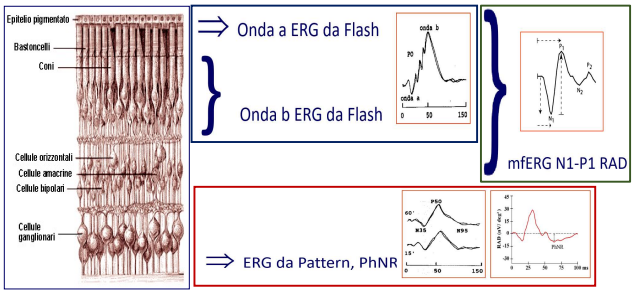
L'Elettroretinogramma: Tipologie e generatori



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L'Elettroretinogramma: Tipologie e generatori

Approccio Farmacologico:

inattivazione dei fotorecettori o blocco delle sinapsi intraretiniche

Approccio "Degenerativo"

taglio del nervo ottico e degenerazione delle fibre ganglionari o modelli patologici con degenerazione delle fibre ganglionari.

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Maffei e Fiorentini, Science, 1981

Dopo taglio del nervo ottico è stata osservata una progressiva diminuzione, fino alla scomparsa, del PERG.

Tale modificazione elettroretinografica era associata alla degenerazione delle fibre e cellule ganglionari.

L'ERG da flash rimaneva invariato.

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Viswanathan et al. *IOVS* 2000;

Experimentally-induced glaucoma or TTX treatment in monkey eyes:

•Reduction of PERG amplitude

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MODELLI UMANI DI NEURODEGENERAZIONE

Correlazioni morfo-funzionali:
PERG vs OCT

1) Multiple Slerosis
2) Alzheimer's Disease
3) CADASIL
4) Eredo-atassie

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MODELLI UMANI DI NEURODEGENERAZIONE

Correlazioni morfo-funzionali:
PERG vs OCT

I modelli umani confermano le evidenze sperimentali:
Il PERG (in particolare l'ampiezza P50-N95) è espressione elettrofunzionale della funzionalità degli strati retinici più interni
(Cellule ganglionari e loro fibre nervose)

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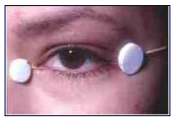
ERG-PERG: Elettrodi


ERG jet


Henkes


DTL


Skin

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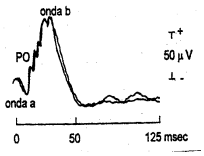
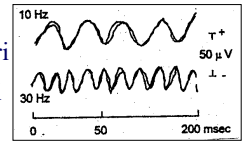
ERG da Flash:

FT 1 Hz, 1 J: Risposta transiente caratterizzata da:

- onda a:
- onda b
- onda c:



FT 1 Hz, 10 J: Potenziali Oscillatori
FT 10 e 20 Hz: Flicker, bastoncelli
FT 30 Hz: Flicker, coni



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ERG da Flash:
aumento del tempo di latenza onda a e b,
riduzione di ampiezza dell'onda a e b, PO in:

- retinite pigmentosa
- distacco di retina
- retinopatie tossiche
- amaurosi di Leber
- acromatopsia
- cecità notturna
- distrofie dei coni
- Vasculopatie (Diabete, Ipertensione)
- Occlusioni arteriose e venose
- Uveiti
- ……...

NO IN PATOLOGIE MACULARI

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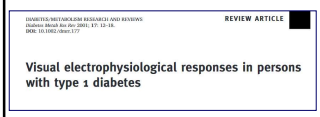
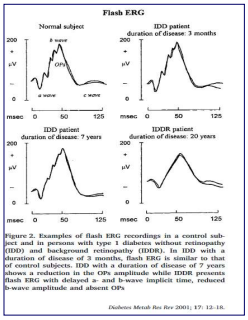
ERG e Diabete


REVIEW ARTICLE

Visual electrophysiological responses in persons with type 1 diabetes



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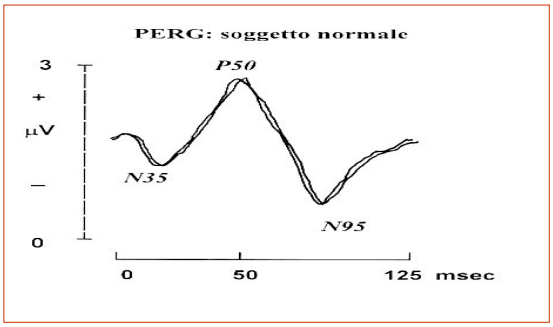
ERG da Pattern



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PERG: METODOLOGIA

1) PREPARAZIONE DEL PAZIENTE

2) POSIZIONAMENTO ELETTRODI

3) LO STIMOLO VISIVO

4) L'ACQUISIZIONE DEL SEGNALE

5) LA TRACCIA

6) IL REFERTO

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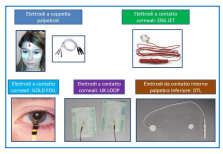
1) PREPARAZIONE DEL PAZIENTE

2) Posizionamento degli elettrodi



Ophthalmology Volume 126, Number 7, July 2019

Electrophysiologic Examinations.

Subjects were seated in a semi-dark, acoustically isolated room, in front of the display and surrounded by a uniform field of luminance of 5 candelas per meter squared. Before the experiment, each subject was adapted to the ambient room light for 10 minutes, with a pupil diameter of approximately 5 mm. No mydriatic or miotic drugs were used. Stimulation was monocular after occlusion of the fellow eye.

Poiché la stimolazione viene fatta sempre in maniera monoculare, seguendo il criterio pubblicato nel 1981 dalla Prof. Adriana Fiorentini e coautori (Fiorentini A, Maffei L, Invest Ophthalmol Vis Sci, 1981; 21:490-493) **il posizionamento degli elettrodi sulla palpebra dell'occhio stimolato e dell'occhio controlaterale occluso permette il vantaggio di ridurre il rumore di fondo legato ai moventi oculari, ai movimenti di ammiccamento palpebrali o all'attività bioelettrica di base.**

Infatti con tale tecnica, all'ingresso del preamplificatore entreranno: **nel polo positivo l'attività bioelettrica successiva alla stimolazione unita ad rumore di fondo e nel polo negativo solo rumore di fondo;** pertanto nella risposta bioelettrica ottenuta poiché il rumore di fondo entra sia nel polo positivo che in quello negativo, in teoria si annullano lasciando solo la componente dell'attività bioelettrica legata alla stimolazione.

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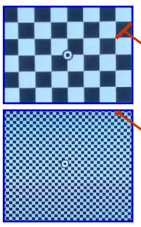
3) LO STIMOLO VISIVO
A) Frequenza spaziale B) Contrasto C) Frequenza temporale

A) Frequenza spaziale: è angolo sotteso dal singolo elemento del pattern, per cui viene calcolata in relazione alla dimensione del singolo elemento (barre- gratings o scacchi-checks) ed alla distanza del soggetto in esame.



a 57 cm: diagonale di 1 cm sottende 1 °= 60'

a 114 cm: diagonale di 2 cm sottende 1 °= 60'

a 114 cm: diagonale di 0.5 cm sottende ¼ di 1 °= 15'

Gli standard ISCEV propongono 40' (?????)

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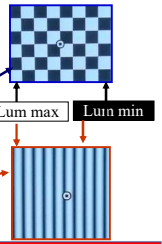
3) LO STIMOLO VISIVO
B) Contrasto: Lmax-Lmin/Lmin+Lmax x 100

Per cui se abbiamo un elemento bianco con massima luminanza (100) ed un elemento nero con minima luminanza (0) il contrasto è del 100%.

In realtà, l'elemento bianco non ha mai una luminanza 100, per cui viene sempre utilizzato un contrasto reale del 70-80 %.



Il contrasto viene definito ad "onda quadra" se il passaggio dalla luminanza dell'elemento bianco a quello nero (sia esso barra o scacchi) avviene in maniera netta, mentre viene definito ad "onda sinusoidale" se il passaggio dalla luminanza dell'elemento bianco a quello nero (sia esso barra o scacchi) avviene in maniera graduale.

L'uso dei gratings è molto importante nei casi in cui non si conoscenza della corretta AV

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3) LO STIMOLO VISIVO
C) Frequenza temporale: tempo di inversione bianco/nero misurata in Hz

- 1-2 Hz: Risposta transiente caratterizzata da serie di onde a polarità alternante negativa-postiva-negativa: N35, P50, N95
- 4, 8, 16 Hz: risposta Steady-State: valutazione della risposta sulla armonica di frequenza doppia rispetto a quella di stimolazione (FFT, fase e ampiezza della II armonica)

Combinando frequenze spaziali, contrasto e frequenza temporale si possono ottenere N all'infinito pattern

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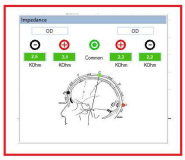
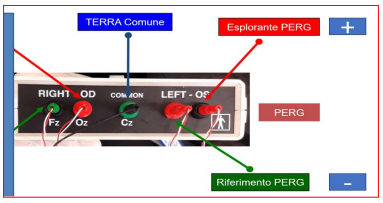
4) ACQUISIZIONE DEL SEGNALE
a) Posizionamento degli elettrodi al pre-amplificatore

Resistenza interelettrodica: < 3 KHoms





Quando si cambia occhio, si invertono gli elettrodi!!!!!!

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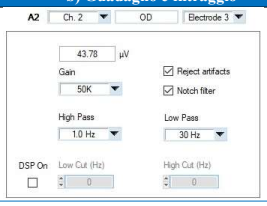
4) L'ACQUISIZIONE DEL SEGNALE
b) Guadagno e filtraggio

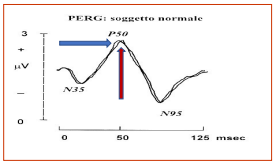


The signal was amplified (gain 50 000), filtered (band pass 1−30 Hz) and averaged with automatic rejection of artefacts (100 events free from artefacts were averaged for every trial) by [redacted] Pisa, Italy). Analysis time was 250 msec.

44

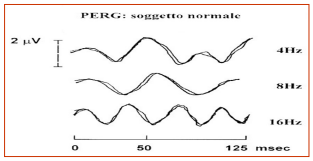
5) LA TRACCIA
FUNZIONE DI FREQUENZA SPAZIALE, CONTRASTO, FREQUENZA TEMPORALE

2 Hz, risposta «transiente»



Si valuta:
1) Tempo implicito N35, P50 e N95
2) Ampiezza picco-picco N35-P50 e P50-N95

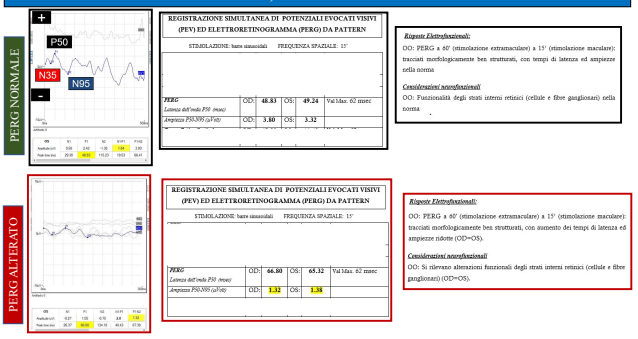
4, 8, 16 Hz, risposta «steady-state»



Si effettua FFT e si valuta
1) fase
2) ampiezza della II armonica

45

6) Il REFERTO



46

ERG da Pattern: aumento del tempo di latenza picchi N35, P50 e N95, riduzione di ampiezza n35-P50 e P50-N95 (transiente), ritardo di fase e riduzione di ampiezza (steady-state) in:

- retinite pigmentosa
- maculopatie
- M. di Stargardt
- M. di Best
- degenerazione maculare senile
- diabete
- glaucoma
- neuriti ottiche (Indice di degenerazione retrograda nella SM)
- Parkinson

CONCOMITANZA DI PATOLOGIE: Abilità dignostica = 0

47

Anomalie retiniche nelle patologie neurodegenerative

1) Glaucoma
2) Multiple Slerosis
3) Alzheimer's Disease
4) CADASIL
5) Eredo-atassie

48

Correlazioni morfo-funzionali: PERG, mfERG vs OCT

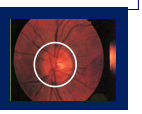
La valutazione "in vivo" delle fibre nervose retiniche

49

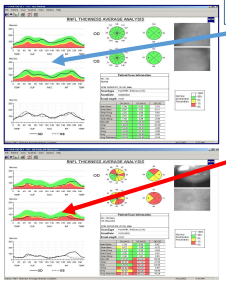
Morfologia: Optical Coherence Tomography (OCT)

- Tecnica ad alta risoluzione che fornisce immagini stratificate della retina dalle quali è possibile ottenere informazioni quantitative sullo strato delle fibre nervose.
- Tecnica analoga all'ecografia B-mode che al posto di un'onda acustica utilizza la riflessione di un'onda luminosa misurando il ritardo del fascio luminoso che incrocia lo strato delle fibre nervose.

- Circular scans
- diameter: 3.4 mm



Normative Database



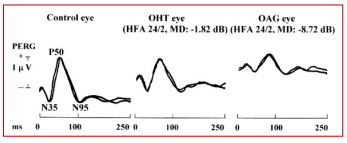
50

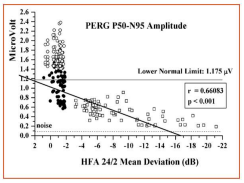
GLAUCOMA

Stimolo checks 15'; FT 2 Hz; Contrasto 70 %

Clinical Ability of Pattern Electroretinograms and Visual Evoked Potentials in Detecting Visual Dysfunction in Ocular Hypertension and Glaucoma

Specificità : 100%
Sensibilità: OAG 100%; OHT 69.2%





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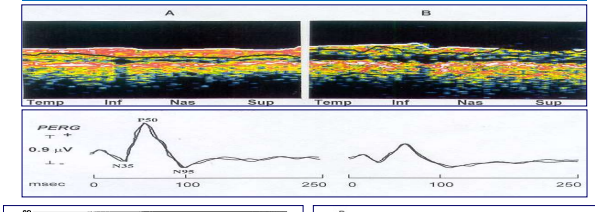
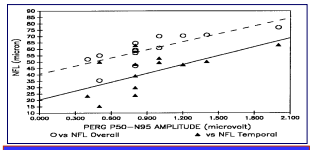
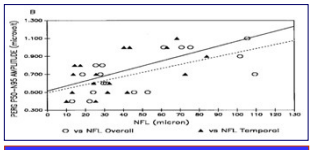
Correlazione tra PERG e spessore del NFL in OHT e POAG







OHT: r = -0.518, P<0.001

POAG: r = -0.847, P<0.001

Parisi et al., IOVS 1999, Ophthalmology 2001, FAN 2021

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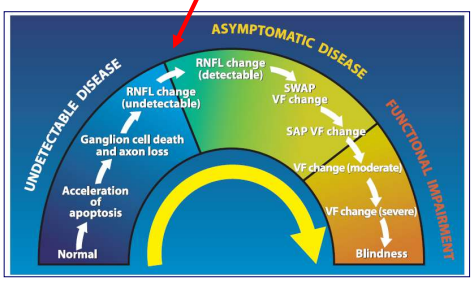
PERG



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Morpho-functional Correlations: Multiple Sclerosis

- Evaluation of RNFL thickness in MS patients with or without Optic Neuritis (NORB)

Correlation between Morphological and Functional Retinal Impairment in Multiple Sclerosis Patients

Vincenzo Parisi,[1,2,3] Gianluca Manni,[1,2] Maria Spadaro,[4] Gaspare Colacino,[1,2] Rita Restuccia,[4] Stefano Marchi,[1] Massimo G. Bucci,[1,2] and Francesco Pierelli[4,5]

Purpose. To assess whether a correlation exists between optic nerve fiber layer (NFL) thickness and the retinal or visual pathway function in multiple sclerosis (MS) patients previously affected by optic neuritis.

