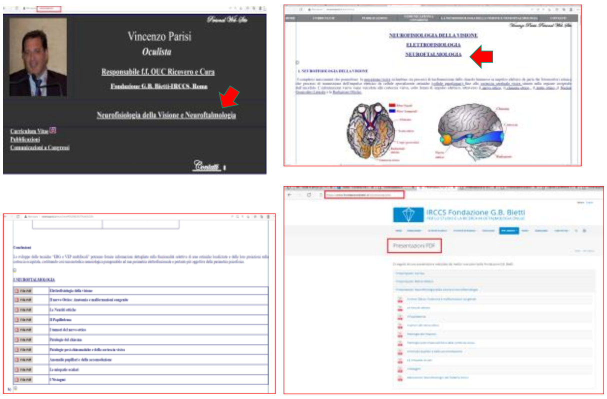
Neurofisiologia della visione

Vincenzo Parisi

IRCCS Fondazione G.B. Bietti, Roma



Vincenzo Parisi
Oculista
Responsabile f.f. OUC Ricovero e Cura
Fondazione G.B. Bietti-IRCCS, Roma
Neurofisiologia della Visione e Neuroftalmologia
Curriculum Vitae
Pubblicazioni
Comunicazioni a Congressi
Contatti

NEUROFISIOLOGIA DELLA VISIONE
ELETTROFISIOLOGIA
NEUROFTALMOLOGIA

3 NEUROFTALMOLOGIA

- Elettrofisiologia della visione
- Il nervo Ottico: Anatomia e malformazioni congenite
- Le Neuriti ottiche
- Il Papilledema
- I tumori del nervo ottico
- Patologie del chiasma
- Patologie post-chiasmatiche e della corteccia visiva
- Anomalie pupillari e della accomodazione
- Le miopatie oculari
- I Nistagmi

IRCCS Fondazione G.B. Bietti

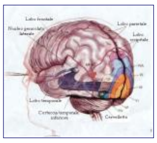
Presentazioni PDF

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

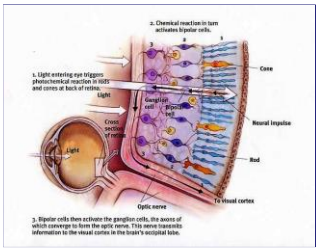
La Visione

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.


Lobo frontale
Nucleo genicolato laterale
Lobo parietale
Lobo occipitale
Lobo temporale
Corteccia temporale inferiore
Cervelletto

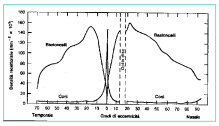
La retina


2. Chemical reaction in turn activates bipolar cells.
3
2
1
Cone
1. Light entering eye triggers photochemical reaction in rods and cones at back of retina.
Light
Ganglion cell
Bipolar cell
Neural impulse
Cross section of retina
Light
Rod
To visual cortex
Optic nerve
3. Bipolar cells then activate the ganglion cells, the axons of which converge to form the optic nerve. This nerve transmits information to the visual cortex in the brain's occipital lobe.

Cellule Fotorecettoriali:

Bastoncelli:

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



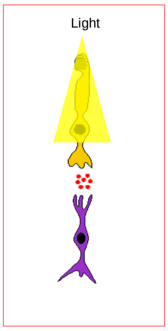
Coni:

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

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



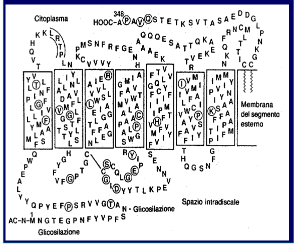
La rodopsina:

- 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)

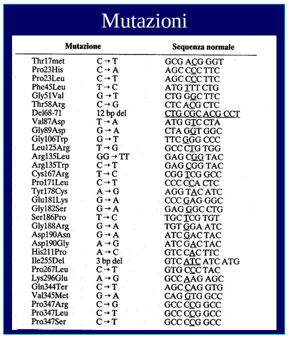
→ Retinite Pigmentosa

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

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	CTC 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

La Retinite Pigmentosa

- Degenerazione retinica progressiva
- Malattia genetica:

- 19 % forma autosomica dominante (cromosomi 3, 6, 8)

- 19 % forma autosomica recessiva

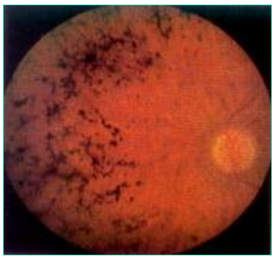
- 8 % X-linked (braccio corto cromosoma X)

- 46 % forma isolata in un membro della famiglia*

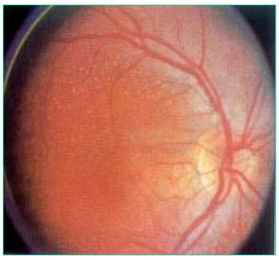
- Differenti forme in relazione al tipo e alla localizzazione del fotorecettore colpito
- Associata a diverse patologie (Sindrome di…..)

* Bunker et al. , Am J Ophthalmol1984

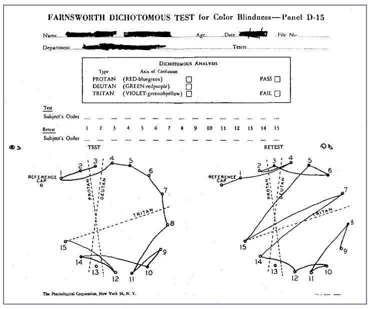
Retinite Pigmentosa



Fondo Albipuntato



Senso Cromatico



FARNSWORTH DICHOTOMOUS TEST for Color Blindness—Panel D-15

Name [redacted] [redacted] Age ...... Date [redacted] File No ......

Department [redacted] Tester ......

DICHOTOMOUS ANALYSIS

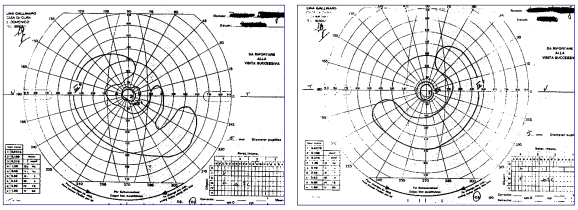
Type	Axis of Confusion		
PROTAN	(RED-bluegreen)	☐	PASS ☐
DEUTAN	(GREEN-redpurple)	☐	
TRITAN	(VIOLET-greenishyellow)	☐	FAIL ☐

Test
Subject's Order

Retest 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Subject's Order

The Psychological Corporation, New York 36, N. Y.

Campo Visivo



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)

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

Decorso della RP

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

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)

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

---

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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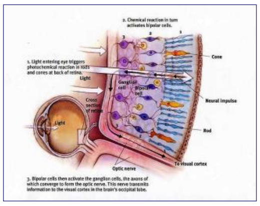
ESPLORAZIONE ELETTOFUNZIONALE DELLA RETINA: L'ERG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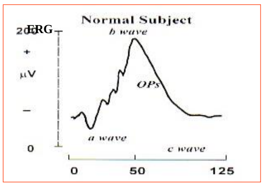
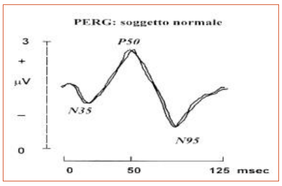
1. Light entering eye triggers photochemical reaction in rods and cones at back of retina.
Light
Ganglion cell
Bipolar cell
Cross section of retina
Cone
Neural impulse
Rod
Light
Optic nerve
To visual cortex
3. Bipolar cells then activate the ganglion cells, the axons of which converge to form the optic nerve. This nerve transmits information to the visual cortex in the brain's occipital lobe.

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





Generatori ERG

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.

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.

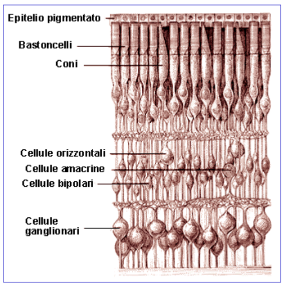
L'ERG da flash rimaneva invariato.

Viswanathan et al. *IOVS* 2000;

Experimentally-induced glaucoma or TTX treatment in monkey eyes:

- Reduction of PERG amplitude

Generatori Elettroretinogramma



⇒ Onda a ERG da Flash

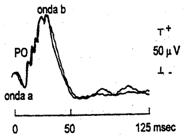
} Onda b ERG da Flash
Potenziali Oscillatori

⇒ ERG da Pattern/PhNR

ERG da Flash:

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

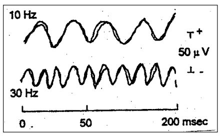
- onda a:
- onda b
- onda c:



FT 1 Hz, 10 J: Potenziali Oscillatori

FT 10 e 20 Hz: Flicker, bastoncelli

FT 30 Hz: Flicker, coni



ERG da Flash:

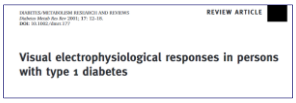
aumento del tempo di latenza onda a e b, riduzione di ampiezza dell'onda a e b, PO in:

- 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

ERG e Diabete


DIABETES/METABOLISM RESEARCH AND REVIEWS
Diabetes Metab Res Rev 2001; 17: 12–18.
DOI: 10.1002/dmrr.177

REVIEW ARTICLE

Visual electrophysiological responses in persons with type 1 diabetes

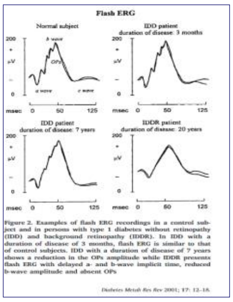


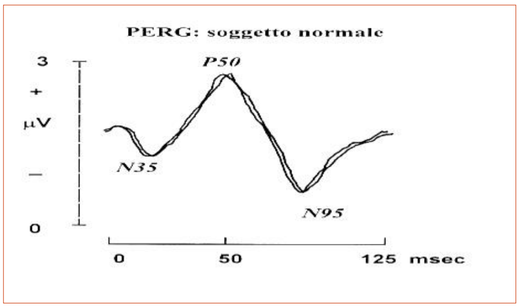
Figure 2. Examples of flash ERG recordings in a control subject and in persons with type 1 diabetes without retinopathy (IDD) and background retinopathy (IDDR). In IDD with a duration of disease of 3 months, flash ERG is similar to that of control subjects. IDD with a duration of disease of 7 years shows a reduction in the OPs amplitude while IDDR presents flash ERG with delayed a- and b-wave implicit time, reduced b-wave amplitude and absent OPs

Diabetes Metab Res Rev 2001; 17: 12–18.

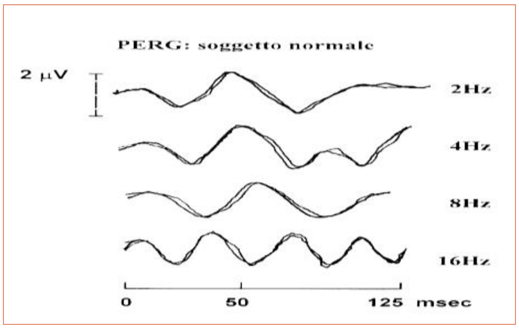
ERG da Pattern

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

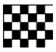
ERG da Pattern



ERG da Pattern



ERG da Pattern: Lo stimolo visivo

- BARRE (gratings)
- SCACCHI (checkerboard) 

se ne valuta:

- **frequenza spaziale** (angolo sotteso dal singolo elemento: minuti di arco o cicli/grado)
- **contrasto** (rapporto di luminanza tra gli elementi del pattern)
- **frequenza temporale** (tempo di inversione)

PERG: Elettrodi

ERG jet

Henkes

DTL

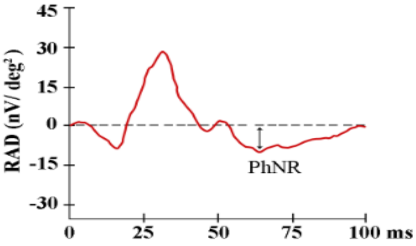
Skin

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

PhNR



Anomalie retiniche nelle patologie neurodegenerative

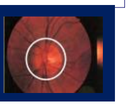
1) Glaucoma
2) Multiple Slerosis
3) Alzheimer’s Disease
4) CADASIL
5) Eredo-atassie

Correlazioni morfo-funzionali: PERG, mfERG vs OCT

La valutazione
“in vivo” delle
fibre nervose retiniche

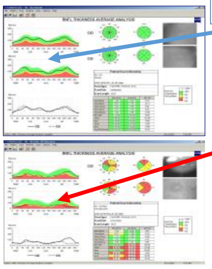
Morfologia: Optical Coherence Tomography (OCT)

- 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.

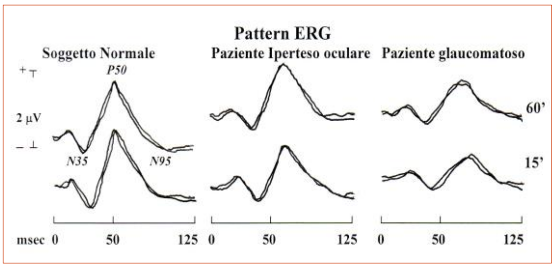


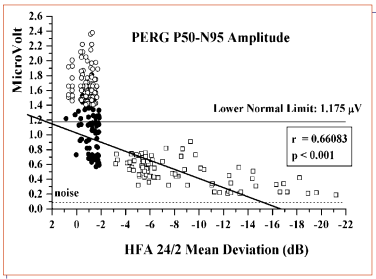
- Circular scans
- diameter: 3.4 mm

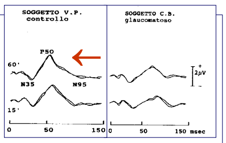
Normative Database



PERG nei pazienti con Ipertensione Oculari o Glaucomatosi





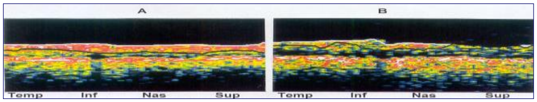


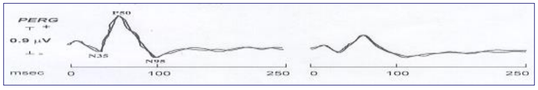
Media± 1SD:
Controlli: 1.695±0.26 µV
OHT: 1.039±0.28 µV
POAG: 0.506±0.17 µV
P<0.01 (Anova)

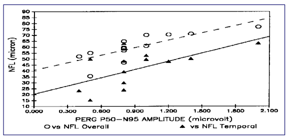
Specificità : 100%
Sensibilità: OAG 100%; OHT 69.2%

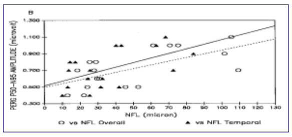
Parisi et al. Ophthalmology 2006

Correlazione tra PERG e spessore del NFL in OHT e POAG







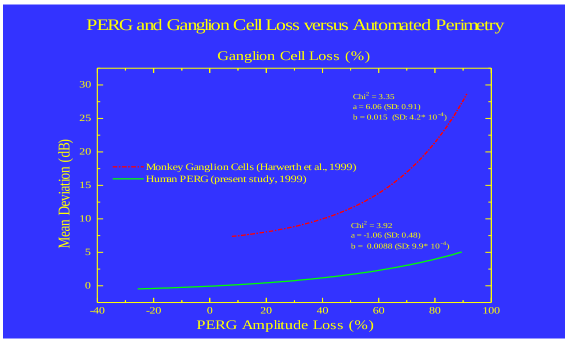


OHT: r = -0.518, P<0.001

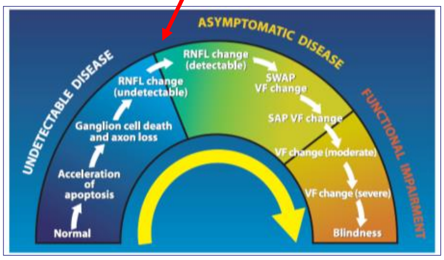
POAG: r = -0.847, P<0.001

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

PERG and Ganglion Cell loss versus Automated Perimetry

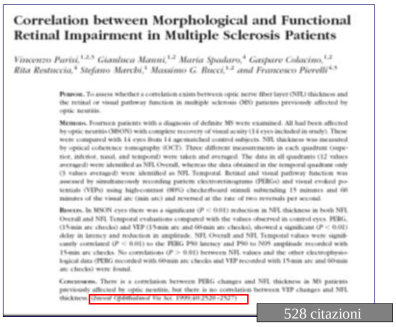


PERG



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,[4] 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

Morpho-functional Correlations: Multiple Sclerosis

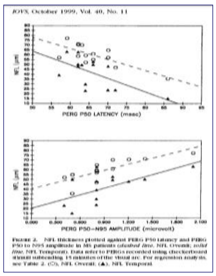


FIGURE 2. NFL thickness plotted against PERG P50 latency and PERG P50 to N95 amplitude in MS patients (*dashed line*, NFL Overall; *solid line*, NFL Temporal). Data refer to PERGs recorded using checkerboard stimuli subtending 15 minutes of the visual arc. For regression analysis, see Table 2. (○), NFL Overall; (▲), NFL Temporal.

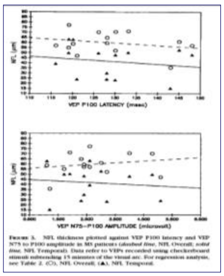
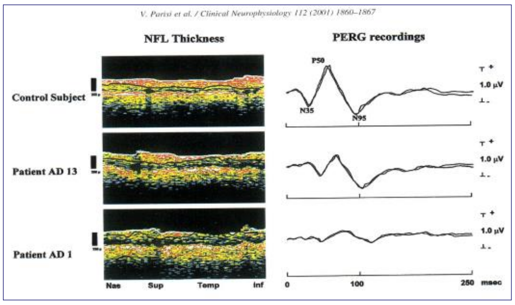


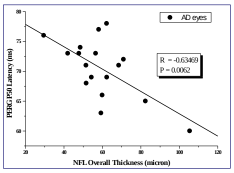
FIGURE 3. NFL thickness plotted against VEP P100 latency and VEP N75 to P100 amplitude in MS patients (*dashed line*, NFL Overall; *solid line*, NFL Temporal). Data refer to VEPs recorded using checkerboard stimuli subtending 15 minutes of the visual arc. For regression analysis, see Table 2. (○), NFL Overall; (▲), NFL Temporal.

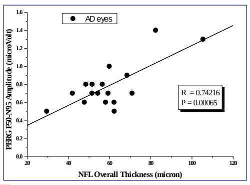
The RNFL thickness was also reduced in MS eyes without NORB!

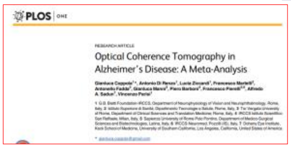
Morpho-functional Correlations: Alzheimer’s Disease



Morpho-functional Correlations: Alzheimer’s Disease







PLOS | ONE

RESEARCH ARTICLE

Optical Coherence Tomography in Alzheimer’s Disease: A Meta-Analysis

Gianluca Coppola[1]*, Antonio Di Renzo[1], Lucia Ziccardi[1], Francesco Martelli[2], Antonello Fadda[2], Gianluca Manni[3], Piero Barboni[4], Francesco Pierelli[5,6], Alfredo A. Sadun[7], Vincenzo Parisi[1]

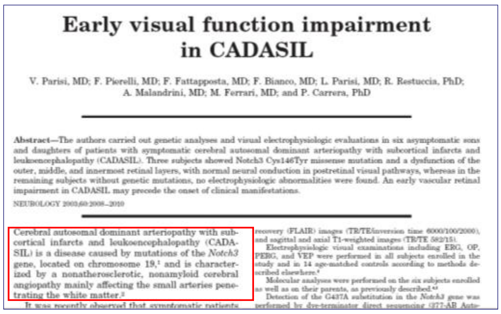
1 G.B. Bietti Foundation-IRCCS, Department of Neurophysiology of Vision and Neurophthalmology, Rome, Italy, 2 Istituto Superiore di Sanità, Dipartimento Tecnologie e Salute, Rome, Italy, 3 Tor Vergata University of Rome, Department of Clinical Sciences and Translation Medicine, Rome, Italy, 4 IRCCS Istituto Scientifico San Raffaele, Milan, Italy, 5 Sapienza University of Rome Polo Pontino, Department of Medico-Surgical Sciences and Biotechnologies, Latina, Italy, 6 IRCCS Neuromed, Pozzilli (IS), Italy, 7 Doheny Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, California, United States of America

* gianluca.coppola@gmail.com

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.