Methods. Fourteen patients with a diagnosis of definite MS were examined. All had been affected by optic neuritis (MSON) with complete recovery of visual acuity (14 eyes included in study). These were compared with 14 eyes from 14 age-matched control subjects. NFL thickness was measured by optical coherence tomography (OCT). Three different measurements in each quadrant (superior, inferior, nasal, and temporal) were taken and averaged. The data in all quadrants (12 values averaged) were identified as NFL Overall, whereas the data obtained in the temporal quadrant only (3 values averaged) were identified as NFL Temporal. Retinal and visual pathway function was assessed by simultaneously recording pattern electroretinograms (PERGs) and visual evoked potentials (VEPs) using high-contrast (80%) checkerboard stimuli subtending 15 minutes and 60 minutes of the visual arc (min arc) and reversed at the rate of two reversals per second.

Results. In MSON eyes there was a significant ($P < 0.01$) reduction in NFL thickness in both NFL Overall and NFL Temporal evaluations compared with the values observed in control eyes. PERG (15-min arc checks) and VEP (15-min arc and 60-min arc checks), showed a significant ($P < 0.01$) delay in latency and reduction in amplitude. NFL Overall and NFL Temporal values were significantly correlated ($P < 0.01$) to the PERG P50 latency and P50 to N95 amplitude recorded with 15-min arc checks. No correlations ($P > 0.01$) between NFL values and the other electrophysiological data (PERG recorded with 60-min arc checks and VEP recorded with 15-min arc and 60-min arc checks) were found.

Conclusions. There is a correlation between PERG changes and NFL thickness in MS patients previously affected by optic neuritis, but there is no correlation between VEP changes and NFL thickness. *Invest Ophthalmol Vis Sci.* 1999;40:2520–2527.

528 citazioni

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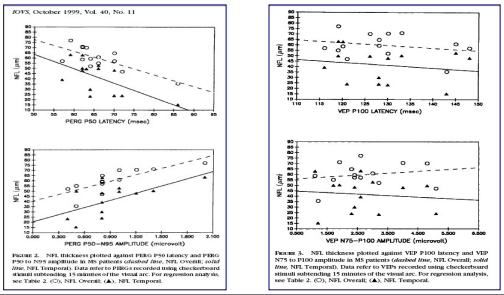
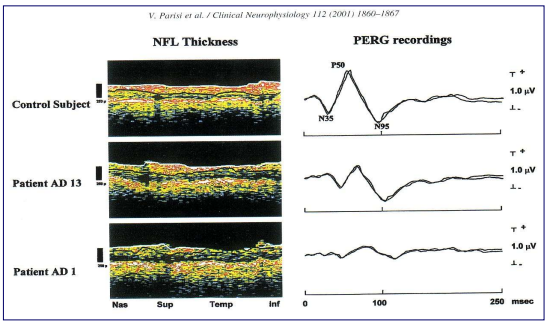
Morpho-functional Correlations: Multiple Sclerosis



The RNFL thickness was also reduced in MS eyes without NORB!

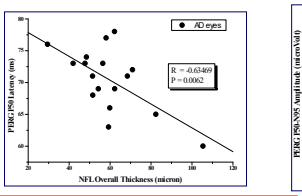
55

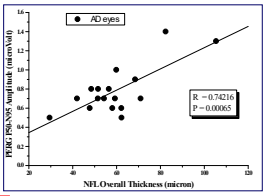
Morpho-functional Correlations: Alzheimer's Disease

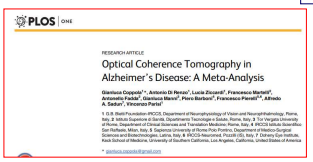


56

Morpho-functional Correlations: Alzheimer's Disease







OCT versus patient's age and psychometric parameters

In AD patients, no significant correlations ($p<0.01$) between the NFL values and age or psychometric parameters (MMSE, ADAS, IVM) were observed.

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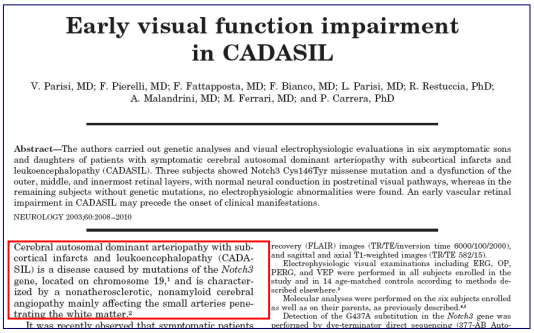
Morpho-functional retinal changes: CADASIL



Early visual function impairment in CADASIL

V. Parisi, MD; F. Pierelli, MD; F. Fattapposta, MD; F. Bianco, MD; L. Parisi, MD; R. Restuccia, PhD; A. Malandrini, MD; M. Ferrari, MD; and P. Carrera, PhD

Abstract—The authors carried out genetic analyses and visual electrophysiologic evaluations in six asymptomatic sons and daughters of patients with symptomatic cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). Three subjects showed Notch3 Cys146Tyr missense mutation and a dysfunction of the outer, middle, and innermost retinal layers, with normal neural conduction in postretinal visual pathways, whereas in the remaining subjects without genetic mutations, no electrophysiologic abnormalities were found. An early vascular retinal impairment in CADASIL may precede the onset of clinical manifestations.

NEUROLOGY 2003;60:2008–2010

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a disease caused by mutations of the *Notch3* gene, located on chromosome 19,[1] and is characterized by a nonatherosclerotic, nonamyloid cerebral angiopathy mainly affecting the small arteries penetrating the white matter.[2]

recovery (FLAIR) images (TR/TE/inversion time 6000/100/2000), and sagittal and axial T1-weighted images (TR/TE 582/15).

Electrophysiologic visual examinations including EEG, OP, PERG, and VEP were performed in all subjects enrolled in the study and in 14 age-matched controls according to methods described elsewhere.[3]

Molecular analyses were performed on the six subjects enrolled as well as on their parents, as previously described.[4,5]

Detection of the G437A substitution in the *Notch3* gene was performed by dye-terminator direct sequencing (377-ABI Auto-

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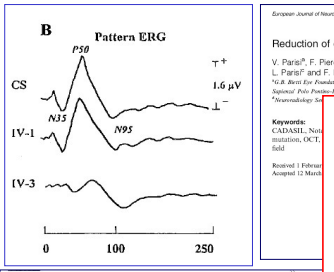
Morpho-functional retinal changes: CADASIL



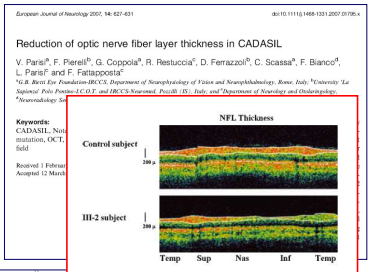


Figure 1 Circular optical coherence tomography (OCT) taken in cylindrical sections of tissue surrounding the optic disc. The most anterior red reflection indicates the nerve fiber layer (NFL). Compared to control eyes, OCT image of subject III-2 (right eye) shows a marked decrease of NFL reflection (lower NFL thickness) in each quadrant.

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Morpho-functional retinal changes: Ataxia

Therefore, the main aim of our work was to evaluate whether the macular functional and morphological abnormalities could be detectable in SP, genetically confirmed and with neurological signs, as well as in SCA-ATXN1-NSC, harboring pathogenic CAG expansion in *ATXN1*. In addition, we investigated whether the macular involvement could be associated or not to an impairment of RGCs and of their fibers and of the neural conduction along the visual pathways.

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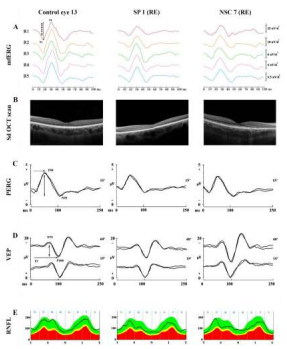
Morpho-functional retinal changes: Ataxia



In four eyes of two SP, visual acuity reduction and chromatic abnormalities were observed; in three of them FO changes associated with macular thinning and outer retinal defects were also detected.

In three NSC eyes, slight FO abnormalities were associated with qualitative macular morphological changes.
By contrast, abnormal mfERG responses (exclusively from foveal and parafoveal areas) were detected in all SP and NSC (18 eyes).

No abnormalities of PERG values, RNFL-T, and VEP responses were found, but in one SP, presenting abnormal papillo-macular bundle neural conduction.

Results from our **SCA-ATXN1** cohort suggest that **a macular dysfunction, detectable by mfERG recordings, may occur in the overt disorder, and unexpectedly in the stage of the disease in which there is still an absence of neurological signs.**
In NSC, an exclusive dysfunction of preganglionic macular elements can be observed, and this is associated with both normal RGCs function and neural conduction along the visual pathways.

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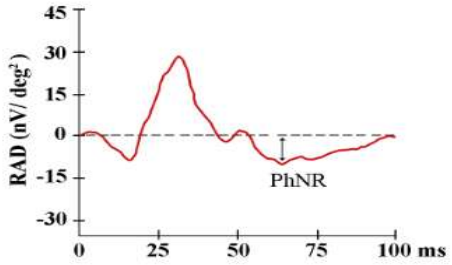
PhNR



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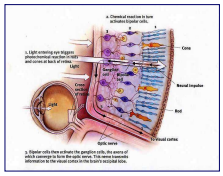
2) ESPLORAZIONE ELETTOFUNZIONALE DA AREE RETINICHE LOCALIZZATE



ERG e PhNR Multifocale

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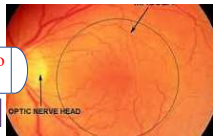
ERG MULTIFOCALE: Problema principale:

Spot luminoso sul nervo ottico registriamo ERG?

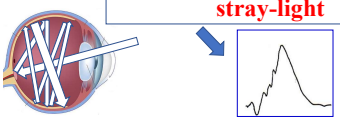
NO non si sono fotorecetori



…..invece…. REGISTRIAMO ERG

Bulbo oculare: Cupola riflettente

stray-light



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Asher (J.P. 1965) e Boynton e Riggs (J.P. 1951) dimostrarono che un piccolo spot luminoso, se orientato sul disco ottico, produceva un ERG la cui ampiezza era eguale o lievemente superiore rispetto a quello ottenibile quando lo stesso spot era orientato sulla fovea.

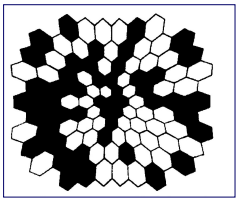
SI PUO' REGISTRARE UNA RISPOSTA BIOLETTRICA DA AREE RETINICHE LOCALIZZATE?

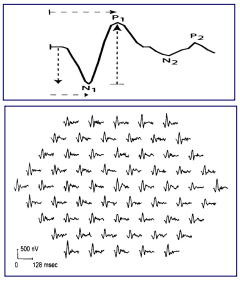
- Risolvere i problemi legati al fenomeno della stray-light

Impiegare uno stimolo test circondato da un background luminoso adattante.

65

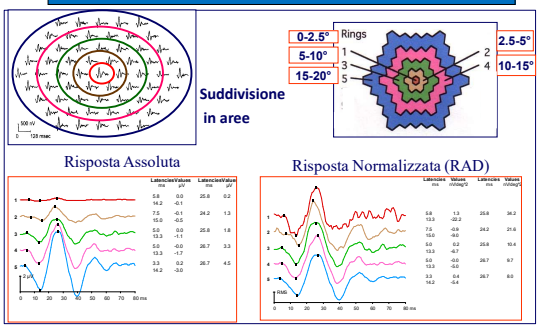
ERG Multifocale: stimolo visivo e risposta elettrofunzionale





66

ERG MULTIFOCALE NORMALE



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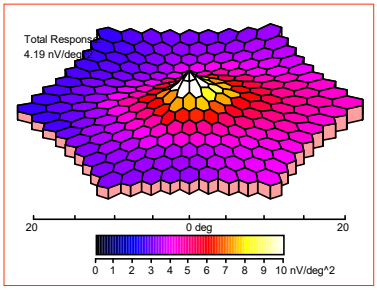
Mappa della funzionalità retinica



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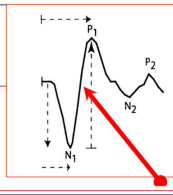
ERG Multifocale: Generatori

Quali sono i generatori retinici della componente N1-P1?

Assessing retinal function with the multifocal technique. **Hood DC.** Prog Retin Eye Res. 2000 Sep;19(5):607-46.

Coni e bipolari off



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Applicazioni Cliniche

-AMD

-CNV Miopica

-Retinite Pigmentosa

-Glaucoma

NO CON CATARATTA, PATOLOGIE CONCOMITANTI, MANCANZA DI FISSAZIONE

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mfERG e AMD:

1. **Correlazioni elettrofisiologia/psicofisica**
2. Correlazioni elettrofisiologia/morfologia
3. Utilità per la valutazione efficacia terapie

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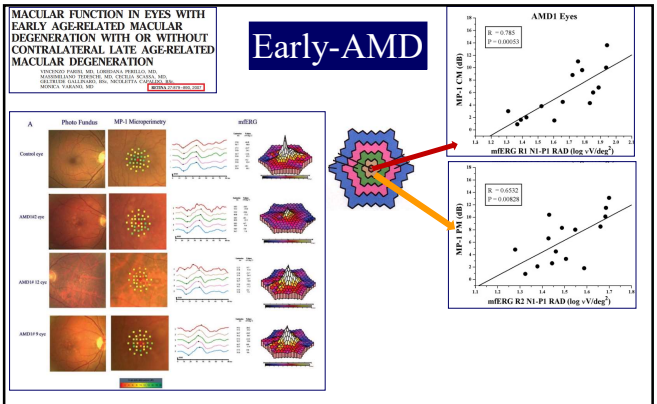
MACULAR FUNCTION IN EYES WITH EARLY AGE-RELATED MACULAR DEGENERATION WITH OR WITHOUT CONTRALATERAL LATE AGE-RELATED MACULAR DEGENERATION

Early-AMD



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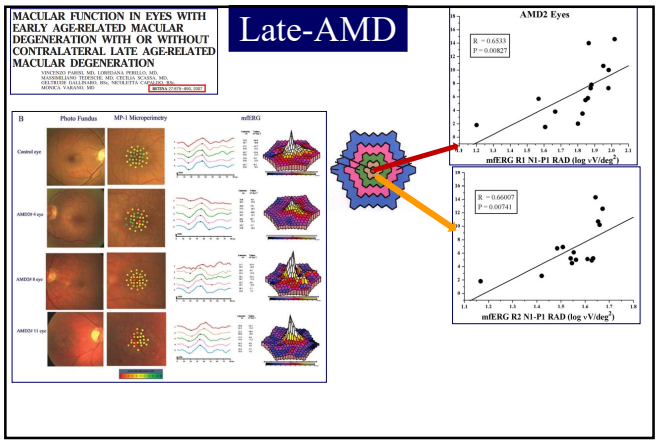

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mfERG e AMD:

1. Correlazioni elettrofisiologia/psicofisica
2. **Correlazioni elettrofisiologia/morfologia**
3. Utilità per la valutazione efficacia terapie

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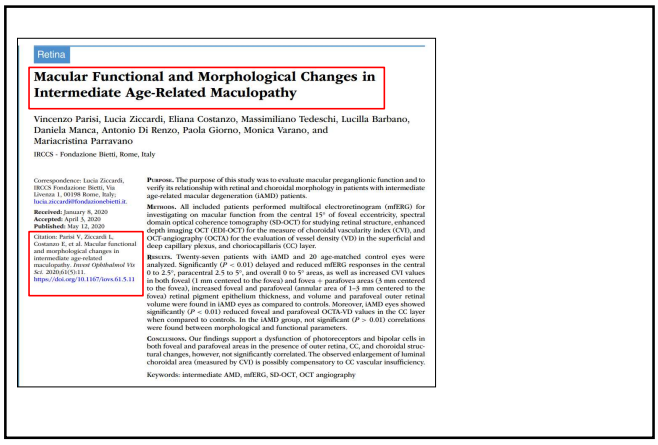
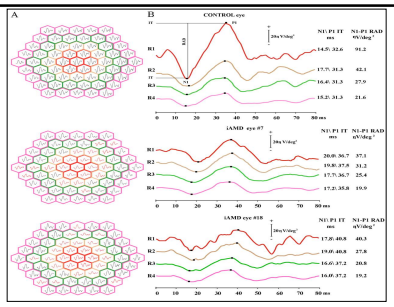


75



Sulla sinistra si osserva la rappresentazione topografica della risposta bioelettrica all'elettroretinogramma multifocale (mfERG) ottenuta nei 15° di eccentricità dalla fovea in un occhio controllo e in due occhi affetti da iAMD.
Sulla destra sono rappresentate le tracce del mfERG ottenute nei 5 Ring centrali [R1 (0°-2,5°), R2 (2,5°-5°), R3 (5°-10°), R4 (10°-15°)] in un occhio controllo e in due occhi affetti da iAMD. Si osserva nei pazienti affetti da iAMD una riduzione della RAD ed un aumento della latenza IT.

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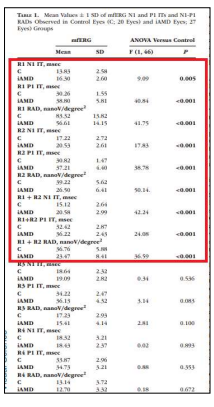


Table 1. Mean Values ± 1 SD of mfERG N1 and P1 ITs and N1-P1 RADs Observed in Control Eyes (C, 20 Eyes) and iAMD Eyes, 27 Eyes) Groups

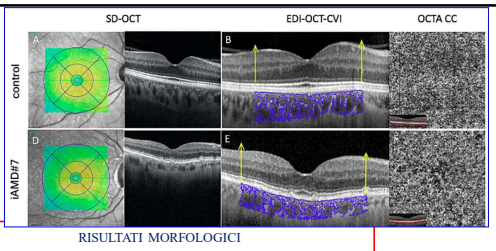
	mfERG Mean	SD	ANOVA Versus Control F (1, 45)	P
R1 N1 IT, msec				
C	13.83	2.58		
iAMD	16.30	2.60	9.09	**0.005**
R1 P1 IT, msec				
C	30.26	1.55		
iAMD	50.80	5.81	40.84	**<0.001**
R1 RAD, nanoV/degree²				
C	83.52	15.82		
iAMD	56.61	14.15	41.75	**<0.001**
R2 N1 IT, msec				
C	17.22	2.72		
iAMD	20.53	2.61	17.83	**<0.001**
R2 P1 IT, msec				
C	30.82	1.47		
iAMD	57.21	4.40	38.78	**<0.001**
R2 RAD, nanoV/degree²				
C	39.22	5.62		
iAMD	25.50	6.41	50.14	**<0.001**
R1 + R2 N1 IT, msec				
C	15.12	2.04		
iAMD	20.58	2.99	42.24	**<0.001**
R1+R2 P1 IT, msec				
C	52.62	2.87		
iAMD	36.22	2.43	24.08	**<0.001**
R1 + R2 RAD, nanoV/degree²				
C	36.76	5.08		
iAMD	23.47	8.41	36.59	**<0.001**
R3 N1 IT, msec				
C	18.64	2.32		
iAMD	19.09	2.82	0.34	0.536
R3 P1 IT, msec				
C	34.22	2.47		
iAMD	36.13	4.32	3.14	0.085
R3 RAD, nanoV/degree²				
C	17.23	2.59		
iAMD	15.41	4.14	2.81	0.100
R4 N1 IT, msec				
C	18.52	3.21		
iAMD	18.63	2.37	0.02	0.893
R4 P1 IT, msec				
C	33.87	2.56		
iAMD	34.73	3.21	0.88	0.353
R4 RAD, nanoV/degree²				
C	13.14	3.72		
iAMD	12.70	3.32	0.18	0.672

RISULTATI FUNZIONALI

Confrontando i valori medi IT e RAD ottenuti nei pazienti iAMD verso i Controlli si evidenzia:

- **Riduzione** della funzione nell'area foveale **(Ring 1)** ovvero tra 0°-2,5° dal centro della fovea.
- **Riduzione** della funzione nell'area parafoveale **(Ring 2)** ovvero tra 2,5°-5° dal centro della fovea.
- **Riduzione** della funzione nell'area foveale + parafoveale **(Ring 1 + Ring 2)** ovvero tra 0°-5° dal centro della fovea.
- **No differenze statisticamente** significative nelle regioni più esterne alla fovea **(Ring 4 e Ring 5)** ovvero tra 5°-10° e tra 10°-15°

77



RISULTATI MORFOLOGICI

SD-OCT:
- Lo spessore ed il volume centrale e parafoveale dell'epitelio pigmentato retinico **(C-RPE, P-RPE)** ed il volume della retina esterna parafoveale **(P-ORV) risultano significativamente aumentati** negli iAMD rispetto ai C.
- I restanti parametri di spessore e volume misurati nei differenti strati retinici foveali e parafoveali non risultano significativamente alterati nei iAMD rispetto ai C.

EDI-OCT:
- L'indice di vascolarizzazione coroideale **(CVI) risulta aumentato** nella regione foveale (1mm) e foveale + parafoveale (3 mm) negli iAMD rispetto ai C.

OCTA:
- La densità vascolare **(VD)** del plesso capillare superficiale **(SCP)** e profondo **(DCP) non mostra differenze statisticamente** significative negli iAMD rispetto ai C.
- La **VD** della **Coriocapillare (CC)** misurata sia nella regione foveale che parafoveale, **risulta significativamente ridotta** negli iAMD rispetto ai C.
- **No differenze statisticamente significative** nella misurazione della zona avascolare foveale **(FAZ)** tra iAMD e C.

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Investigative Ophthalmology & Visual Science

RISULTATI DELLE CORRELAZIONI MORFO-FUNZIONALI

Conclusions. Our findings support a dysfunction of photoreceptors and bipolar cells in both foveal and parafoveal areas in the presence of outer retina, CC, and choroidal structural changes, however, not significantly correlated. The observed enlargement of luminal choroidal area (measured by CVI) is possibly compensatory to CC vascular insufficiency.

Non si osservano correlazioni statisticamente significative tra i parametri morfologici (SD-OCT, EDI-OCT, OCTA) e funzionali (mfERG IT e mfERG RAD) di aree retiniche corrispondenti.

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mfERG e AMD:

1. Correlazioni eletrofisiologia/psicofisica
2. Correlazioni elettrofisiologia/morfologia
3. **Utilità per la valutazione efficacia terapie:**

a) **Carotenoidi**

b) **Terapie intravitreali**

80

1) Carotenoidi

Ophthalmology 2008;115:324–333 © 2008 by the American Academy of Ophthalmology.

Carotenoids and Antioxidants in Age-Related Maculopathy Italian Study

Multifocal Electroretinogram Modifications after 1 Year

Vincenzo Parisi, MD,[1] Massimiliano Tedeschi, MD,[1] Gektrude Gallinaro, BSc,[1] Monica Varano, MD,[1] Sandro Saviano, MD,[2] Stefano Piermarocchi, MD,[3] CARMIS Study Group[4,5]

Objective: To evaluate the influence of short-term carotenoid and antioxidant supplementation on retinal function in nonadvanced age-related macular degeneration (AMD).
Methods: Multifocal electroretinograms in response to 61 M-stimuli presented to the central 20° of the visual field were assessed in pretreatment (baseline) conditions and, in nonadvanced AMD patients, after 6 and 12 months.

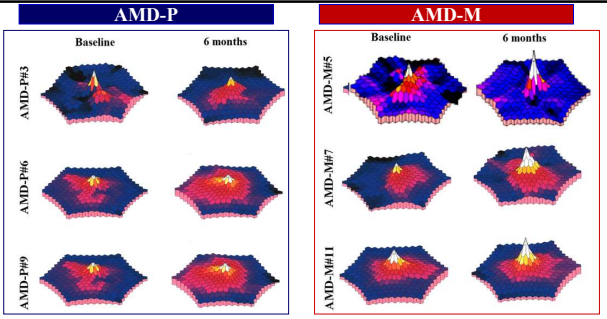
Adv Ther (2019) 36:2493–2505
https://doi.org/10.1007/s12325-019-01016-2

Effects of Macuprev® Supplementation in Age-Related Macular Degeneration: A Double-Blind Randomized Morpho-Functional Study Along 6 Months of Follow-Up

Mariacristina Parravano · Massimiliano Tedeschi · Daniela Manca · Eliana Costanzo · Antonio Di Renzo · Paola Giorno · Lucilla Barbano · Lucia Ziccardi · Monica Varano · Vincenzo Parisi

Background: To evaluate the effects of Macuprev® supplementation on macular function and structure in intermediate age-related macular degeneration (AMD) along 6 months of follow-up.

81



82

2) Trattamenti intravitreali

Doc Ophthalmol (2013) 127:217–225
DOI 10.1007/s10633-013-9404-z

Single-session photodynamic therapy combined with intravitreal ranibizumab for neovascular age-related macular degeneration: a comprehensive functional retinal assessment

Mariacristina Parravano · Vincenzo Parisi · Lucia Ziccardi · Adele Chiaravalloti · Massimiliano Tedeschi · Andrea Cacciamani · Barbara Boccassini · Antonluca Boninfante · Monica Varano

Purpose To explore functional retinal changes in neovascular AMD patients (nAMD) treated with ranibizumab 0.5 mg combined with photodynamic therapy (PDT) 3 days after the first injection in the long term.

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	R1: 0-2.5°	R2: 2.5-5 °	R3: 5-10°	R4: 10-15°	R5: 15-20°
Baseline	30.4 ± 8.15	18.7 ± 4.90	13.9 ± 4.01	15.14 ± 6.90	13.00 ± 7.21
3 months	41.7 ± 14.95	25.8 ± 10.54	19.4 ± 8.54	13.08 ± 5.82	10.44 ± 5.15
ANOVA, $f(1, 23)$ versus baseline	$f = 5.22$, $p = 0.032$	$f = 4.55$, $p = 0.043$	$f = 4.64$, $p = 0.042$	$f = 0.05$, $p = 0.822$	$f = 0.08$, $p = 0.775$
12 months	52.7 ± 20.58	28.60 ± 13.10	21.2 ± 10.9	11.91 ± 4.52	10.54 ± 4.23
ANOVA, $f(1, 23)$ versus Baseline	$f = 12.2$, $p = 0.002$	$f = 6.12$, $p = 0.021$	$f = 4.67$, $p = 0.041$	$f = 0.15$, $p = 0.699$	$f = 0.09$, $p = 0.771$

Conclusions Ranibizumab 0.5 mg combined with standard PDT 3 days after the first injection determines an improvement of mfERG values in the retinal central area in nAMD patients in long-term follow-up.

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Conclusioni

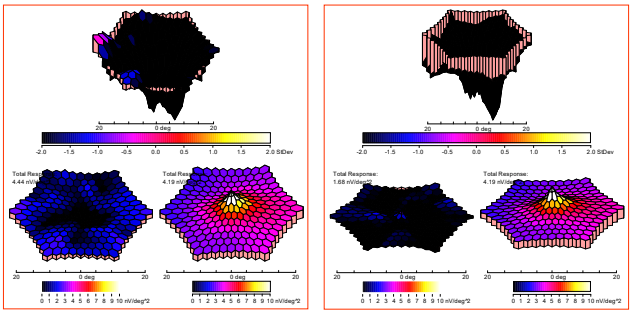
mfERG e AMD:

1. Identificazioni di disfunzioni precoci nell'area foveale
2. Modificazioni del mfERG correlate con psicofisica (microperimetria), ma non con OCT/A-OCT
3. Utilità per la valutazione efficacia terapie

85

Soggetto: Di Ma 44 anni, CNV miopica, OD

Soggetto: Di Mi 54 anni, CNV miopica, OD



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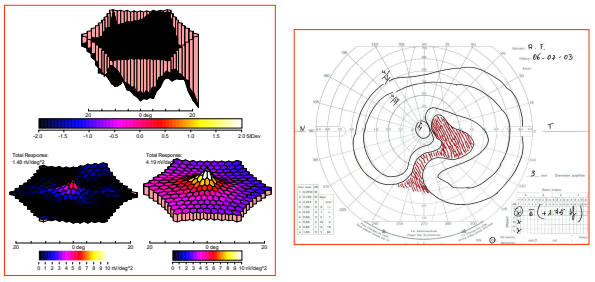
Soggetto B.A.: 34 anni, RP, OD

M-ERG Campo Visivo



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Nei pazienti con RP si ha la possibilità di rilevare aree retiniche "ancora" funzionanti e di quantificarne la funzionalità residua in maniera oggettiva.

- Particolare utilità nella valutazione funzionale residua della regione maculare

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L'ERG MULTIFOCALE

Visual Neuroscience

Macular Function in Eyes with Open-Angle Glaucoma Evaluated by Multifocal Electroretinogram

Invest Ophthalmol Vis Sci. 2012; 53:6973-80

Vincenzo Parisi,[1] Lucia Ziccardi,[1] Marco Centofanti,[1,2] Lucia Tanga,[1] Geltrude Gallinaro,[3] Benedetto Falsini,[4] and Massimo G. Bucci[1]

Abstract

Purpose. To evaluate macular function in patients with open-angle glaucoma (OAG) by means of multifocal electroretinogram (mfERG). Methods. Twenty-four OAG patients (mean age 54.6 ± 9.1 years) and 14 age-similar controls were enrolled. OAG patients had intraocular pressure (IOP) less than 18 mm Hg with topical medical treatment. 24-2 visual field (Humphrey Field Analyzer [HFA]) with mean deviation (MD) between -2 and -12 dB, and corrected pattern standard deviation (CPSD) between +2 and +10 dB and no history or presence of cataract and/or macular disease. MfERGs in response to 61 M-stimuli presented to the central 20° of the visual field were assessed in OAG patients (24 eyes) and in controls (14 eyes). Ring (R) analysis was performed every five retinal eccentricities in areas between the fovea and midperiphery: 0° to 2.5° (R1), 2.5° to 5° (R2), 5° to 10° (R3), 10° to 15° (R4), and 15° to 20° (R5). MfERG response amplitude density of the N1-P1 components (N1-P1 RAD, nV/deg(2)) and P1 implicit time (P1 IT, ms) of the first-order binary kernel were measured for each ring. Results. OAG patients showed a significant ($P < 0.01$) decrease in N1-P1 RADs and an increase in P1 IT in both R1 and R2 with respect to controls. The reduction in N1-P1 RADs was significantly ($P < 0.01$) correlated with HFA MD and CPSD. No other significant differences between OAG and controls were found. Conclusions. OAG patients show macular dysfunction detectable by the mfERG technique. Since the mfERG N1-P1 component is thought to be generated by preganglionic elements (photoreceptors and OFF bipolar cells), our data support the functional impairment of the neural generators of the macular region in patients with glaucoma.