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]

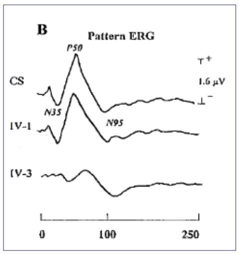
recovery (FLAIR) images (TR/TE/inversion time 6000/100/2000), and sagittal and axial T1-weighted images (TR/TE 582/15).

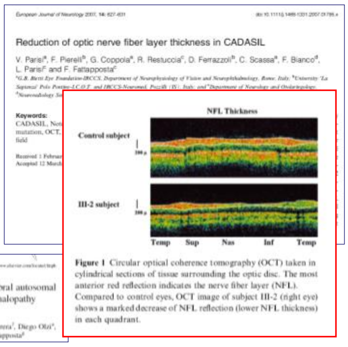
Electrophysiologic visual examinations including ERG, OP, PERG, and VEP were performed in all subjects enrolled in the study and in 14 age-matched controls according to methods described elsewhere.[4]

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

Morpho-functional retinal changes: CADASIL





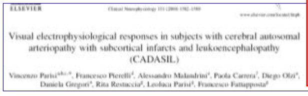
European Journal of Neurology 2007, 14: 627–631

Reduction of optic nerve fiber layer thickness in CADASIL

V. Parisi, F. Pierelli, G. Coppola, R. Restuccia, D. Ferrazzoli, C. Scassa, F. Bianco, L. Parisi and F. Fattapposta

Keywords: CADASIL, Notch3 mutation, OCT, visual field

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.

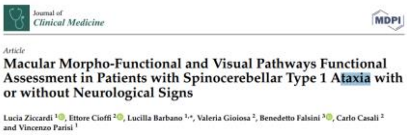


ELSEVIER

Visual electrophysiological responses in subjects with cerebral autosomal arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)

Vincenzo Parisi, Francesco Pierelli, Alessandro Malandrini, Paola Carrera, Diego Olzi, Daniela Gregori, Rita Restuccia, Leoluca Parisi, Francesco Fattapposta

Morpho-functional retinal changes: Ataxia



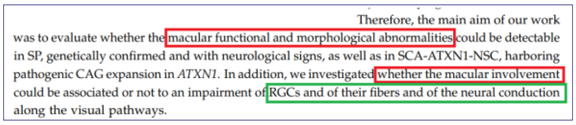
Journal of *Clinical Medicine*

MDPI

Article

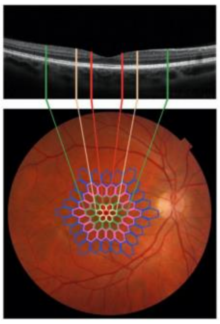
Macular Morpho-Functional and Visual Pathways Functional Assessment in Patients with Spinocerebellar Type 1 Ataxia with or without Neurological Signs

Lucia Ziccardi [1], Ettore Cioffi [2], Lucilla Barbano [1,*], Valeria Gioiosa [2], Benedetto Falsini [3], Carlo Casali [2] and Vincenzo Parisi [1]



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.

Morpho-functional retinal changes: Ataxia

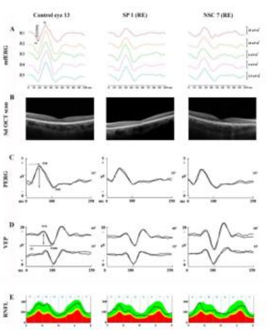


OCT scans

mfERG visual stimuli

⬡ R1: 0°–2.5°
⬡ R2: 2.5°–5°
⬡ R3: 5°–10°
⬡ R4: 10°–15°
⬡ R5: 15°–20°

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.

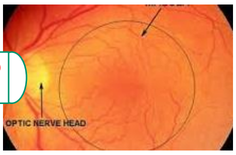
Results from our **SCA-ATXN1** cohort suggest that **a macular dysfunction, detectable by mfERG recordings, may occur in the overt disorder, and unexpectedly in the stage of the disease in which there is still an absence of neurological signs.**
In NSC, an exclusive dysfunction of preganglionic macular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

ESPLORAZIONE ELETTOFUNZIONALE DI AREE LOCALIZZATE RETINICHE:

- ERG multifocale

- PhNR multifocale

Problema principale:



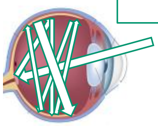
Spot luminoso sul nervo ottico registriamo ERG?

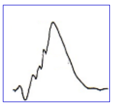
NO non si sono fotorecetori

…..invece…. REGISTRIAMO ERG

Bulbo oculare: Cupola riflettente

stray-light





Problema principale:

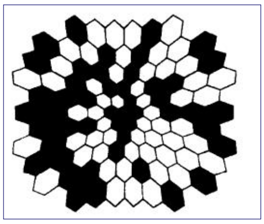
Asher (J.P. 1965) e Boynton e Riggs (J.P. 1951) dimostrarono che un piccolo spot luminoso, se orientato sul disco ottico, produceva un ERG la cui ampiezza era eguale o lievemente superiore rispetto a quello ottenibile quando lo stesso spot era orientato sulla fovea.

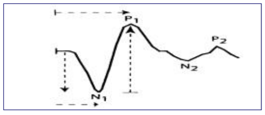
SI PUO’ REGISTRARE UNA RISPOSTA BIOLETTRICA DA AREE RETINICHE LOCALIZZATE?

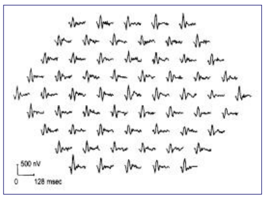
- Risolvere i problemi legati al fenomeno della stray-light

Impiegare uno stimolo test circondato da un background luminoso adattante.

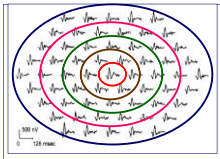
ERG Multifocale: stimolo visivo e risposta elettrofunzionale



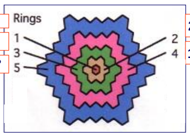




ERG MULTIFOCALE NORMALE



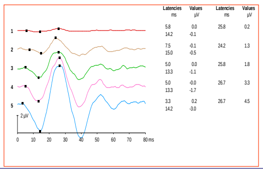
0-2.5°
5-10°
15-20°



2.5-5°
10-15°

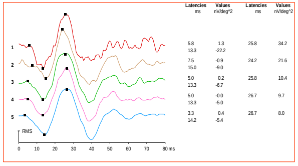
Suddivisione in aree

Risposta Assoluta



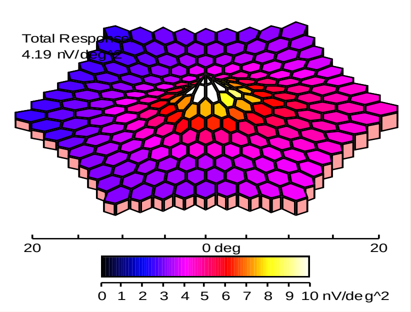
Latencies ms	Values µV	Latencies ms	Values µV
5.8	0.0	25.8	0.2
14.2	-0.1		
7.5	-0.1	24.2	1.3
15.0	-0.5		
5.0	0.0	25.8	1.8
13.3	-1.1		
5.0	-0.0	26.7	3.3
13.3	-1.7		
3.3	0.2	26.7	4.5
14.2	-3.0		

Risposta Normalizzata (RAD)



Latencies ms	Values nV/deg^2	Latencies ms	Values nV/deg^2
5.8	1.3	25.8	34.2
13.3	-22.2		
7.5	-0.9	24.2	21.6
15.0	-9.0		
5.0	0.2	25.8	10.4
13.3	-6.7		
5.0	-0.0	26.7	9.7
13.3	-5.0		
3.3	0.4	26.7	8.0
14.2	-5.4		

Mappa della funzionalità retinica

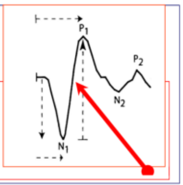


ERG Multifocale: Generatori

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



Applicazioni Cliniche

-AMD
-CNV Miopica
-Retinite Pigmentosa
-Glaucoma

NO CON CATARATTA, PATOLOGIE CONCOMITANTI, MANCANZA DI FISSAZIONE

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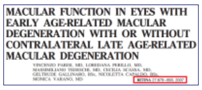
mfERG e AMD:

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

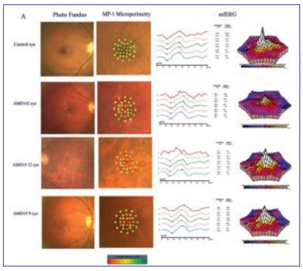


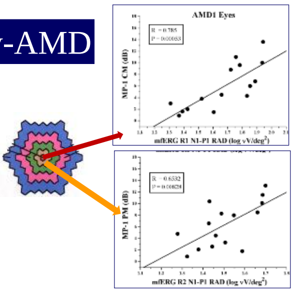
MACULAR FUNCTION IN EYES WITH EARLY AGE-RELATED MACULAR DEGENERATION WITH OR WITHOUT CONTRALATERAL LATE AGE-RELATED MACULAR DEGENERATION

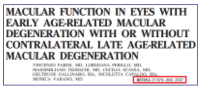
VINCENZO PARISI, MD, LOREDANA PERILLO, MD, MASSIMILIANO TEDESCHI, MD, CECILIA SCASSA, MD, GELTRUDE GALLINARO, BSc, NICOLETTA CAPALDO, BSc, MONICA VARANO, MD

RETINA 27:879–890, 2007

Early-AMD







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

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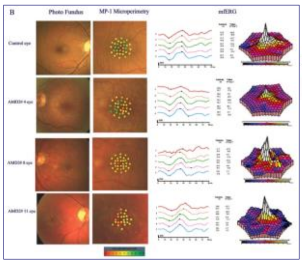
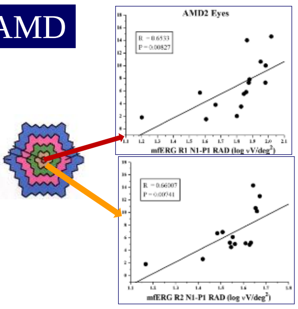
RETINA 27:879–890, 2007

Late-AMD





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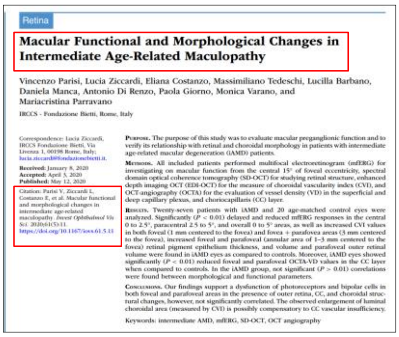
mfERG e AMD:

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



Retina

Macular Functional and Morphological Changes in Intermediate Age-Related Maculopathy

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

IRCCS - Fondazione Bietti, Rome, Italy

Correspondence: Lucia Ziccardi, IRCCS Fondazione Bietti, Via Livenza 1, 00198 Rome, Italy; lucia.ziccardi@fondazionebietti.it.