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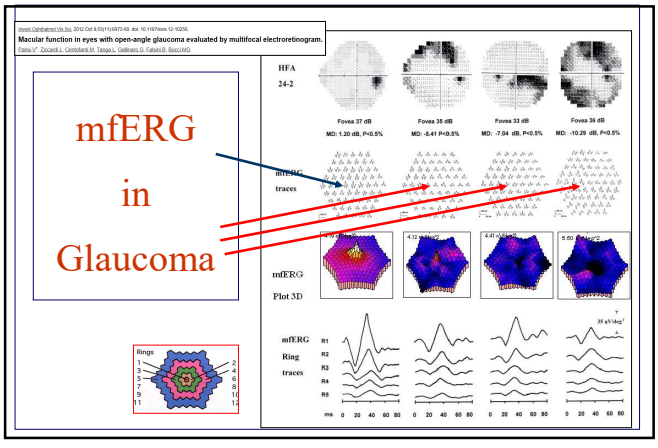

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Standards, Recommendations and Guidelines

mfERG (= multifocal ERG)

Hood DC, Bach M, Brigell M, Keating D, Kondo M, Lyons JS, Marmor MF, McCulloch DL and Palmowski-Wolfe AM (2012) ISCEV Standard for clinical multifocal electroretinography (2011 edition). Doc Ophthalmol 124:1–13

mfERG Standard (Springer) | local copy [PDF]

ERG

Marmor MF, Fulton AB, Holder GE, Miyake Y, Brigell M, Bach M (2009) Standard for clinical electroretinography (2008 update). Doc Ophthalmol 118:69–77

ERG Standard (Springer) | local copy [PDF]

EOG

Marmor MF, Brigell MG, Westall CA, Bach M. ISCEV Standard for Clinical Electro-oculography (2010 Update). Doc Ophthalmol (2011) 122:1–7

EOG Standard (Springer) | local copy [PDF]

PERG (= Pattern ERG)

Bach M, Brigell MG, Hawlina M, Holder GE, Johnson MA, McCulloch DL, Meigen T, Viswanathan S (2013) ISCEV standard for clinical pattern electroretinography (PERG) – 2012 update. Doc Ophthalmol 124:1–13 [DOI]

PERG Standard (Springer) | local copy [PDF]

VEP

Odom JV, Bach M, Brigell M, Holder GE, McCulloch DL, Tormene AP, Vaegan (2010). ISCEV standard for clinical visual evoked potentials(2009 update). Doc Ophthalmol 120:111–119

VEP Standard (Springer) | local copy [PDF]

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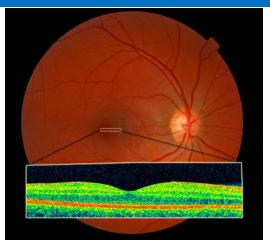
L'AREA MACULARE:
MODELLO DI STUDIO DEI PROCESSI NEURODEGENERATIVI
(POST-NEURITICI ?)



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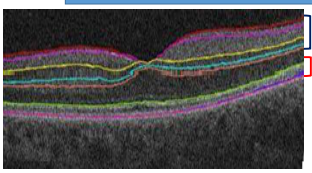
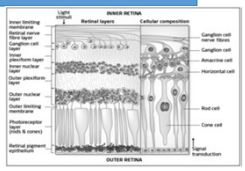
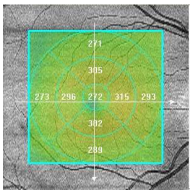
OCT: Macular Thickness and Macular Volume







Thickness

Section	Thick(μm)
Fovea	272
ParaFovea	305
S. Hemisphere	305
I. Hemisphere	304
Tempo	296
Superior	305
Nasal	315
Inferior	302
Perifovea	291
S. Hemisphere	274
I. Hemisphere	289
Tempo	270
Superior	271
Nasal	293
Inferior	289

Volume

Section	Vol(mm³)
Fovea	0.214
ParaFovea	1.914
S. Hemisphere	0.959
I. Hemisphere	0.955
Tempo	0.464
Superior	0.479
Nasal	0.495
Inferior	0.475
Perifovea	3.535
S. Hemisphere	1.720
I. Hemisphere	1.815
Tempo	0.856
Superior	0.850
Nasal	0.920
Inferior	0.909

Vol within: 0.214(1mm) 2.128(3mm) 5.663(6mm)

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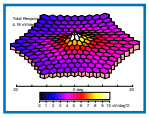
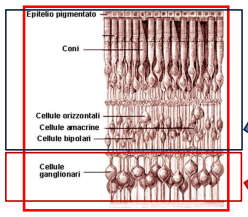
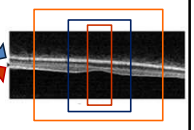
Dove si estende il processo neurodegenerativo?

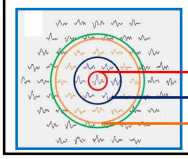
FUNZIONE





MORFOLOGIA: Volume maculare





0-5°
5-10°
10-15°

Vol within 0.064 (1mm) → Area 1
1.010 (3mm) → 3 mm - 1 mm: Area 2
2.610 (6mm) → 6 mm - 3 mm: Area 3
Area 1+2+3

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1) STUDIO MORFOLOGICO

frontiers in Neurology

ORIGINAL RESEARCH

Morphological Outer Retina Findings in Multiple Sclerosis Patients With or Without Optic Neuritis

Lucia Ziccardi[1], Lucilla Barbano[1], Laura Boffa[1], Maria Albanese[2], Andrzej Grzybowski[3,4], Diego Centonze[1,2] and Vincenzo Parisi[1]*

Purpose: To investigate on the morphology of the macular inner (IR) and outer (OR) layers in multiple sclerosis (MS) patients with and without history of optic neuritis (ON), followed by good or poor recovery of best corrected visual acuity (BCVA).

Methods: Thirty-five normal control subjects and 93 relapsing remitting MS patients were enrolled. Of this, 40 MS patients without ON (MS-noON, 40 eyes), 27 with history of ON and good BCVA recovery (MS-ON-G, 27 eyes), and 26 with history of ON and poor BCVA recovery (MS-ON-P, 26 eyes) were studied. Controls and MS patients underwent an extensive ophthalmological examination including spectral-domain optical coherence tomography evaluating in 3 localized macular areas (0–1 mm, Area 1; 1–3 mm, Area 2; 3- 6 mm, Area 3), volumes (MV), and thicknesses (MT) of the whole retina (WR), further segmented in IR and OR. The differences of MV and MT between the groups were tested by ANOVA. In the MS-ON-P group, the correlations between MV and MT and BCVA were evaluated by Pearson's test.

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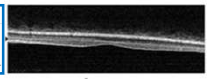
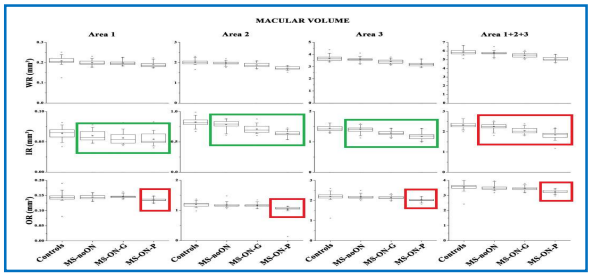
1) STUDIO MORFOLOGICO

frontiers in Neurology

Morphological Outer Retina Findings in Multiple Sclerosis Patients With or Without Optic Neuritis



Volume maculare



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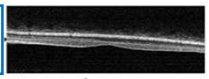
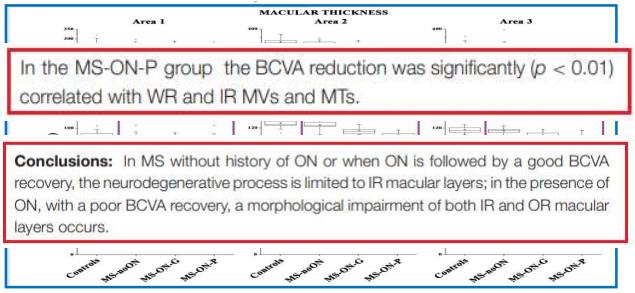
1) STUDIO MORFOLOGICO

Morphological Outer Retina Findings in Multiple Sclerosis Patients With or Without Optic Neuritis



Spessore maculare



In the MS-ON-P group the BCVA reduction was significantly ($p < 0.01$) correlated with WR and IR MVs and MTs.

Conclusions: In MS without history of ON or when ON is followed by a good BCVA recovery, the neurodegenerative process is limited to IR macular layers; in the presence of ON, with a poor BCVA recovery, a morphological impairment of both IR and OR macular layers occurs.

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1) STUDIO FUNZIONALE

THE LANCET Neurology

Retinal layer segmentation in multiple sclerosis: a systematic review and meta-analysis

Functional Assessment of Outer and Middle Macular Layers in Multiple Sclerosis

A limitation to the available studies is the difficulty in obtaining retinal tissue for detailed histological investigations.[9] A potential advantage is the availability of electrophysiological techniques.[10,11] Clinically, it is well recognised that conduction block can be caused by any structural or inflammatory lesion affecting the optic pathways. Typically these lesions are shown by MRI in the brain. Therefore, the application of MRI-based diagnostic criteria for multiple sclerosis[12] to many of the participants included in the present meta-analysis mean that contamination by retinal damage unrelated to optic neuritis is unlikely. The potential to combine OCT with pattern and multifocal electroretinogram, visual-evoked potentials and MRI provide a powerful means to assess structure and function in cohorts of homogeneous pathology.[4,11]

Abstract: The involvement of macular preganglionic elements' function, during the neurodegenerative process of multiple sclerosis (MS), is controversial. In this case-control observational and retrospective study, we assessed multifocal electroretinogram (mfERG) responses from 41 healthy Controls, 41 relapsing-remitting MS patients without optic neuritis (ON) (MS-noON Group), and 47 MS patients with ON: 27 with full recovery of high-contrast best corrected visual acuity (BCVA) (MS-ON-G Group) and 20 with poor recovery (between 0.2 and 1 LogMAR) of BCVA, (MS-ON-P Group).

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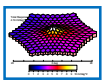
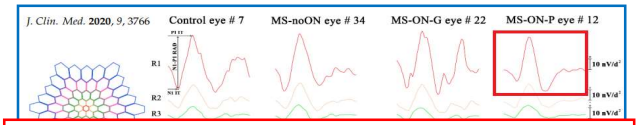
1) STUDIO FUNZIONALE

Functional Assessment of Outer and Middle Macular Layers in Multiple Sclerosis



Funzionalità pre-ganglionare maculare



5. Conclusions

In conclusion, in our study we detected an absence of mfERG abnormalities in MS patients without and with ON followed by full recovery of BCVA. Thus, our results suggest that in MS the function of preganglionic elements located in the O-MR layers is not modified by the occurrence of ON itself. By contrast, the MS neurodegenerative processes could induce a dysfunction of the preganglionic elements of the fovea and the retinal nasal sector after an event of ON followed by permanent impairment of visual acuity (poor recovery of BCVA after ON). This functional impairment was associated, but not correlated, with OR and IR structural changes.

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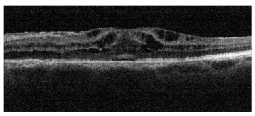
Effetti avversi del Fingolimod a livello oculare

Dai clinical trial FREEDOMS and TRANSFORMS (2010) e' stato riportato come principale effetto collaterale del Fingolimod **l'edema maculare** (Fingolimod-associated macular edema FAME) nello 0,5% dei pazienti trattati nei con Fingolimod 0-5 mg nei **primi 3-4 mesi** dopo inizio del trattamento.

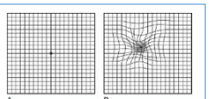
Altri effetti avversi avversi descritti in letteratura sono:

- ➢Emorragia retinica
- ➢Uveite infiammatoria



Sintomatologia

- ➢Riduzione visiva
- ➢Metamorfopsie (visione distorta presente alla valutazione con test di Amsler)



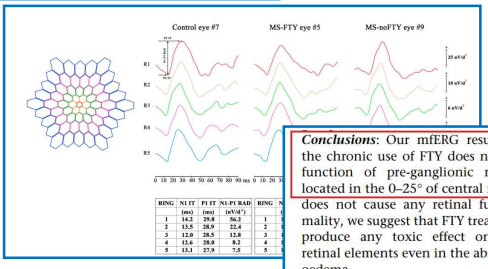
Kappos L, O'Connor P, Radue EW, et al. Long-term effects of fingolimod in multiple sclerosis: the randomized FREEDOMS extension trial. Neurology. 2015;84:1582–91.

Cohen JA, Barkhof F, Comi G, Hartung HP, et al; TRANSFORMS Study Group. Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis. N Engl J Med. 2010;362:402–15.

101

Effetti avversi del Fingolimod a livello oculare

Assessment of Macular Function by Multifocal Electroretinogram in Patients with Multiple Sclerosis Treated with Fingolimod



RING	N1 IT (ms)	P1 IT (ms)	N1-P1 RAD (nV/d²)
1	14.2	29.8	56.2
2	13.5	28.9	22.4
3	12.6	28.5	12.8
4	12.6	28.0	8.2
5	13.1	27.9	7.5

Conclusions: Our mfERG results suggest that the chronic use of FTY does not induce a dysfunction of pre-ganglionic retinal elements located in the 0–25° of central retina. Since FTY does not cause any retinal functional abnormality, we suggest that FTY treatment could not produce any toxic effect on pre-ganglionic retinal elements even in the absence of macular oedema.

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Effetti avversi del Fingolimod a livello oculare

Diagnosi differenziale con Corioretinopatia Sierosa Centrale

Choriocapillaris Integrity in Relapsed Central Serous Chorioretinopathy in a Patient Treated With Fingolimod for Multiple Sclerosis: New Insights From Optical Coherence Tomography Angiography

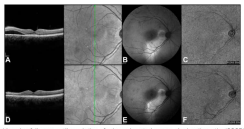


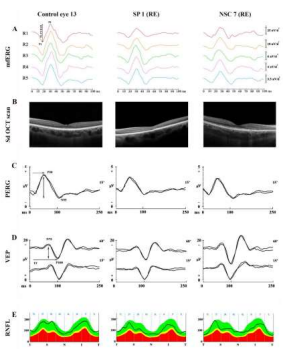
FIG. 2. Multimodal imaging follow-up until resolution of relapsed central serous chorioretinopathy (CSCR) during fingolimod treatment. Three months after the appearance of relapsed CSCR, neuroretinal detachment (NRD) height was reduced (**A**) for partial reabsorption of the subretinal fluid, that resolved completely (**D**) at the 6-month evaluation, as seen in the spectral domain optical coherence tomography (Spectralis HRA; Heidelberg Engineering, Heidelberg, Germany) scans. Short-wave fundus autofluorescence remained stable, showing diffuse hyperautofluorescence corresponding to the NRD with a gravitational track (**B** and **E**). OCTA images (PLEX Elite 9000; Carl Zeiss Meditec Inc, Dublin, CA) confirmed the absence of clear ischemic features at the level of the choriocapillaris (**C** and **F**). OCTA, optical coherence tomography angiography.

Trattamento:
E' raccomandato **sospendere** l'assunzione di Fingolimod in presenza di FAME.
In letteratura tuttavia è descritto beneficio con la seguente terapia:
- Azetazolamide per via os
- Colliri antinfiammatori: es: Nepafenac 0.1% 1 gtt per 3 volte al giorno
- Iniezione intravitreale di triamcinolone

N:B se non sono presenti aree ischemiche alla FAG o OCTA si può non sospendere il Fingolimod e osservare la progressione dell'edema. (Ziccardi L et al. J Neuroophthalmol. 2021 Mar 1;41:e51-e53)

103

Morpho-functional retinal changes: Ataxia



In four eyes of two SP, visual acuity reduction and chromatic abnormalities were observed; in three of them FO changes associated with macular thinning and outer retinal defects were also detected.

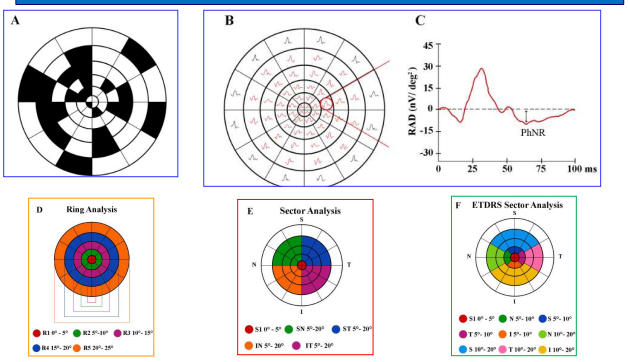
In three NSC eyes, slight FO abnormalities were associated with qualitative macular morphological changes.
By contrast, abnormal mfERG responses (exclusively from foveal and parafoveal areas) were detected in all SP and NSC (18 eyes).