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Citation: Parisi V, Ziccardi L, Costanzo E, et al. Macular functional and morphological changes in intermediate age-related maculopathy. *Invest Ophthalmol Vis Sci.* 2020;61(5):11. https://doi.org/10.1167/iovs.61.5.11

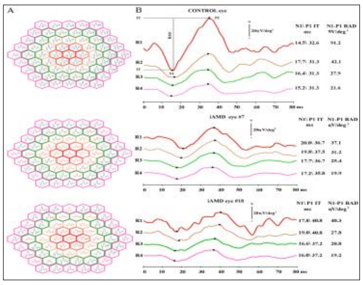
PURPOSE. The purpose of this study was to evaluate macular preganglionic function and to verify its relationship with retinal and choroidal morphology in patients with intermediate age-related macular degeneration (iAMD) patients.

METHODS. All included patients performed multifocal electroretinogram (mfERG) for investigating on macular function from the central 15° of foveal eccentricity, spectral domain optical coherence tomography (SD-OCT) for studying retinal structure, enhanced depth imaging OCT (EDI-OCT) for the measure of choroidal vascularity index (CVI), and OCT-angiography (OCTA) for the evaluation of vessel density (VD) in the superficial and deep capillary plexus, and choriocapillaris (CC) layer.

RESULTS. Twenty-seven patients with iAMD and 20 age-matched control eyes were analyzed. Significantly ($P < 0.01$) delayed and reduced mfERG responses in the central 0 to 2.5°, paracentral 2.5 to 5°, and overall 0 to 5° areas, as well as increased CVI values in both foveal (1 mm centered to the fovea) and fovea + parafovea areas (3 mm centered to the fovea); increased foveal and parafoveal (annular area of 1–3 mm centered to the fovea) retinal pigment epithelium thickness, and volume and parafoveal outer retinal volume were found in iAMD eyes as compared to controls. Moreover, iAMD eyes showed significantly ($P < 0.01$) reduced foveal and parafoveal OCTA-VD values in the CC layer when compared to controls. In the iAMD group, not significant ($P > 0.01$) correlations were found between morphological and functional parameters.

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.

Keywords: intermediate AMD, mfERG, SD-OCT, OCT angiography



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.

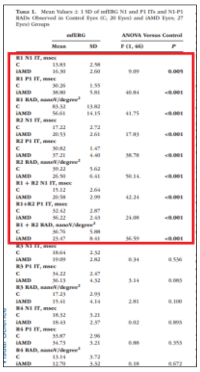


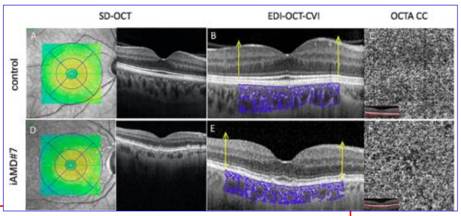
Table 1. Mean Values ± 1 SD of mfERG N1 and P1 ITs and N1-P1 RADs Observed in Control Eyes (C; 20 Eyes) and iAMD Eyes; 27 Eyes) Groups

	mfERG		ANOVA Versus Control	
	Mean	SD	F (1, 46)	P
R1 N1 IT, msec				
C	13.83	2.58		
iAMD	16.90	2.60	9.09	**0.005**
R1 P1 IT, msec				
C	30.26	1.55		
iAMD	38.80	5.81	40.84	**<0.001**
R1 RAD, nanoV/degree²				
C	83.32	13.82		
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	37.21	4.40	38.78	**<0.001**
R2 RAD, nanoV/degree²				
C	39.22	5.62		
iAMD	26.50	6.41	50.14.	**<0.001**
R1 + R2 N1 IT, msec				
C	15.12	2.64		
iAMD	20.58	2.99	42.24	**<0.001**
R1+R2 P1 IT, msec				
C	32.42	2.87		
iAMD	36.22	2.43	24.08	**<0.001**
R1 + R2 RAD, nanoV/degree²				
C	36.76	5.88		
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	4.52	3.14	0.083
R3 RAD, nanoV/degree²				
C	17.23	2.93		
iAMD	15.41	4.14	2.81	0.100
R4 N1 IT, msec				
C	18.52	3.21		
iAMD	18.43	2.37	0.02	0.893
R4 P1 IT, msec				
C	33.87	2.96		
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°



RISULTATI MORFOLOGICI

SD-OCT:

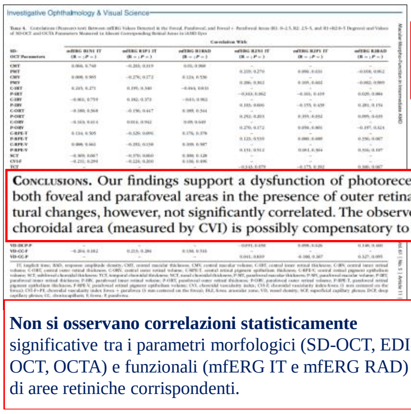
- Lo spessore ed il volume centrale e parafoveale dell'epitelio pigmentato retinico **(C-RPE, P-RPE)** ed il volume della retina esterna parafoveale **(P-ORV)** **risultano significativamente aumentati** negli iAMD rispetto ai C.
- I restanti parametri di spessore e volume misurati nei differenti strati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



Investigative Ophthalmology & Visual Science

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.

RISULTATI DELLE CORRELAZIONI MORFO-FUNZIONALI

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.

mfERG e AMD:

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

a) Carotenoidi

b) Terapie intravitreali

mfERG: VARIABILITA'

COME STUDIARLA E PER COSA PUO' ESSERE UTILE

1) Test-Retest

a) Almeno due misurazioni nell'arco della giornata

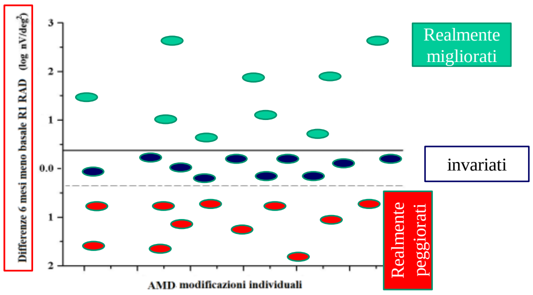
b) Misurare le differenze (log µV)

Es: *paz 1 = - 0.21* log µV
paz 2 = + 0.18 log µV
paz 3 = + 0.23 log µV
paz 4 = - 0.19 log µV …………

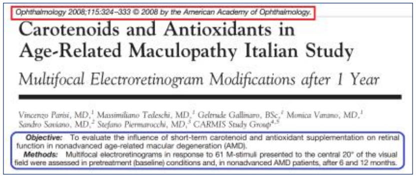
Media 0.01, ± 2 SD (0.24)
Variabilità da – 0.47 log µV a + 0.49

mfERG: VARIABILITA’

COME STUDIARLA



1) Carotenoidi



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

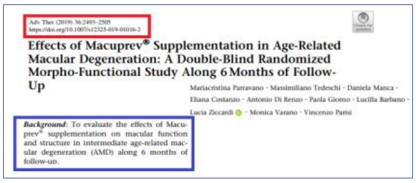
Carotenoids and Antioxidants in Age-Related Maculopathy Italian Study

Multifocal Electroretinogram Modifications after 1 Year

Vincenzo Parisi, MD,[1] Massimiliano Tedeschi, MD,[1] Geltrude 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

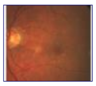
Effects of Macuprev® Supplementation in Age-Related Macular Degeneration: A Double-Blind Randomized Morpho-Functional Study Along 6 Months of Follow-Up

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.

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

Pazienti



- N= 30 pazienti
- Early AMD, categoria 3 dello studio AREDS
- ETDRS ≥ 0.2 LogMAR

- Suddivisi Random in due gruppi paragonalbili per età e grado di AMD

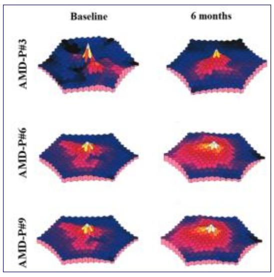
N=15, AMD-M: Trattati, età media: 68.5±8.79 anni;
supplementazione orale di cocktail con antiossidanti
(Macuprev, Farmaplus Italia s.r.l., Italy).)* 2 cps/giorno per 6 mesi

*(constituenti: lutein (20 mg), zeaxanthin (4 mg), N-acetylcysteine (140 mg), bromelain 2500GDU (80 mg), vitamin B12 (18 mg), vitamin D3 (800 IU), alphalipoic acid (140 mg), rutin (157 mg), vitamin C (160 mg), zinc oxide (16 mg), Vaccinium myrtillus 36% anthocyanosides (90 mg), Ganoderma lucidum (600 mg)

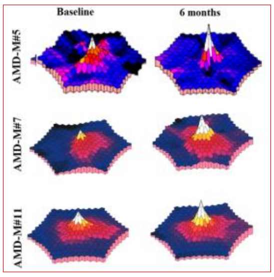
N= 15 AMD- Placebo, età media: 70.1±9.87 annni;
2 cps/giorno per 6 mesi

Risultati:
esempi di risposte individuali di mfERG in occhi AMD-P e AMD-M

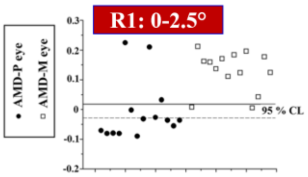
AMD-P



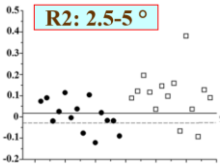
AMD-M

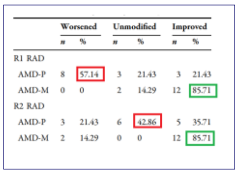


R1: 0-2.5°



R2: 2.5-5 °





	Worsened		Unmodified		Improved	
	n	%	*n*	%	*n*	%
R1 RAD						
AMD-P	8	57.14	3	21.43	3	21.43
AMD-M	0	0	2	14.29	12	85.71
R2 RAD						
AMD-P	3	21.43	6	42.86	5	35.71
AMD-M	2	14.29	0	0	12	85.71

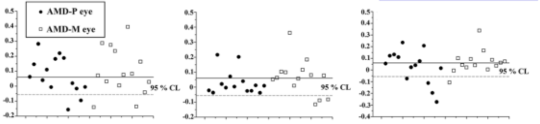
AMD-P: p>0.05 vs Basale

AMD-M: p<0.01 vs Basale

R3: 5-10°

R4: 10-15°

R5: 15-20°



	Worsened		Unmodified		Improved	
	n	%	n	%	n	%
R3 RAD						
AMD-P	2	14.29	6	42.86	6	42.86
AMD-M	2	14.29	4	28.57	8	57.14
R4 RAD						
AMD-P	0	0	11	78.57	3	21.43
AMD-M	3	21.43	4	28.57	7	50
R5 RAD						
AMD-P	4	28.57	4	28.57	6	42.86
AMD-M	1	7.143	7	50	6	42.86

AMD-P e AMD-M: p>0.05 vs Basale

Conclusions: In intermediate AMD, Macuprev® supplementation increases the function of the macular pre-ganglionic elements, with no associated retinal and choroidal ultra-structural changes.

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.

	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.

Conclusioni

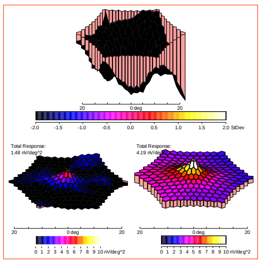
mfERG e AMD:

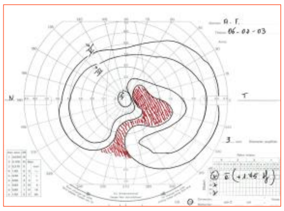
1. Identificazioni di disfunzioni precoci nell’area foveale
2. Modificazioni del mfERG correlate con psicofisica (microperimetria), ma non con OCT/A-OCT
3. Utilità per la valutazione efficacia terapie

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

M-ERG

Campo Visivo

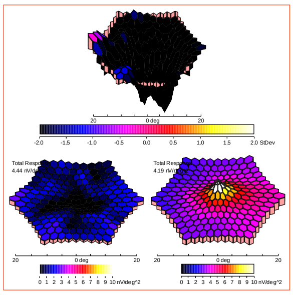




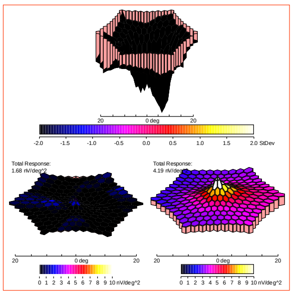
Nei pazienti con RP si ha la possibilità di rilevare aree retiniche “ancora” funzionanti e di quantificarne la funzionalità residua in maniera oggettiva.

- Particolare utilità nella valutazione funzionale residua della regione maculare

Soggetto: Di Ma 44 anni, CNV miopica, OD



Soggetto: Di Mi 54 anni, CNV miopica, OD

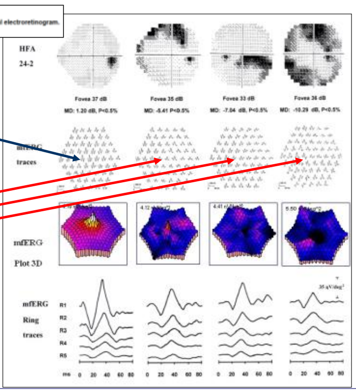


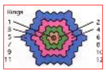
Macular function in eyes with open-angle glaucoma evaluated by multifocal electroretinogram.

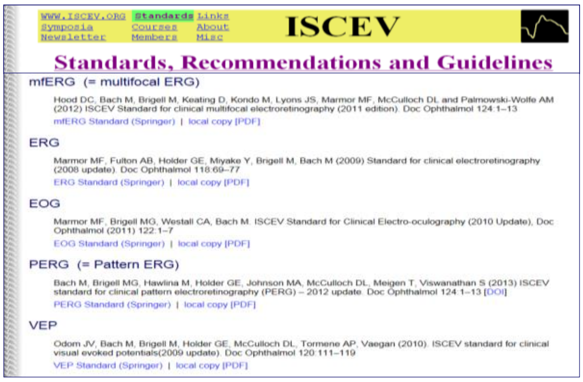
mfERG

in

Glaucoma


HFA
24-2
Fovea 37 dB
MD: 1.20 dB, P<0.5%
Fovea 35 dB
MD: -8.41 P<0.5%
Fovea 33 dB
MD: -7.04 dB, P<0.5%
Fovea 36 dB
MD: -10.29 dB, P<0.5%
mfERG
traces
mfERG
Plot 3D
mfERG
Ring
traces
R1
R2
R3
R4
R5
ms
0
20
40
60
80





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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]

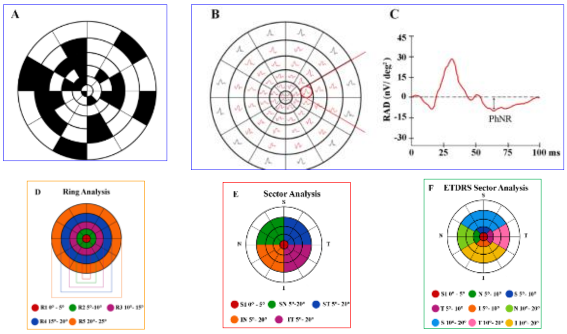
PERG Standard (Springer) | local copy [PDF]

VEP

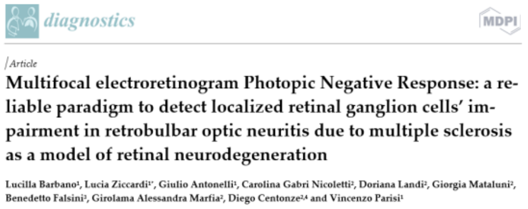
Odom JV, Bach M, Brigell M, Holder GE, McCulloch DL, Tormene AP, Vaegan (2010). ISCEV standard for clinical visual evoked potentials(2009 update). Doc Ophthalmol 120:111–119

VEP Standard (Springer) | local copy [PDF]

PhNR Multifocale: stimolo visivo e risposta elettrofunzionale


A
B
C
RAD (nV/ deg²)
45
30
15
0
-15
-30
0
25
50
75
100 ms
PhNR
D
Ring Analysis
E
Sector Analysis
F
ETDRS Sector Analysis
S
N
T
I

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



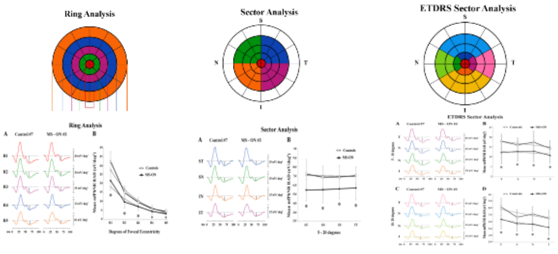
diagnostics MDPI

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

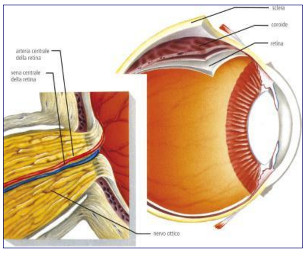
Lucilla Barbano[1], Lucia Ziccardi[1*], Giulio Antonelli[1], Carolina Gabri Nicoletti[2], Doriana Landi[2], Giorgia Mataluni[2], Benedetto Falsini[3], Girolama Alessandra Marfia[2], Diego Centonze[2,4] and Vincenzo Parisi[1]

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

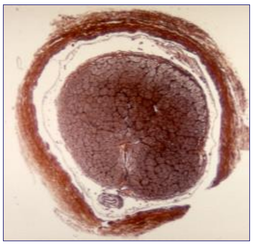


The mfPhNR RAD values observed in all rings or sectors in MS-ON eyes were significantly reduced ($p<0.01$) with respect to control ones. Our results suggest that mfPhNR recordings may detect localized IRL dysfunction in the pathologic condition of selective RGCs neurodegeneration.

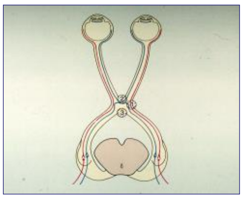
Il nervo Ottico

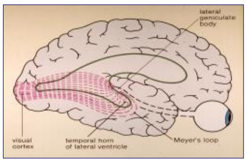

sclera
coroide
retina
arteria centrale della retina
vena centrale della retina
nervo ottico

- 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.