No abnormalities of PERG values, RNFL-T, and VEP responses were found, but in one SP, presenting abnormal papillo-macular bundle neural conduction.

Results from our **SCA-ATXN1** cohort suggest that **a macular dysfunction, detectable by mfERG recordings, may occur in the overt disorder, and unexpectedly in the stage of the disease in which there is still an absence of neurological signs.**
In NSC, an exclusive dysfunction of preganglionic macular elements can be observed, and this is associated with both normal RGCs function and neural conduction along the visual pathways.

104

PhNR Multifocale: stimolo visivo e risposta elettrofunzionale



105

PhNR Multifocale: può riflettere disfunzioni della retina interna di aree retiniche localizzate?

diagnostics MDPI

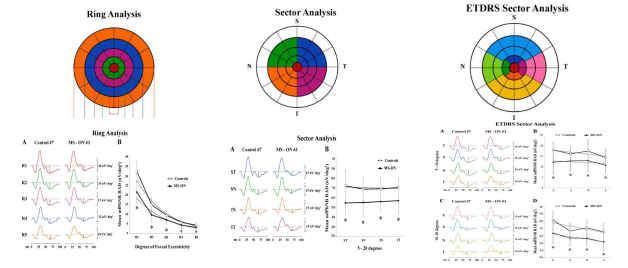
Article

Multifocal electroretinogram Photopic Negative Response: a reliable paradigm to detect localized retinal ganglion cells' impairment in retrobulbar optic neuritis due to multiple sclerosis as a model of retinal neurodegeneration

Lucilla Barbano[1], Lucia Ziccardi[1*], Giulio Antonelli[1], Carolina Gabri Nicoletti[2], Doriana Landi[2], Giorgia Mataluni[2], Benedetto Falsini[3], Girolama Alessandra Marfia[2], Diego Centonze[2,4] and Vincenzo Parisi[1]

106

PhNR Multifocale: può riflettere disfunzioni della retina interna di aree retiniche localizzate?



The mfPhNR RAD values observed in all rings or sectors in MS-ON eyes were significantly reduced ($p<0.01$) with respect to control ones. Our results suggest that mfPhNR recordings may detect localized IRL dysfunction in the pathologic condition of selective RGCs neurodegeneration.

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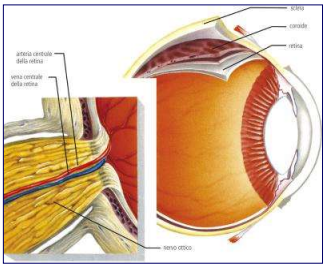
Il nervo Ottico



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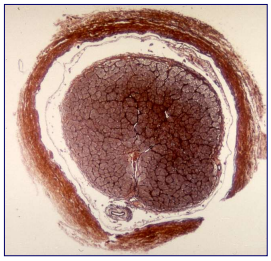
- Il ***nervo ottico*** (II paio dei nervi cranici) non è un nervo nell'accezione abituale del termine, ma, morfologicamente e funzionalmente, una proiezione diencefalica.
- **Costituito dall'insieme degli assoni delle cellule gangliari della retina,** si estende da questa al chiasma ottico rivestito dalle sue guaine, dura madre, aracnoide e pia madre, che sono in continuità con quelle meningee.



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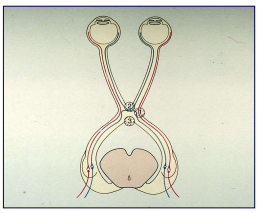
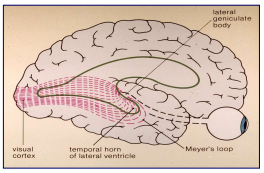
LE VIE OTTICHE POST-CHIASMATICHE





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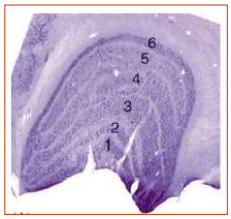
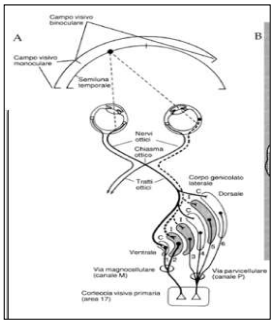
Il Nucleo Genicolato laterale

- Sistema magno/parvo cellulare

Diviso in 6 strati: ipsi e controlaterale



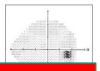


111

Fisiologia della via nervosa visiva

1) Rilascio di neurotrasmettitore

Normale percezione visiva



Plasticità cerebrale:

1) Capacità di formare sinapsi
2)Stabilizzazione sinaptica a lungo termine
3) Il periodo critico

Fattori neurotrofici (NGF, BDNF…)

visiva

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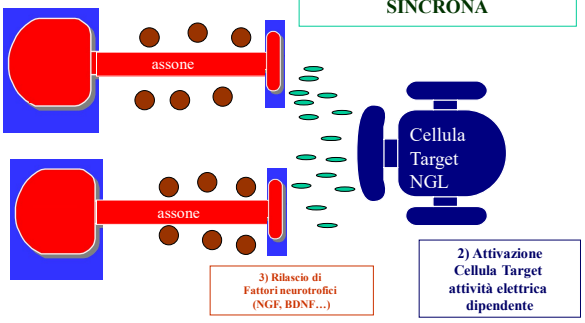
Nucleo Genicolato laterale e visione binoculare

1) Rilascio di neurotrasmettitore SINCRONA



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Nucleo Genicolato laterale e deficit della visione binoculare

1) Rilascio di neurotrasmettitore ASINCRONO

Modificazioni della plasticità cerebrale:

1) anomala formazione di sinapsi
2)Anomala stabilizzazione sinaptica a lungo termine

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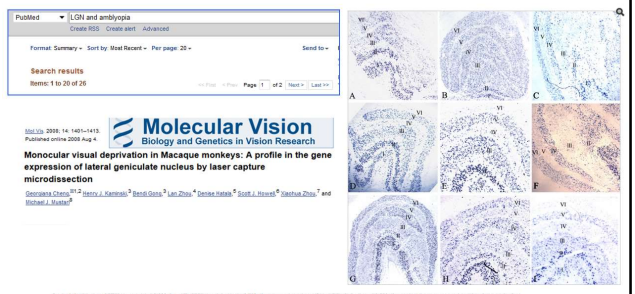
NGL e Ampliopia



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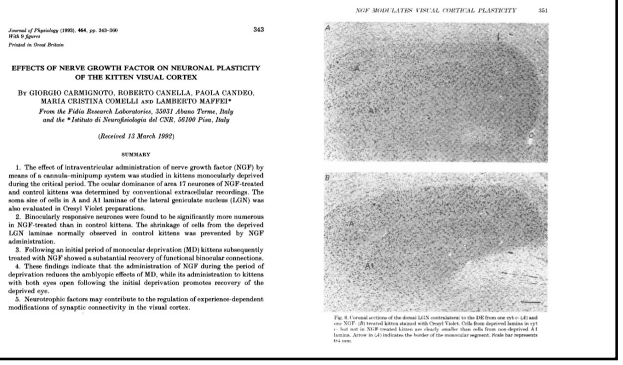
Plasticità cerebrale: ruolo del NGF



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Plasticità cerebrale: ruolo dell'ambiente

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Corteccia deficit della visione binoculare

1) Rilascio di neurotrasmettitore ASINCRONO

DEFICIT VISIONE BINOCULARE

Amblyopia (AM) is a disorder of the visual system, characterized by reduced visual function in one eye, that has been estimated to affect 1% to 5% of the population.[1] The disorder is associated with strabismus, anisometropia, or a form of deprivation early in life.[2–6]
(*Invest Ophthalmol Vis Sci.* 2010;51:5041–5048)

Deprivazione o strabismo

assone

con attività elettrica asincrona

degenerazione degli strati relativi all'occhio deprivato

3) Minor Rilascio di Fattori neurotrofici all'occhio deprivato(NGF, BDNF…) "Competizione per il fattore neurotrofico"

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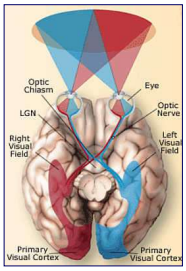
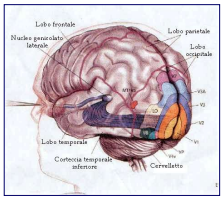
La Corteccia Visiva





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La corteccia visiva

- Aree occipitali 17, 18, 19
- Rappresentazione retinotopica
- Cellule semplici, complesse, ipercomplesse
- Le colonne di dominanza oculare

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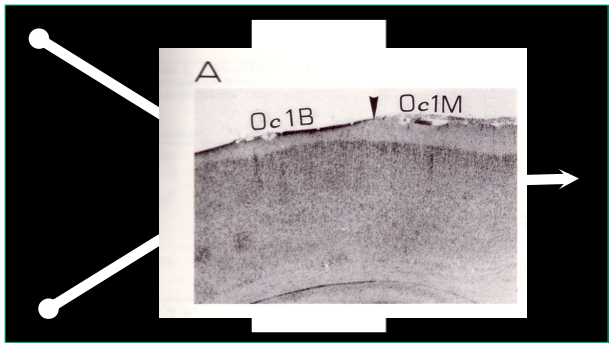
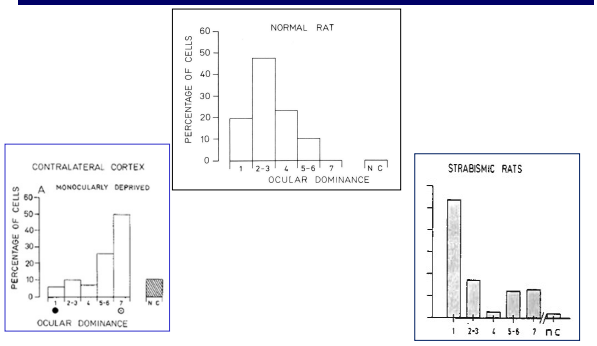
Cellule semplici, complesse ipercomplesse



121

Colonne di Dominanza Oculare



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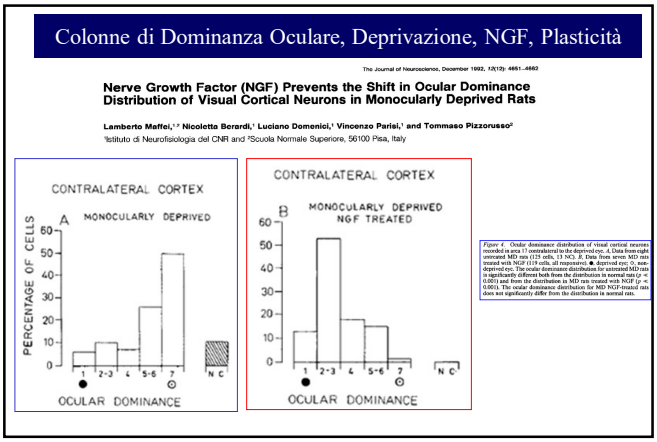
Colonne di Dominanza Oculare, Deprivazione, NGF, Plasticità



Nerve Growth Factor (NGF) Prevents the Shift in Ocular Dominance Distribution of Visual Cortical Neurons in Monocularly Deprived Rats

Lamberto Maffei,[1,2] Nicoletta Berardi,[1] Luciano Domenici,[1] Vincenzo Parisi,[1] and Tommaso Pizzorusso[2]

[1]Istituto di Neurofisiologia del CNR and [2]Scuola Normale Superiore, 56100 Pisa, Italy

CONTRALATERAL CORTEX
A MONOCULARLY DEPRIVED
B MONOCULARLY DEPRIVED NGF TREATED
PERCENTAGE OF CELLS
OCULAR DOMINANCE

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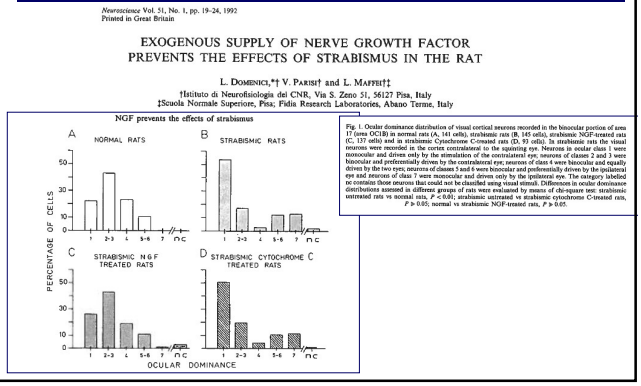
Colonne di Dominanza Oculare, Strabismo, NGF, Plasticità



Neuroscience Vol. 51, No. 1, pp. 19-24, 1992
Printed in Great Britain

EXOGENOUS SUPPLY OF NERVE GROWTH FACTOR PREVENTS THE EFFECTS OF STRABISMUS IN THE RAT

L. Domenici,*† V. Parisi† and L. Maffei†‡
†Istituto di Neurofisiologia del CNR, Via S. Zeno 51, 56127 Pisa, Italy
‡Scuola Normale Superiore, Pisa; Fidia Research Laboratories, Abano Terme, Italy

NGF prevents the effects of strabismus
A NORMAL RATS
B STRABISMIC RATS
C STRABISMIC NGF TREATED RATS
D STRABISMIC CYTOCHROME C TREATED RATS
PERCENTAGE OF CELLS
OCULAR DOMINANCE

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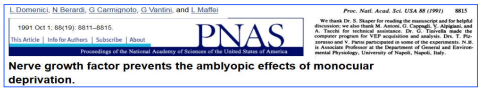
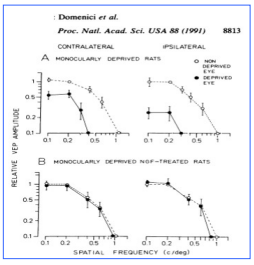
Acuità visiva, Deprivazione, NGF, Plasticità



L. Domenici, N. Berardi, G. Carmignoto, G. Vantini, and L. Maffei

PNAS

Nerve growth factor prevents the amblyopic effects of monocular deprivation.



Supplementazione di NGF (Riattivazione Plasticità)

↓

Attivazione del NGL

↓

Riduzione deficit visivo

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Corteccia deficit della visione binoculare

1) Rilascio di neurotrasmettitore ASINCRONO

Miglioramento binocularità e AV

assone

> RILASCIO NEUROTRAS

Cellula Target NGL

Attività sincrona a livello della corteccia

Deprivazione o strabismo

assone

Attività biolettrica meno Asincrona nel NGL

SUPPLEMETAZIONE DI NGF

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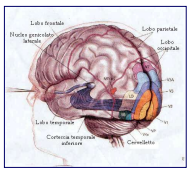
3) ESPLORAZIONE ELETTOFUNZIONALE DELLA DELLE VIE OTTICHE:



I Potenziali Evocati Visivi

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I POTENZIALI EVOCATI VISIVI (PEV)

Variazioni dei potenziali bioelettrici della corteccia occipitale evocati da stimoli visivi.

Manifestazione di raffinati e complessi eventi neurosensoriali legati a fenomeni di traduzione e trasmissione dell'impulso nervoso lungo le vie visive, cioè dai fotorecettori retinici fino alla corteccia cerebrale occipitale.

INTERNATIONAL SOCIETY FOR CLINICAL ELECTROPHYSIOLOGY OF VISION

Doc Ophthalmol (2016) 133:1–9

ISCEV standard for clinical visual evoked potentials: (2016 update) J. Vernon Odom · Michael Bach · Mitchell Brigell · Graham E. Holder · Daphne L. McCulloch · Atsushi Mizota · Alma Patrizia Tormene ·

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PEV: METODOLOGIA

1) PREPARAZIONE DEL PAZIENTE

2) POSIZIONAMENTO ELETTRODI

3) LO STIMOLO VISIVO

4) L'ACQUISIZIONE DEL SEGNALE

5) LA TRACCIA

6) IL REFERTO

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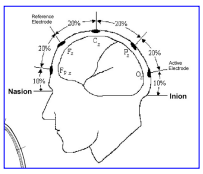
1) PREPARAZIONE DEL PAZIENTE

2) Posizionamento degli elettrodi

Ophthalmology Volume 126, Number 7, July 2019

Electrophysiologic Examinations.

Subjects were seated in a semi-dark, acoustically isolated room, in front of the display and surrounded by a uniform field of luminance of 5 candelas per meter squared. Before the experiment, each subject was adapted to the ambient room light for 10 minutes, with a pupil diameter of approximately 5 mm. No mydriatic or miotic drugs were used. Stimulation was monocular after occlusion of the fellow eye.



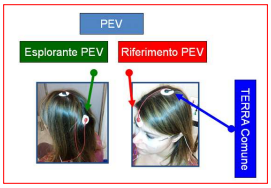


Table 1 ISCEV standard for VEP assessment

	Electrode montage (international 10/20 channel system)		Filters (−3 dB)		
	Active	Common reference	Low freq	High freq	Sweeps averaged
Pattern stimulation	Oz	Fz	≤1	≥100	≥50

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3) LO STIMOLO VISIVO

A) Frequenza spaziale | B) Contrasto | C) Frequenza Temporale

Table 1 ISCEV standard for VEP assessment

Stimulus type	Field size (minimum)	Presentation	Stimulus	Mean luminance (cd · m^{-2})	Michaelson contrast (%)	Presentation rate
Pattern reversal	15°	Monocular	Check widths: 1° (0.8°–1.2°); 0.25° (0.2°–0.3°)	50 (40–60)	≥80	2 (1.8–2.2) reversals/s

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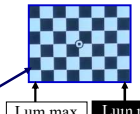
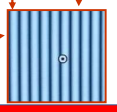
3) LO STIMOLO VISIVO
B) Contrasto: Lmax-Lmin/Lmin+Lmax x 100

Per cui se abbiamo un elemento bianco con massima luminanza (100) ed un elemento nero con minima luminanza (0) il contrasto è del 100%.

In realtà, l'elemento bianco non ha mai una luminanza 100, per cui viene sempre utilizzato un contrasto reale del 70-80 %.



Il contrasto viene definito ad "onda quadra" se il passaggio dalla luminanza dell'elemento bianco a quello nero (sia esso barra o scacchi) avviene in maniera netta, mentre viene definito ad "onda sinusoidale" se il passaggio dalla luminanza dell'elemento bianco a quello nero (sia esso barra o scacchi) avviene in maniera graduale.



L'uso dei gratings è molto importante nei casi in cui non si conoscenza della corretta AV

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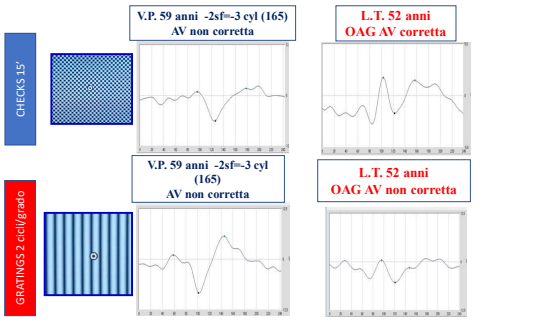
3) Risposta e stimolo visivo: fonti di errore legati al difetto refrettivo



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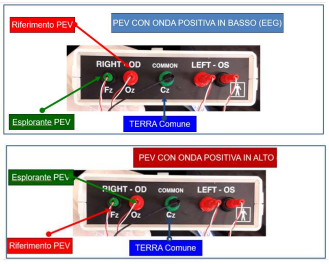
4) ACQUISIZIONE DEL SEGNALE
a) Posizionamento degli elettrodi al pre-amplificatore

Resistenza interelettrodica: < 3 KHoms



Traccia con polarità positiva in basso/alto:

MOLTO IMPORTANTE PER EVITARE ERRORI DI VISUALIZZAZIONE DEI PICCHI

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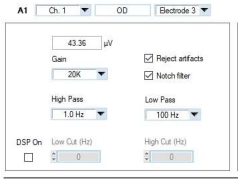
4) L'ACQUISIZIONE DEL SEGNALE
b) Guadagno e filtraggio

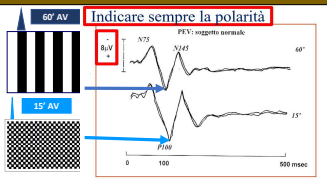


Visual Evoked Potential Recordings.

The bioelectric signal was amplified (gain, 20 000), filtered (band pass, 1–100 Hz), and averaged (200 events free from artifacts were averaged for every trial) by Analysis time was 250 milliseconds.

135

5) LA TRACCIA
FUNZIONE DI FREQUENZA SPAZIALE, CONTRASTO, FREQUENZA TEMPORALE

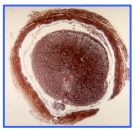


Valutazione funzione degli assoni di grosso calibro

Valutazione funzione del fascio papillo-maculare

Basse frequenze spaziali (60'): risposta più "rapida" → assoni con più rapida velocità di conduzione → assoni di grosso calibro

Alte frequenze spaziali (15'): risposta + ritardata → assoni con più lenta velocità di conduzione → assoni di piccolo calibro



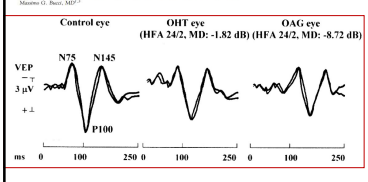
136

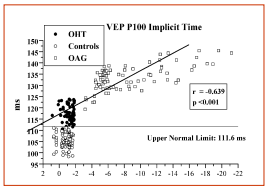
5) LA TRACCIA
FUNZIONE DI FREQUENZA SPAZIALE, CONTRASTO, FREQUENZA TEMPORALE

Stimolo checks 15'; FT 2 Hz; Contrasto 70 %

Clinical Ability of Pattern Electroretinograms and Visual Evoked Potentials in Detecting Visual Dysfunction in Ocular Hypertension and Glaucoma

Specificità : 100%
Sensibilità: OAG 100%; OHT 85.3%

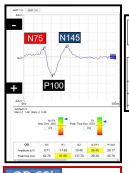


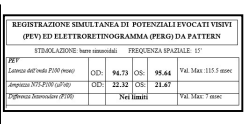


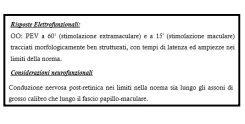
137

6) Il REFERTO

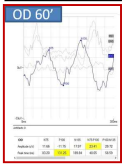
PEV NORMALE

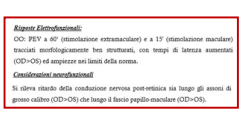






PEV ALTERATO

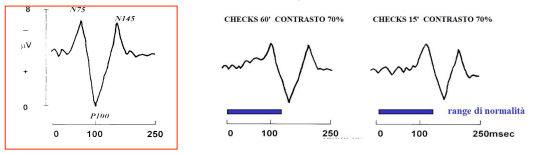




138

6) APPLICAZIONI CLINICHE
PEV con latenze aumentate ed ampiezze ridotte:

Normale **Patologico**



Disfunzione retinica,
del nervo ottico, del chiasma,
del tratto ottico…….ecc?

139

7) APPLICAZIONI CLINICHE
PEV NELLA SCLEROSI MULTIPLA

2013-2017 Optical coherence tomography (OCT) in the diagnosis and the monitoring of the neurodegenerative process in multiple sclerosis

Patients

	MS Patients	MS patients with NORB*	MS patients without NORB	Controls
Number	261	108	153	69
Age (ys)	37.5±5.4	39.5±7.2	33.8±4.2	38.2±8.6

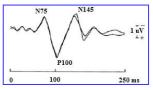
*At list 12 month elapsed from the NORB, VA 20/20 on 96 eyes; Kupfer C. *Arch Ophthalmol* 1983; 70:256-260

Italian MOH: Ricerca Finalizzata 2012,
Morphofunctional visual pathways evaluation in multiple sclerosis: possible identificationf neurodegenerative bio-markers
Principal investigator: Vincenzo Parisi — Istitution: IRCCS Fondazione G.B. Bietti
Unit 1: Diego Centonze — Istitution: Tor Vergata University
Unit 2: Marco Bozzali — Istitution: IRCCS Santa Lucia

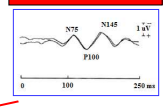
140

RESULTS — VEP 60' vs OCT OVERALL

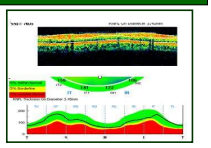
Normal VEP
Normal Neural Conduction



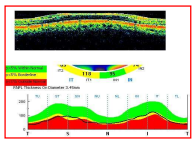
Delayed and reduced VEP
Impaired Neural Conduction



Normal NFLT Overall

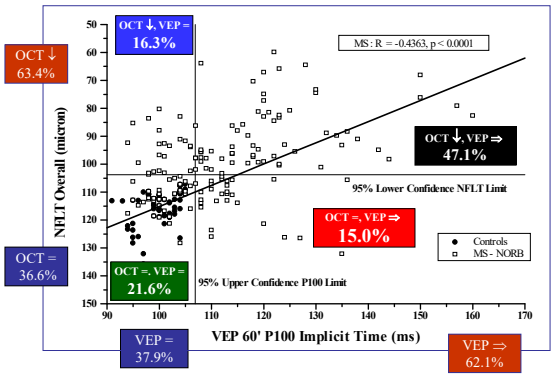


Reduced NFLT Overall



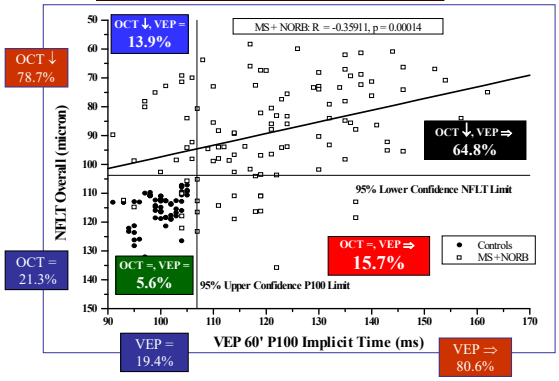
141

MS WITHOUT NORB (N=153)



142

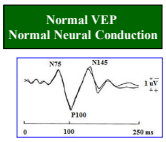
MS WITH NORB (N=108)



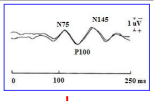
143

RESULTS — VEP 15' vs OCT TEMPORAL

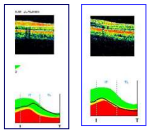
Normal VEP
Normal Neural Conduction



Delayed and reduced VEP
Impaired Neural Conduction

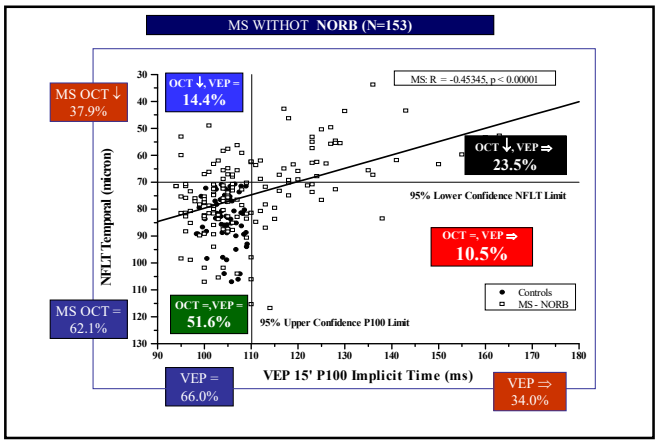


Normal NFLT Temporal

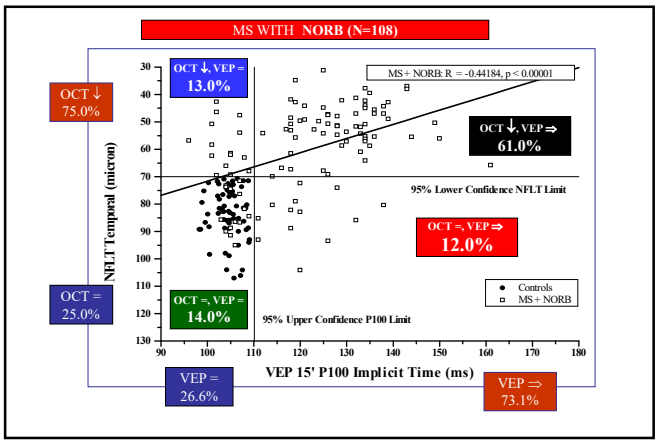


Reduced NFLT Temporal

144



145



146

Commenti OCT vs VEP in MS

- OCT Overall Abnormal on
63% MS without NORB and **78%** with NORB

- OCT Temporal Abnormal on
38% MS without NORB and **75%** with NORB

Author	Patients and Method	Sensitivity, %	Specificity, %
Naismith et al., 2009	OCT in 65 subjects with at least 1 clinical ON episode at least 6 months prior.	60	66

147

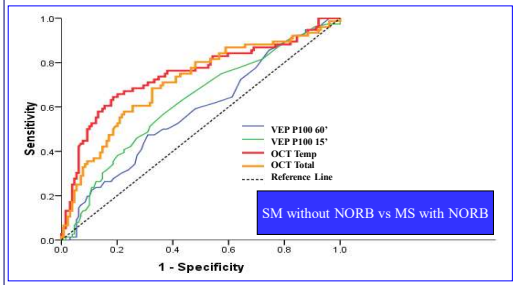
Commenti OCT vs VEP in MS

- VEP Abnormal on
62% MS without NORB and **80%** with NORB

Author	Patients and Method	Sensitivity, %	Specificity, %
Matthews et al., 1982	VEP in 84 patients in whom the diagnosis of MS was under consideration.	53.6	87.8
Hume & Waxman, 1988	VEP 14 patients with definite MS, 222 patients suspected of having MS, 26 patients with isolated optic neuritis.	83	78.5
Lee et al., 1991	VEP in 200 patients with suspected multiple sclerosis.	60.7	80.5
Filippini et al., 1994	VEP in 82 patients in whom MS was suspected but diagnosis of clinically definite multiple sclerosis was not possible entered the study prospectively	25	63
Frederiksen & Petrera, 1999	90 untreated patients at the onset of optic neuritis (ON) and after 2, 4, 12, and 52 weeks	89	65
Naismith et al., 2009	VEP in 65 subjects with at least 1 clinical ON episode at least 6 months prior.	81	76
Lascano et al., 2009	A 256-channel VEP was recorded in 44 healthy subjects and in 26 patients with MS.	72	100

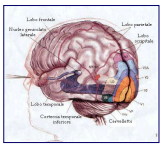
148

Accuracy



149

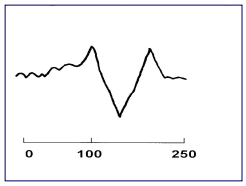
4) ESPLORAZIONE ELETTOFUNZIONALE DELLA DELLE VIE OTTICHE POST-RETINICHE



Registrazione simultanea di PERG+ERG

150

PEV: latenze aumentate/ampiezze ridotte:



Diagnosi differenziale tra:

- Patologie retiniche -Patologie postretiniche

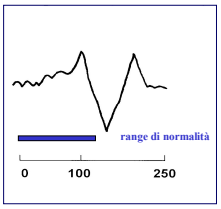
E' necessario associare:

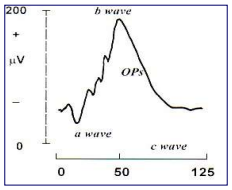
PEV + ERG PEV + PERG

151

PEV+ ERG

PEV Alterato + ERG Normale





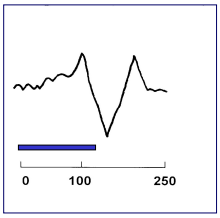
patologia post-fotorecettoriale:

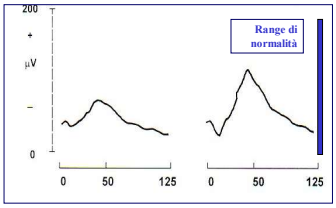
cellule ganglionari, nervo ottico, vie ottiche

152

PEV+ ERG

PEV Alterato + ERG Alterato

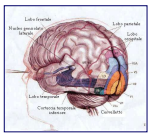




Patologia fotorecettoriale che determina un ritardo della conduzione nervosa lungo le vie ottiche

153

5) ESPLORAZIONE ELETTOFUNZIONALE DELLA DELLE VIE OTTICHE POST-RETINICHE



Registrazione simultanea di PERG+PEV

154

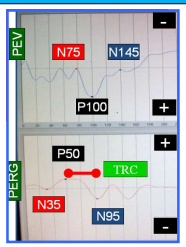
PEV+ PERG: il Tempo Retino-Corticale

PEV P100 Tempo Implicito:
Risposta bioelettrica corteccia visiva

PERG P50 Tempo Implicito ed Ampiezza:
risposta bioelettrica delle cellule ganglionari

Differenza PEV P100- PERG P50 Tempi Impliciti è indicato come "Tempo Retinocorticale (TRC)"
(indice elettrofisiologico della conduzione nervosa tra le cellule ganglionari e corteccia visiva)

Celesia et al, IOVS, 1985.