LE VIE OTTICHE POST-CHIASAMTICHE

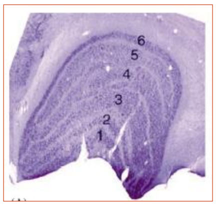


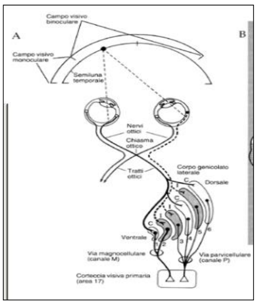

lateral geniculate body
visual cortex
temporal horn of lateral ventricle
Meyer's loop

Il Nucleo Genicolato laterale

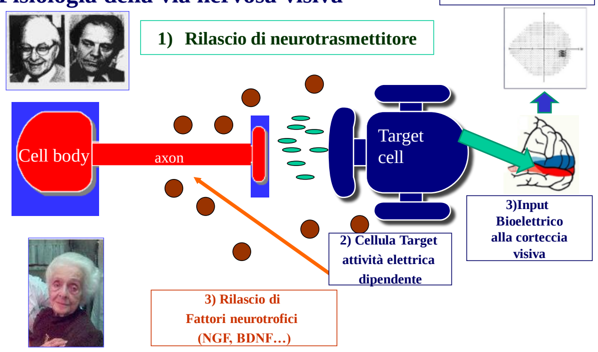
- Sistema magno/parvo cellulare

Diviso in 6 strati: ipsi e controlaterale




A
B
Campo visivo binoculare
Campo visivo monoculare
Semiluna temporale
Nervi ottici
Chiasma ottico
Tratti ottici
Corpo genicolato laterale
Dorsale
Ventrale
C
I
1
2
3
4
5
6
Via magnocellulare (canale M)
Via parvicellulare (canale P)
Corteccia visiva primaria (area 17)

Fisiologia della via nervosa visiva



Normale percezione visiva

1) **Rilascio di neurotrasmettitore**

Cell body

axon

Target cell

2) Cellula Target attività elettrica dipendente

3)Input Bioelettrico alla corteccia visiva

3) Rilascio di Fattori neurotrofici (NGF, BDNF…)

Fisiologia della via nervosa visiva

Normale percezione visiva

1) **Rilascio di neurotrasmettitore**

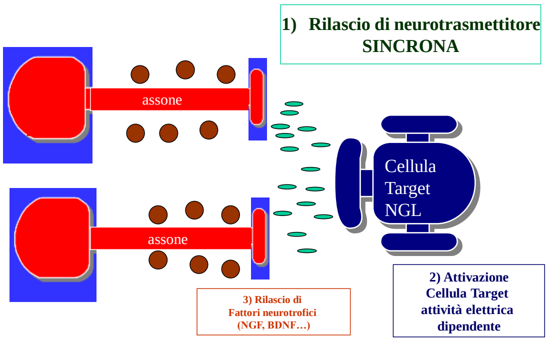
Plasticità cerebrale:

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

Fattori neurotrofici (NGF, BDNF…)

visiva

Nucleo Genicolato laterale e visione binoculare



1) **Rilascio di neurotrasmettitore SINCRONA**

assone

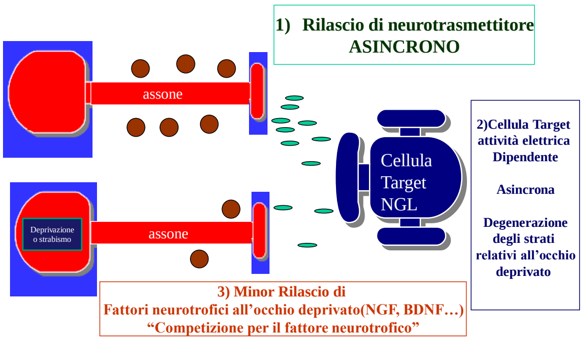
assone

Cellula Target NGL

2) Attivazione Cellula Target attività elettrica dipendente

3) Rilascio di Fattori neurotrofici (NGF, BDNF…)

Nucleo Genicolato laterale e deficit della visione binoculare



1) **Rilascio di neurotrasmettitore ASINCRONO**

assone

Deprivazione o strabismo

assone

Cellula Target NGL

2)Cellula Target attività elettrica Dipendente

Asincrona

Degenerazione degli strati relativi all'occhio deprivato

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

Nucleo Genicolato laterale e deficit della visione binoculare

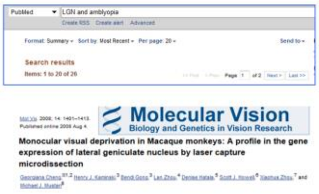
1) **Rilascio di neurotrasmettitore ASINCRONO**

Modificazioni della plasticità cerebrale:

1) anomala formazione di sinapsi

2)Anomala stabilizzazione sinaptica a lungo termine

NGL e Ampliopia



PubMed | LGN and amblyopia

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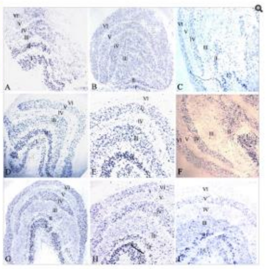
Page 1 of 2 Next > Last >>

Mol Vis. 2008; 14: 1401–1413.
Published online 2008 Aug 4.

Molecular Vision
Biology and Genetics in Vision Research

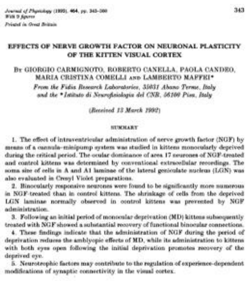
Monocular visual deprivation in Macaque monkeys: A profile in the gene expression of lateral geniculate nucleus by laser capture microdissection

Georgiana Cheng,[1,2] Henry J. Kaminski,[3] Bendi Gong,[3] Lan Zhou,[4] Denise Hatala,[5] Scott J. Howell,[6] Xiaohua Zhou,[7] and Michael J. Mustari[8]



In situ hybridization of CRH in control and LGN. A and B: CRH expression in the LGN of two control monkeys (C1and C2). C: Ipsilateral LGN of a monkey that was monocular vision-deprived for four months (MD5). D: CRH showed decreased expression in deprived layers (layers I, IV, and VI) in the LGN contralateral to the eye from a monkey that was monocular vision-deprived for four months (MD3). E: Higher-magnification photomicrograph of D. F: Ipsilateral LGN from a monkey that was monocular vision-deprived for two (MD2). G: CRH showed decreased expression in deprived layers (layers II, III, and V) in the LGN ipsilateral to the eye from a monkey that was monocular vision-deprived for four months (MD4). H: Higher-magnification photomicrograph of G. I: Contralateral LGN eye from a monkey that was monocular vision-deprived for four months (MD4).

Plasticità cerebrale: ruolo del NGF



Journal of Physiology (1993), 464, pp. 343–360 343
With 9 figures
Printed in Great Britain

EFFECTS OF NERVE GROWTH FACTOR ON NEURONAL PLASTICITY OF THE KITTEN VISUAL CORTEX

BY GIORGIO CARMIGNOTO, ROBERTO CANELLA, PAOLA CANDEO, MARIA CRISTINA COMELLI AND LAMBERTO MAFFEI*

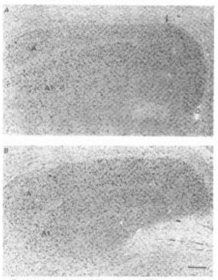
*From the Fidia Research Laboratories, 35031 Abano Terme, Italy and the *Istituto di Neurofisiologia del CNR, 56100 Pisa, Italy*

(Received 13 March 1992)

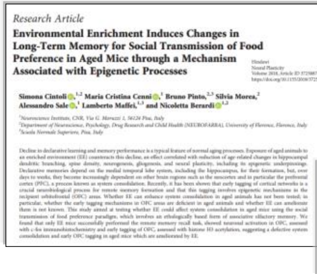
SUMMARY

1. The effect of intraventricular administration of nerve growth factor (NGF) by means of a cannula–minipump system was studied in kittens monocularly deprived during the critical period. The ocular dominance of area 17 neurones of NGF-treated and control kittens was determined by conventional extracellular recordings. The soma size of cells in A and A1 laminae of the lateral geniculate nucleus (LGN) was also evaluated in Cresyl Violet preparations.
2. Binocularly responsive neurones were found to be significantly more numerous in NGF-treated than in control kittens. The shrinkage of cells from the deprived LGN laminae normally observed in control kittens was prevented by NGF administration.
3. Following an initial period of monocular deprivation (MD) kittens subsequently treated with NGF showed a substantial recovery of functional binocular connections.
4. These findings indicate that the administration of NGF during the period of deprivation reduces the amblyopic effects of MD, while its administration to kittens with both eyes open following the initial deprivation promotes recovery of the deprived eye.
5. Neurotrophic factors may contribute to the regulation of experience-dependent modifications of synaptic connectivity in the visual cortex.

NGF MODULATES VISUAL CORTICAL PLASTICITY 351



Plasticità cerebrale: ruolo dell'ambiente



Research Article

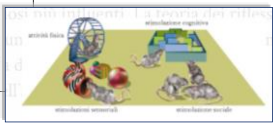
Environmental Enrichment Induces Changes in Long-Term Memory for Social Transmission of Food Preference in Aged Mice through a Mechanism Associated with Epigenetic Processes

Hindawi
Neural Plasticity
Volume 2018, Article ID 3725087, 12 pages
https://doi.org/10.1155/2018/3725087

Simona Cintoli,[1,2] Maria Cristina Cenni,[1] Bruno Pinto,[2,3] Silvia Morea,[2] Alessandro Sale,[1] Lamberto Maffei,[1,3] and Nicoletta Berardi[1,2]

[1]Neuroscience Institute, CNR, Via G. Moruzzi 1, 56124 Pisa, Italy
[2]Department of Neuroscience, Psychology, Drug Research and Child Health (NEUROFARBA), University of Florence, Florence, Italy
[3]Scuola Normale Superiore, Pisa, Italy

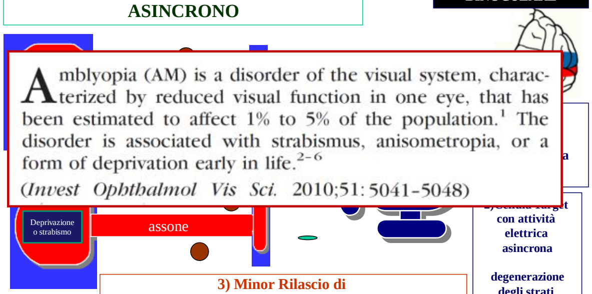
Decline in declarative learning and memory performance is a typical feature of normal aging processes. Exposure of aged animals to an enriched environment (EE) counteracts this decline, an effect correlated with reduction of age-related changes in hippocampal dendritic branching, spine density, neurogenesis, gliogenesis, and neural plasticity, including its epigenetic underpinnings. Declarative memories depend on the medial temporal lobe system, including the hippocampus, for their formation, but, over days to weeks, they become increasingly dependent on other brain regions such as the neocortex and in particular the prefrontal cortex (PFC), a process known as system consolidation. Recently, it has been shown that early tagging of cortical networks is a crucial neurobiological process for remote memory formation and that this tagging involves epigenetic mechanisms in the recipient orbitofrontal (OFC) areas. Whether EE can enhance system consolidation in aged animals has not been tested; in particular, whether the early tagging mechanisms in OFC areas are deficient in aged animals and whether EE can ameliorate them is not known. This study aimed at testing whether EE could affect system consolidation in aged mice using the social transmission of food preference paradigm, which involves an ethologically based form of associative olfactory memory. We found that only EE mice successfully performed the remote memory recall task, showed neuronal activation in OFC, assessed with c-fos immunohistochemistry and early tagging of OFC, assessed with histone H3 acetylation, suggesting a defective system consolidation and early OFC tagging in aged mice which are ameliorated by EE.



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]

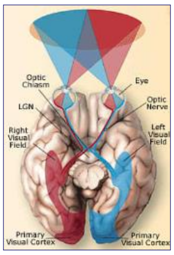
(*Invest Ophthalmol Vis Sci.* 2010;51:5041-5048)

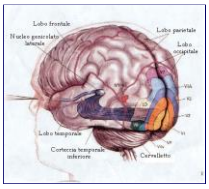
2)Cellula target con attività elettrica asincrona

degenerazione degli strati relativi all'occhio deprivato

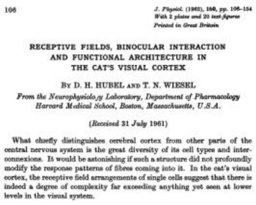
3) Minor Rilascio di Fattori neurotrofici all'occhio deprivato(NGF, BDNF…) "Competizione per il fattore neurotrofico"

La Corteccia Visiva





La corteccia visiva



106 J. Physiol. (1962), 160, pp. 106–154
With 2 plates and 20 text-figures
Printed in Great Britain

RECEPTIVE FIELDS, BINOCULAR INTERACTION AND FUNCTIONAL ARCHITECTURE IN THE CAT'S VISUAL CORTEX

By D. H. HUBEL and T. N. WIESEL

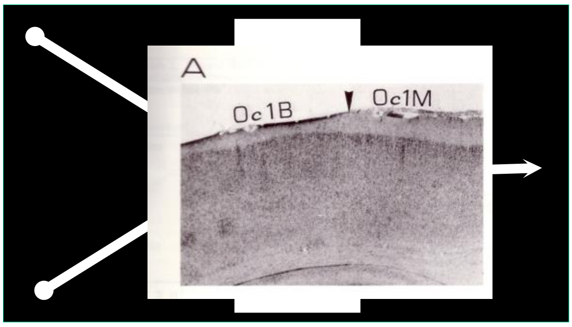
From the Neurophysiology Laboratory, Department of Pharmacology Harvard Medical School, Boston, Massachusetts, U.S.A.

(*Received* 31 *July* 1961)

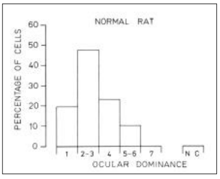
What chiefly distinguishes cerebral cortex from other parts of the central nervous system is the great diversity of its cell types and interconnexions. It would be astonishing if such a structure did not profoundly modify the response patterns of fibres coming into it. In the cat's visual cortex, the receptive field arrangements of single cells suggest that there is indeed a degree of complexity far exceeding anything yet seen at lower levels in the visual system.

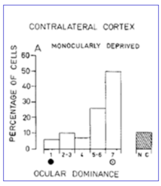
- **Aree occipitali 17, 18, 19**
- **Rappresentazione retinotopica**
- **Cellule semplici, complesse, ipercomplesse**
- **Le colonne di dominanza oculare**

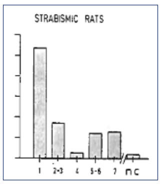
Cellule semplici, complesse ipercomplesse



Colonne di Dominanza Oculare







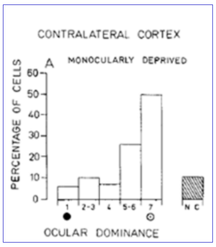
Colonne di Dominanza Oculare, Deprivazione, NGF, Plasticità

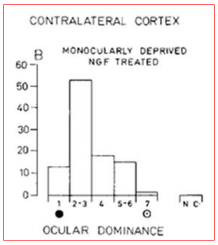
The Journal of Neuroscience, December 1992, 12(12): 4651–4662

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





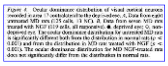


Figure 4. Ocular dominance distribution of visual cortical neurons recorded in area 17 contralateral to the deprived eye. *A*, Data from eight untreated MD rats (125 cells, 13 NC). *B*, Data from seven MD rats treated with NGF (119 cells, all responsive). ●, deprived eye; ○, nondeprived eye. The ocular dominance distribution for untreated MD rats is significantly different both from the distribution in normal rats (p < 0.001) and from the distribution in MD rats treated with NGF (p < 0.001). The ocular dominance distribution for MD NGF-treated rats does not significantly differ from the distribution in normal rats.

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

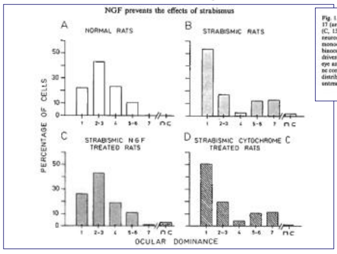


Fig. 1. Ocular dominance distribution of visual cortical neurons recorded in the binocular portion of area 17 (area OC1B) in normal rats (A, 141 cells), strabismic rats (B, 145 cells), strabismic NGF-treated rats (C, 137 cells) and in strabismic Cytochrome C-treated rats (D, 93 cells). In strabismic rats the visual neurons were recorded in the cortex contralateral to the squinting eye. Neurons in ocular class 1 were monocular and driven only by the stimulation of the contralateral eye; neurons of classes 2 and 3 were binocular and preferentially driven by the contralateral eye; neurons of class 4 were binocular and equally driven by the two eyes; neurons of classes 5 and 6 were binocular and preferentially driven by the ipsilateral eye and neurons of class 7 were monocular and driven only by the ipsilateral eye. The category labelled nc contains those neurons that could not be classified using visual stimuli. Differences in ocular dominance distributions assessed in different groups of rats were evaluated by means of chi-square test: strabismic untreated rats vs normal rats, $P < 0.01$; strabismic untreated vs strabismic cytochrome C-treated rats, $P \geqslant 0.05$; normal vs strabismic NGF-treated rats, $P \geqslant 0.05$.

Acuità visiva, Deprivazione, NGF, Plasticità

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

1991 Oct 1; 88(19): 8811–8815.

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PNAS

Proceedings of the National Academy of Sciences of the United States of America

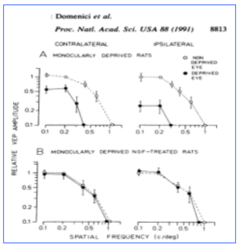
Nerve growth factor prevents the amblyopic effects of monocular deprivation.

Proc. Natl. Acad. Sci. USA 88 (1991) 8815

We thank Dr. S. Skaper for reading the manuscript and for helpful discussion; we also thank M. Antoni, G. Cappagli, V. Alpigiani, and A. Tacchi for technical assistance. Dr. G. Tiniella made the computer program for VEP acquisition and analysis. Drs. T. Pizzorusso and V. Parisi participated in some of the experiments. N.B. is Associate Professor at the Department of General and Environmental Physiology, University of Napoli, Napoli, Italy.

Domenici *et al.*

Proc. Natl. Acad. Sci. USA 88 (1991) 8813



Supplementazione di NGF (Riattivazione Plasticità)

↓

Attivazione del NGL

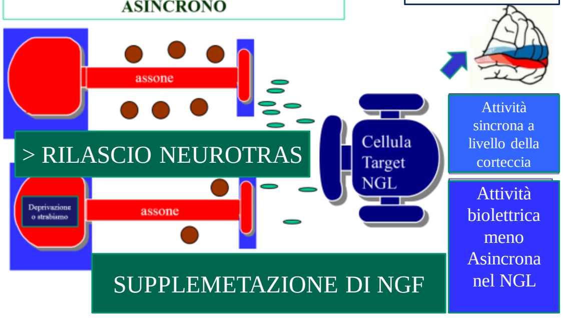
↓

Riduzione deficit visivo

Corteccia deficit della visione binoculare

1) Rilascio di neurotrasmettitore ASINCRONO

Miglioramento binocularità e AV



> RILASCIO NEUROTRAS

SUPPLEMETAZIONE DI NGF

Attività sincrona a livello della corteccia

Attività biolettrica meno Asincrona nel NGL

ESPLORAZIONE FUNZIONALE DELLE VIE OTTICHE: I POTENZIALI EVOCATI VISIVI

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

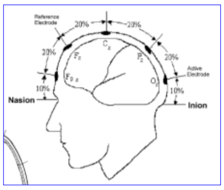
Doc Ophthalmol (2016) 133:1–9

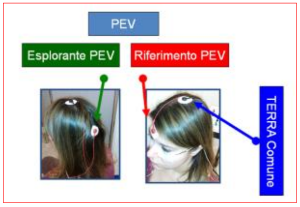
ISCEV standard for clinical visual evoked potentials: (2016 update)

J. Vernon Odom · Michael Bach · Mitchell Brigell · Graham E. Holder · Daphne L. McCulloch · Atsushi Mizota · Alma Patrizia Tormene ·

1) PREPARAZIONE DEL PAZIENTE

Posizionamento degli elettrodi





RESISTENZA INTERELETTRODICA < 3 KHoms

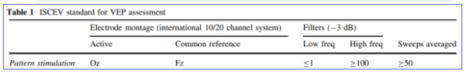
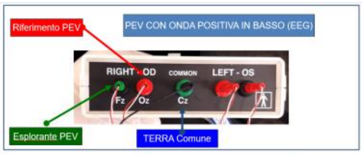


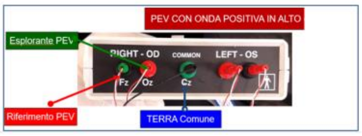
Table 1 ISCEV standard for VEP assessment

	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

1) PREPARAZIONE DELL'ESAME

Posizionamento degli elettrodi
NEL PREAMPLIFICATORE



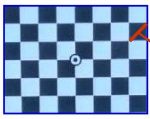


Traccia con polarità positiva in basso/alto:

MOLTO IMPORTANTE PER EVITARE ERRORI DI VISUALIZZAZIONE DEI PICCHI

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

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’

Table 1 ISCEV standard for VEP assessment

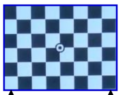
Stimulus type	Field size (minimum)	Presentation	Stimulus	Mean luminance (cd · m^{-2})	Michaelson contrast (%)	Presentation rate
Pattern reversal	15°	Monocular	Check widths: 1° (0.8°–1.2°); 0.25° (0.2°–0.3°)	50 (40–60)	≥80	2 (1.8–2.2) reversals/s

---

2) LO STIMOLO VISIVO
C) 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%.