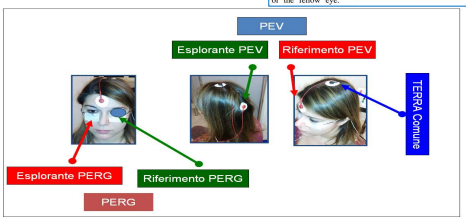


155

1) PREPARAZIONE DEL PAZIENTE

2) Posizionamento degli elettrodi

Ophthalmology Volume 126, Number 7, July 2019
Electrophysiologic Examinations.
Subjects were seated in a semi-dark, acoustically isolated room, in front of the display and surrounded by a uniform field of luminance of 5 candelas per meter squared. Before the experiment, each subject was adapted to the ambient room light for 10 minutes, with a pupil diameter of approximately 5 mm. No mydriatic or miotic drugs were used. Stimulation was monocular after occlusion of the fellow eye.



Stimolazione monoculare

156

1) PREPARAZIONE DEL PAZIENTE

2) Posizionamento degli elettrodi

157

3) LO STIMOLO VISIVO

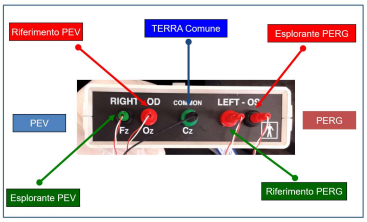
A) Frequenza spaziale | B) Contrasto | C) Frequenza Temporale

Table 1 ISCEV standard for VEP assessment

Stimulus type	Field size (minimum)	Presentation	Stimulus	Mean luminance (cd · m^{-2})	Michaelson contrast (%)	Presentation rate
Pattern reversal	15°	Monocular	Check widths: 1° (0.8°–1.2°); 0.25° (0.2°–0.3°)	50 (40–60)	≥80	2 (1.8–2.2) reversals/s

158

4) ACQUISIZIONE DEL SEGNALE
a) Posizionamento degli elettrodi al pre-amplificatore



Traccia con polarità positiva in basso per il PEV

Traccia con polarità positiva in alto per il PERG

MOLTO IMPORTANTE PER EVITARE ERRORI DI VISUALIZZAZIONE DEI PICCHI

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POSSIBILI COMBINAZIONE DI RISPOSTE BIOELETTRICHE PERG+PEV

5) LA TRACCIA
FUNZIONE DI FREQUENZA SPAZIALE, CONTRASTO, FREQUENZA TEMPORALE

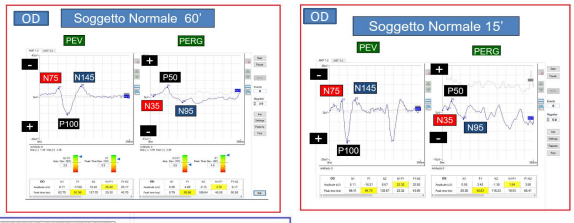
6) Il REFERTO

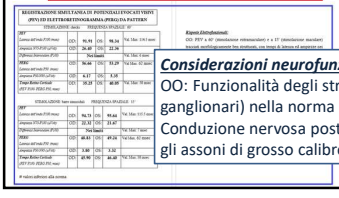
160

POSSIBILI COMBINAZIONE DI RISPOSTE BIOELETTRICHE PERG+PEV

161

1 PEV e PERG con impliciti ed ampiezze normali, TRC nella norma





Considerazioni neurofunzionali

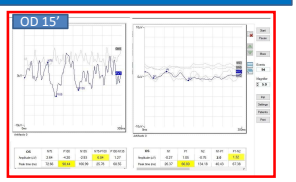
OO: Funzionalità degli strati interni retinici (cellule e fibre ganglionari) nella norma

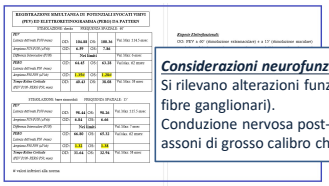
Conduzione nervosa post-retinica nei limiti nella norma sia lungo gli assoni di grosso calibro che lungo gli assoni di piccolo calibro

162

2

60’ e 15’ PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti aumentati ed ampiezze ridotte ed TRC normali





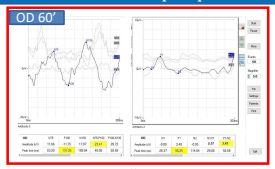
Considerazioni neurofunzionali

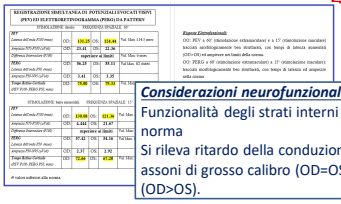
Si rilevano alterazioni funzionali degli strati interni retinici (cellule e fibre ganglionari).
Conduzione nervosa post-retinica nei limiti nella norma sia lungo gli assoni di grosso calibro che lungo gli assoni di piccolo calibro

163

3

60’ e 15’ PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti ed ampiezze normali, TRC aumentati





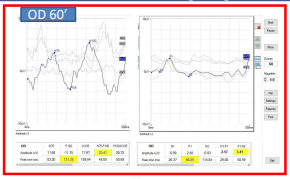
Considerazioni neurofunzionali

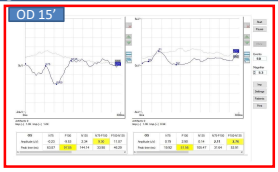
Funzionalità degli strati interni retinici (cellule e fibre ganglionari) nella norma
Si rileva ritardo della conduzione nervosa post-retinica sia lungo gli assoni di grosso calibro (OD=OS) che lungo gli assoni di piccolo calibro (OD>OS).

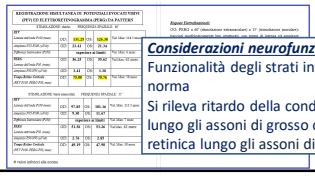
164

4

1. 60’ PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti ed ampiezze normali, TRC aumentati
2. 15’ PEV P100 tempi impliciti ed ampiezze normali, PERG tempi impliciti ed ampiezze normali, TRC normali







Considerazioni neurofunzionali

Funzionalità degli strati interni retinici (cellule e fibre ganglionari) nella norma
Si rileva ritardo della conduzione nervosa post-retinica esclusivamente lungo gli assoni di grosso calibro (OD=OS); conduzione nervosa post-retinica lungo gli assoni di piccolo calibro nella norma.

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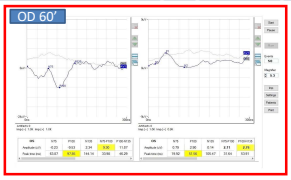
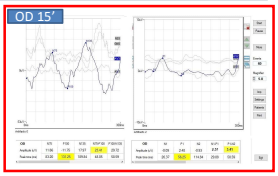
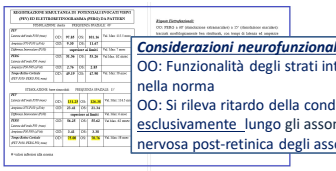
5

1. 60’ PEV P100 tempi impliciti ed ampiezze normali, PERG tempi impliciti ed ampiezze normali, TRC normali
2. 15’ PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti ed ampiezze normali, TRC aumentati







Considerazioni neurofunzionali

OO: Funzionalità degli strati interni retinici (cellule e fibre ganglionari) nella norma
OO: Si rileva ritardo della conduzione nervosa post-retinica esclusivamente lungo gli assoni di piccolo calibro (OD=OS); conduzione nervosa post-retinica degli assoni di grosso calibro limiti della norma.

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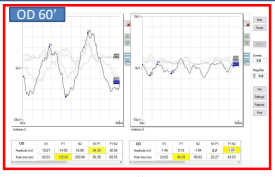
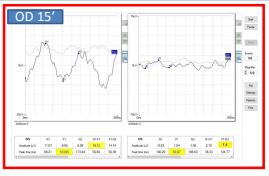
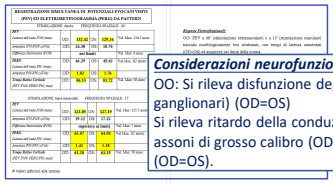
6

60’ e 15’ PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti aumentati ed ampiezze ridotte, TRC aumentati







Considerazioni neurofunzionali

OO: Si rileva disfunzione degli strati interni retinici (cellule e fibre ganglionari) (OD=OS)
Si rileva ritardo della conduzione nervosa post-retinica sia lungo gli assoni di grosso calibro (OD=OS) che lungo gli assoni di piccolo calibro (OD=OS).

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Applicazioni cliniche

1) **Ipertensione oculare**
2) **Glaucoma**
3) **Sclerosi multipla con NORB**
4) **Sclerosi Multipla no NORB**
5) **Ambliopia**
6) **NOIA**
7) **LHON**

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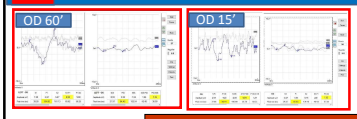
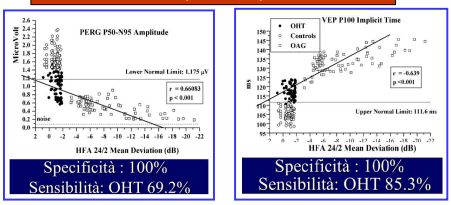
1 IPERTENSIONE OCULARE:



Considerazioni neurofunzionali
Si rilevano alterazioni funzionali degli strati interni retinici (cellule e fibre ganglionari).
Conduzione nervosa post-retinica nei limiti nella norma sia lungo gli assoni di grosso calibro che lungo gli assoni di piccolo calibro

Stimolo checks 15'; FT 2 Hz; Contrasto 70 %



Specificità : 100%
Sensibilità: OHT 69.2%

Specificità : 100%
Sensibilità: OHT 85.3%

PERG RIDOTTO, VEP RITARDATO E TRC NELLA NORMA

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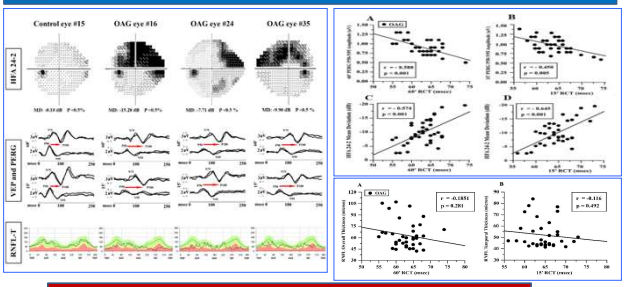
2 GLAUCOMA



PERG RIDOTTO, VEP RITARDATO TRC: AUMENTATO IN PROPORZIONE ALLA RIDUZIONE DEL PERG, CORRELATO CON LA MD, NON CORRELATO CON RNFL

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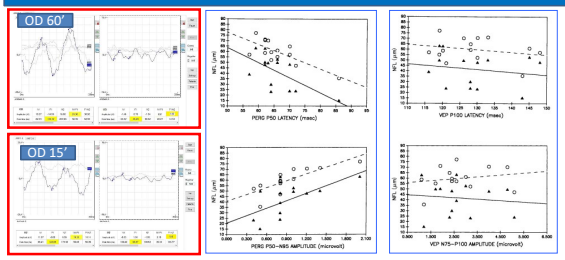
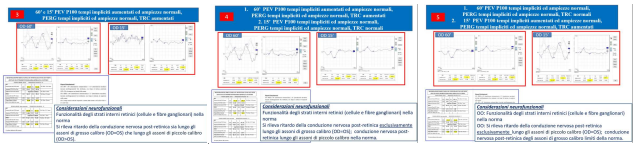
3 SCLEROSI MULTIPLA CON NORB



PERG RIDOTTO, VEP RITARDATO TRC AUMENTATO NON PROPORZIONE ALLA RIDUZIONE DEL PERG, NON CORRELATO CON RNFL

171

4 SCLEROSI MULTIPLA SENZA NORB



PERG NORMALE, VEP RITARDATO E TRC AUMENTATO

60 o 15' di stimolazione PERG RIDOTTO, VEP RITARDATO TRC: AUMENTATO NON PROPORZIONE ALLA RIDUZIONE DEL PERG, NON CORRELATO CON RNFL

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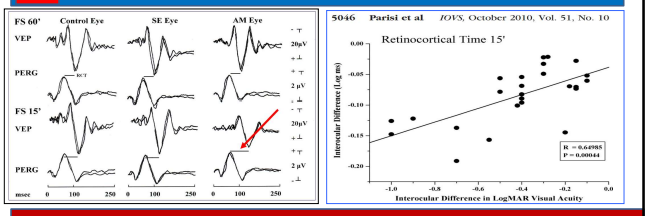
5 AMBLIOPIA



60' di stimolazione PERG VEP E TRC NELLA NORMA

15' di stimolazione PERG: NELLA NORMA, VEP: RITARDATO, TRC AUMENTATO

LA DIFFERENZA INTEROCULARE DEL TRC CORRELATA CON LA DIFFERENZA INTEROCULARE AV

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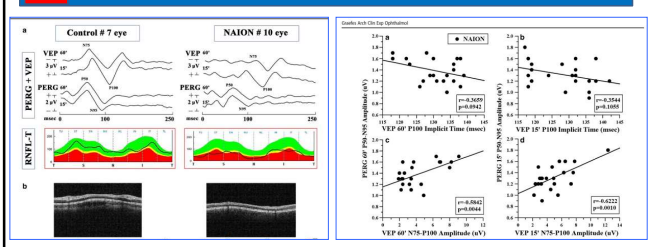
6 NOIA



PERG RIDOTTO, VEP RITARDATO

TRC: AUMENTATO IN PROPORZIONE ALLA RIDUZIONE DEL PERG, CORRELATO CON LA MD, CORRELATO CON RNFL

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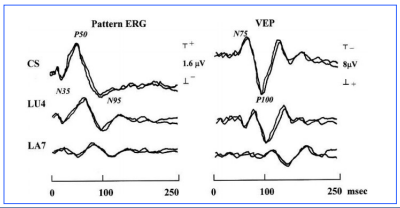
7 NEURITE OTTICA DI LEBER E CARRIER



Simolazione a 60' e 15'
PERG RIDOTTO sia negli AFFETTI che nei CARRIER
VEP: RITARDATO negli AFFETTI, normale nei CARRIER
TRC: AUMENTATO negli AFFETTI, normale nei CARRIER

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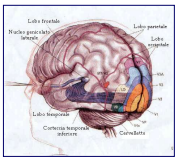
5) ESPLORAZIONE ELETTOFUNZIONALE DELLA DELLE VIE OTTICHE:



I PEV Multifocali

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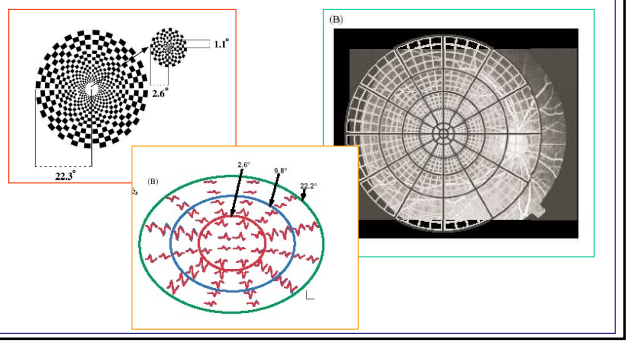
VEP Multifocale: stimolo visivo e risposta elettrofunzionale



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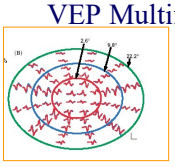
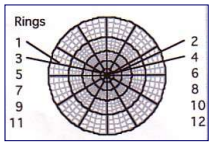
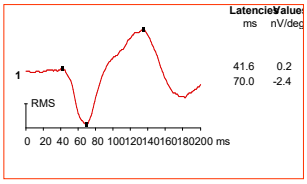
VEP Multifocale Normale

Rings

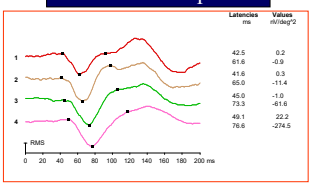




Absolute Response



Normalized Response



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Applicazioni Cliniche

- Retinite Pigmentosa
- Maculopatie
- Glaucoma
- Neuriti Ottiche

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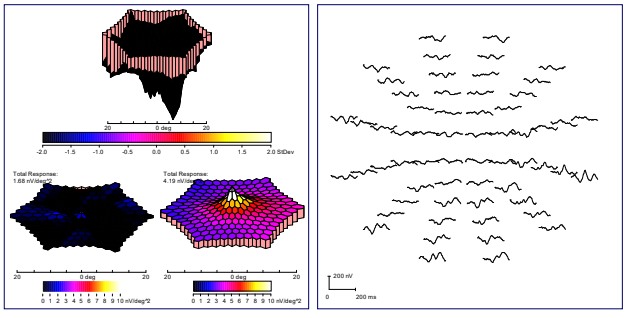
Subject: V. C. 45 years, myopic CNV, RE

Mf-ERG | Mf-VEP



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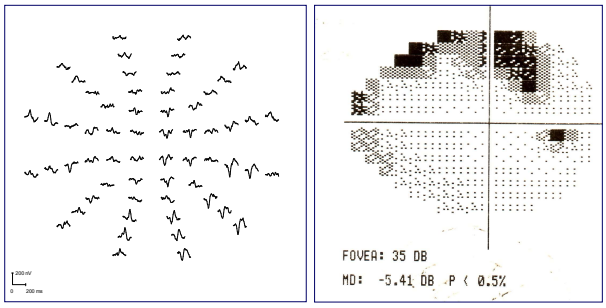
Subject C.A.: 56 years, Glaucoma

Mf-VEP | Visual Field



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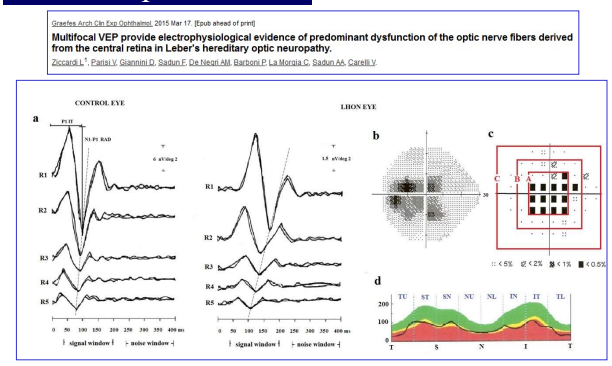
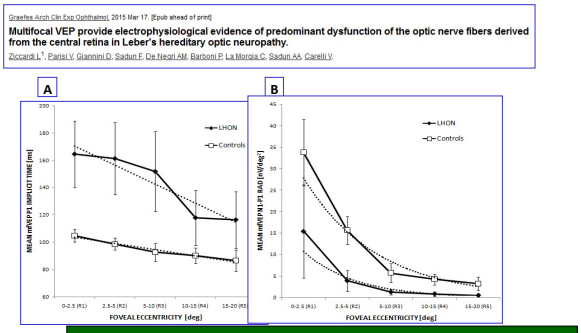
Leber's Optic Neuritis



182

Leber's Optic Neuritis



Greatest delay in the papillo-macular bundle

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Quanto viene influenzata la risposta corticale da eventuali deficit localizzati retinici?

Può esistere un meccanismo di plasticità o di rimodellamento cerebrale tale da incrementare la funzionalità retinica?

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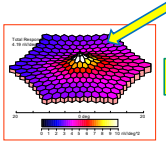
Quanto viene influenzata la risposta corticale da eventuali deficit localizzati retinici?

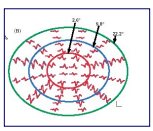
Metodo

RISPOSTE MULTIFOCALI



mfERG

mfVEP



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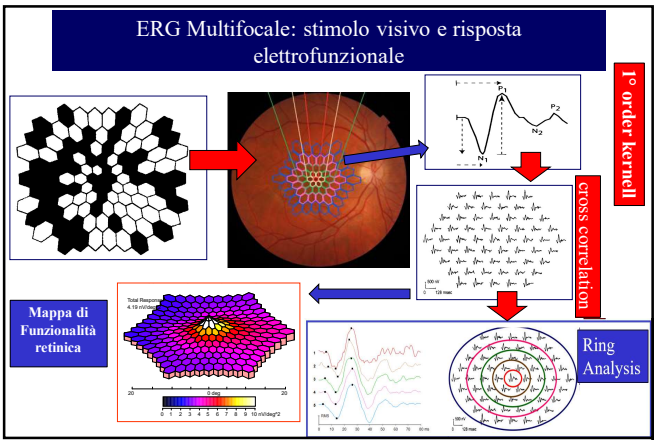
ERG Multifocale: stimolo visivo e risposta elettrofunzionale



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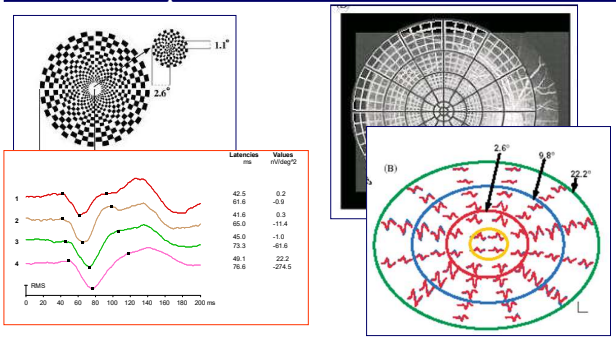
VEP Multifocale: stimolo visivo e risposta elettrofunzionale



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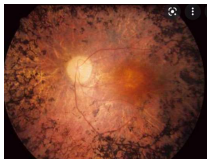
Modello umano di deficit funzionale retinico: retinite pigmentosa



malattia genetica dell'occhio caratterizzata dalla degenerazione degli elementi sensoriali (fotorecettori) e nervosi (cellule ganglionari della retina), con conseguente perdita del campo visivo

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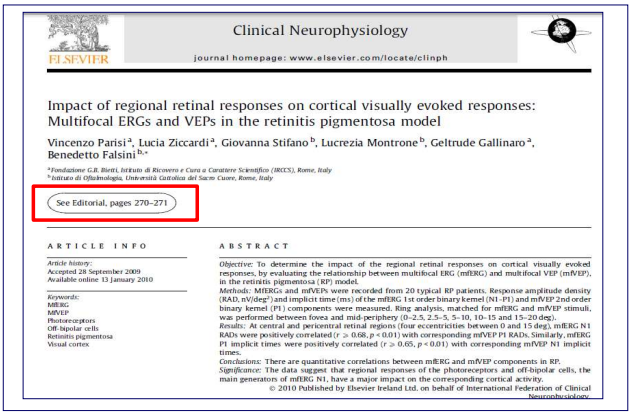
Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Impact of regional retinal responses on cortical visually evoked responses: Multifocal ERGs and VEPs in the retinitis pigmentosa model

Vincenzo Parisi [a], Lucia Ziccardi [a], Giovanna Stifano [b], Lucrezia Montrone [b], Geltrude Gallinaro [a], Benedetto Falsini [b,*]

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[b] Istituto di Oftalmologia, Università Cattolica del Sacro Cuore, Rome, Italy

See Editorial, pages 270–271

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MfVEP
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Retinitis pigmentosa
Visual cortex

ABSTRACT

Objective: To determine the impact of the regional retinal responses on cortical visually evoked responses, by evaluating the relationship between multifocal ERG (mfERG) and multifocal VEP (mfVEP), in the retinitis pigmentosa (RP) model.
Methods: MfERGs and mfVEPs were recorded from 20 typical RP patients. Response amplitude density (RAD, nV/deg²) and implicit time (ms) of the mfERG 1st order binary kernel (N1–P1) and mfVEP 2nd order binary kernel (P1) components were measured. Ring analysis, matched for mfERG and mfVEP stimuli, was performed between fovea and mid-periphery (0–2.5, 2.5–5, 5–10, 10–15 and 15–20 deg).
Results: At central and pericentral retinal regions (four eccentricities between 0 and 15 deg), mfERG N1 RADs were positively correlated ($r \geq 0.68$, $p < 0.01$) with corresponding mfVEP P1 RADs. Similarly, mfERG P1 implicit times were positively correlated ($r \geq 0.65$, $p < 0.01$) with corresponding mfVEP N1 implicit times.
Conclusions: There are quantitative correlations between mfERG and mfVEP components in RP.
Significance: The data suggest that regional responses of the photoreceptors and off-bipolar cells, the main generators of mfERG N1, have a major impact on the corresponding cortical activity.

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Patients

N = 20

Mean age: 36 yrs, range: 15-56

Median visual acuity: 20/25, range: 20/30 – 20/20

Goldmann visual field (V/4e target): mean field (major diameter): 45°, range 30-55

Fundus: typical RP appearance

Ganzfeld ERG (ISCEV standard)

Rod-mediated response	Non-recordable
Maximal response	Severely reduced amplitude (< 35% of the normal mean)
Single-flash cone-mediated response	Severely reduced amplitude (< 40% of the normal mean) & delayed implicit time (3-8 ms slower than the normal mean)
Flicker response	Severely reduced amplitude (< 40% of the normal mean)

Inheritance Mode	N
Dominant	2
Recessive	3
Isolated	12
X-linked	3

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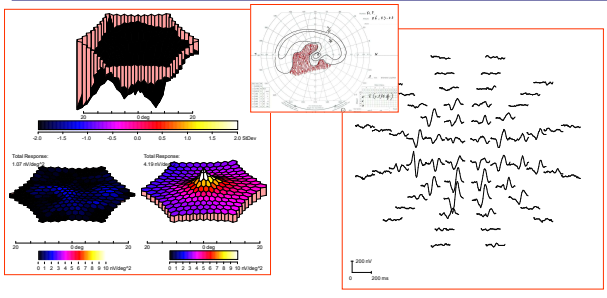
Soggetto B.A.: 34 anni, RP, OS

mfERG Campo Visivo mfVEP



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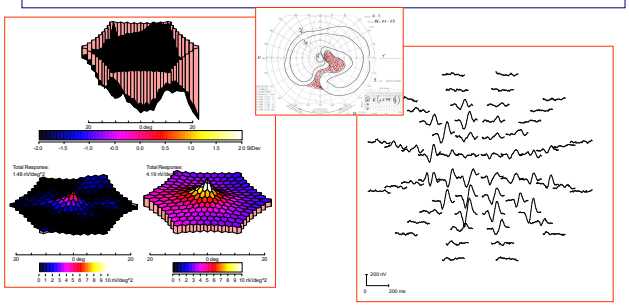
Soggetto B.A.: 34 anni, RP, OD

mfERG Campo Visivo mfVEP



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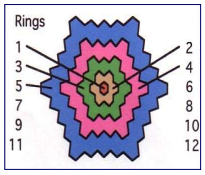
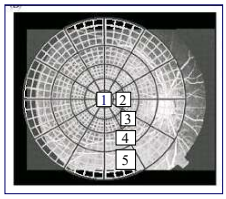
CORRELAZIONI TRA AREE RETINICHE E LE RELATIVE PROIEZIONI CORTICALI:

5 LIVELLI DI ECCENTRICITA'

	MERG	MVEP
R1:0-2.5 gradi		
R2:2.5-5 gradi		
R3: 5-10 gradi		
R4:10-15 gradi		
R5:15-20 gradi		

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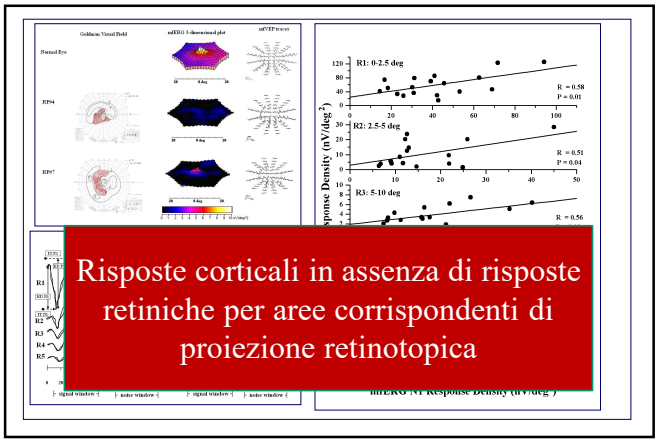

Risposte corticali in assenza di risposte retiniche per aree corrispondenti di proiezione retinotopica

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ELSEVIER

Editorial

Degeneration/re-organization coupling in retinitis pigmentosa

This groundbreaking approach allowed for the first time the investigators to show the presence of a tight correlation between local retinal function (mfERG response) and its cortical projection as probed with the mfVEPs. Specifically it was shown that a negative component of the mfERG first-order Kernel has a major impact on the mfVEP signal characteristics. The more severe the local retinal functional loss, the more profound the functional re-organization of cortical activity, suggesting that the cortical circuitry may undergo substantial remodelling following primary photoreceptor loss. The results warrant further studies to shed more light on the time course of degeneration/re-organization coupling in retinitis pigmentosa.

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MODELLO RP:

possibilità di rilevare aree retiniche "ancora" funzionanti e di quantificarne la funzionalità residua in maniera oggettiva.

Correlazioni tra ERG e VEP multifocali:

CORTECCIA VISIVA E' IN GRADO DI RIMODELLARE LE INFORMAZIONI BIOELETTRICHE PROVENIENTI DALLA RETINA

196

forma, colore, dimensioni, contrasto,

posizione nello spazio,…

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CONCLUSIONI

Gli esami elettrofunzionali

- PEV a 60' e 15': Permettono di differenziare una disfunzione degli assoni di grosso calibro (PEV a 60') da quella degli assoni di piccolo calibro (PEV a 15')
- PERG +PEV=TRC: Permettono di ottenere un indice della conduzione nervosa lungo le vie ottiche post-retiniche rilevando:

a) Disfunzioni delle RGC primarie o dovute a fenomeni di degerazione retrograda post-neuritica

b) Disfunzioni delle vie ottiche post-retiniche

sia nella componente degli assoni di grosso calibro

che nella componente degli assoni di piccolo calibro

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Neural conduction along post-retinal visual pathways in glaucoma
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