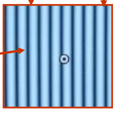
In realtà, l’elemento bianco non ha mai una luminanza 100, per cui viene sempre utilizzato un contrasto reale del 70-80 %.



Lum max

Lum min

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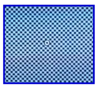
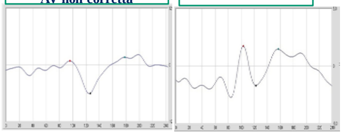
3) Risposta e stimolo visivo: fonti di errore legati al difetto refrettivo

CHECKS,

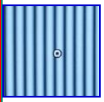


V.P. 59 anni -2sf=-3 cyl (165)
AV non corretta

A.T 36 anni
LHON AV corretta

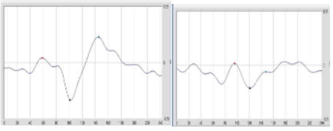


GRATINGS



V.P. 59 anni -2sf=-3 cyl (165)
AV non corretta

A.T 36 anni
LHON AV corretta



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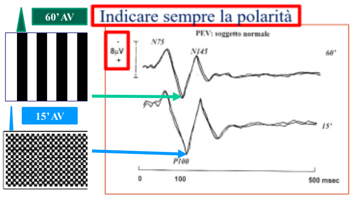
3) Le risposte bioelettriche corticali



Valutazione funzione degli assoni di grosso calibro

Valutazione funzione del fascio papillo-maculare

Eye Movements, Strabismus, Amblyopia, and Neuro-Ophthalmology

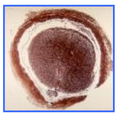
Electrophysiological Detection of Delayed Postretinal Neural Conduction in Human Amblyopia

Eye Movements, Strabismus, Amblyopia, and Neuro-Ophthalmology

Retinal Function and Neural Conduction Along the Visual Pathways in Affected and Unaffected Carriers With Leber's Hereditary Optic Neuropathy

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



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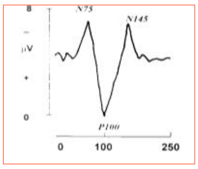
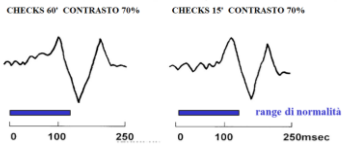
4) APPLICAZIONI CLINICHE
PEV con latenze aumentate ed ampiezze ridotte:

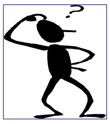
Normale



Patologico

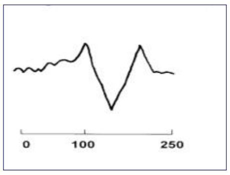


Disfunzione retinica,
del nervo ottico, del chiasma,
del tratto ottico…….ecc?



ESPLORAZIONE ELETTOFUNZIONALE DELLE VIE OTTICHE POSTRETINICHE

PEV: latenze aumentate/ampiezze ridotte:



Diagnosi differenziale tra:

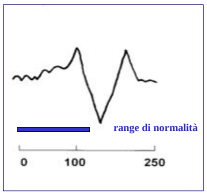
- Patologie retiniche **-Patologie postretiniche**

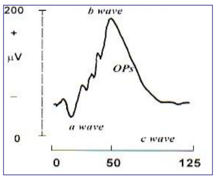
E' necessario associare:

PEV + ERG **PEV + PERG**

PEV+ ERG

PEV Alterato + **ERG Normale**



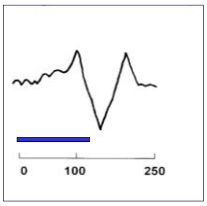


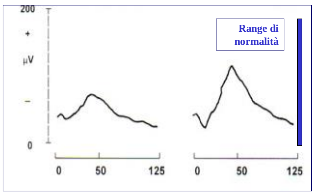
patologia post-fotorecettoriale:

cellule ganglionari, nervo ottico, vie ottiche

PEV+ ERG

PEV Alterato + **ERG Alterato**





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

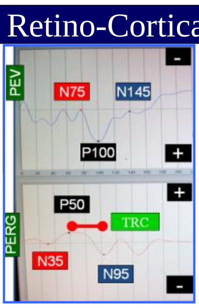
PEV+ PERG: il Tempo Retino-Corticale

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.



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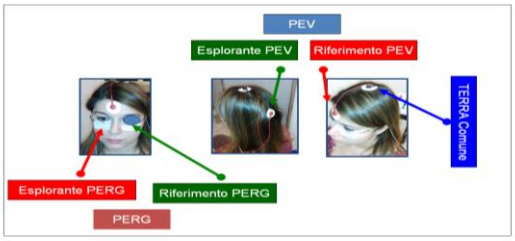
1) PREPARAZIONE DEL PAZIENTE

Posizionamento degli elettrodi


PEV
Esplorante PEV
Riferimento PEV
TERRA Comune
Esplorante PERG
Riferimento PERG
PERG

Stimolazione monoculare

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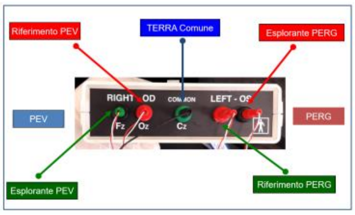
1) PREPARAZIONE DELL'ESAME

Posizionamento degli elettrodi
NEL PREAMPLIFICATORE


Riferimento PEV
TERRA Comune
Esplorante PERG
RIGHT - OD
COMMON
LEFT - OS
Fz
Oz
Cz
PEV
PERG
Esplorante PEV
Riferimento PERG

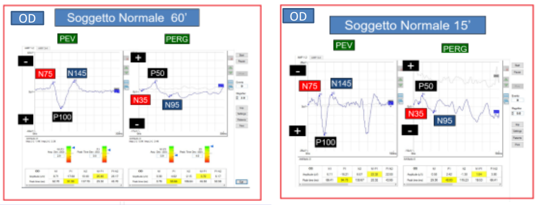
Traccia con polarità positiva in basso per il PEV

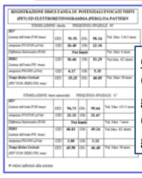
Traccia con polarità positiva in alto per il PERG

MOLTO IMPORTANTE PER EVITARE ERRORI DI VISUALIZZAZIONE DEI PICCHI

POSSIBILI COMBINAZIONE DI RISPOSTE BIOELETTRICHE PERG+PEV

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



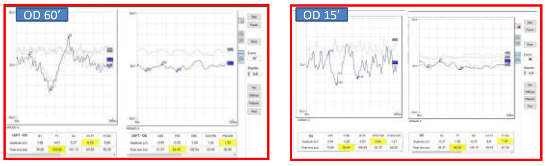


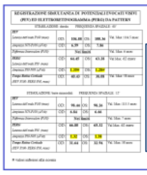
Considerazioni neurofunzionali

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

2 60' e 15' PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti aumentati ed ampiezze ridotte ed TRC normali



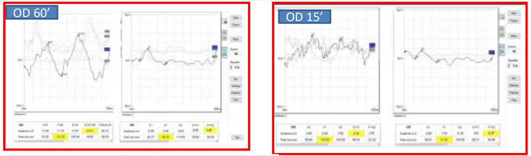


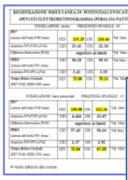
Considerazioni neurofunzionali

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

3 60' e 15' PEV P100 tempi impliciti aumentati ed ampiezze normali, PERG tempi impliciti ed ampiezze normali, TRC aumentati



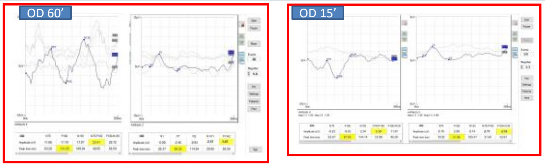


Considerazioni neurofunzionali

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).

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



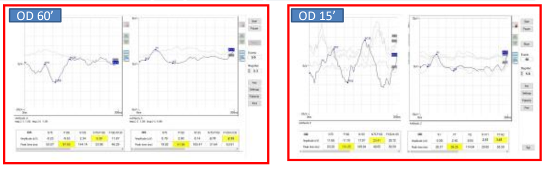
Considerazioni neurofunzionali

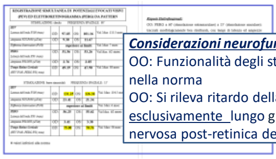
Funzionalità degli strati interni retinici (cellule e fibre ganglionari) nella norma

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.

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




REGISTRAZIONE SIMULTANEA DI POTENZIALI EVOCATI VISIVI (PEV) ED ELETTRORETINOGRAMMA (PERG) DA PATTERN

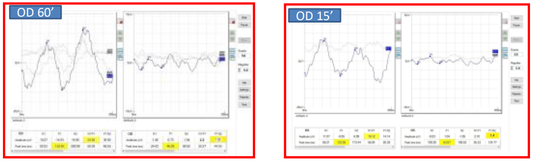
Considerazioni neurofunzionali

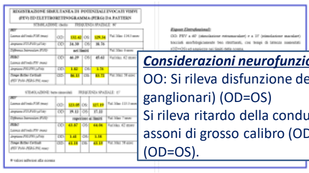
OO: Funzionalità degli strati interni retinici (cellule e fibre ganglionari) nella norma

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.

6

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




REGISTRAZIONE SIMULTANEA DI POTENZIALI EVOCATI VISIVI (PEV) ED ELETTRORETINOGRAMMA (PERG) DA PATTERN

Considerazioni neurofunzionali

OO: Si rileva disfunzione degli strati interni retinici (cellule e fibre ganglionari) (OD=OS)

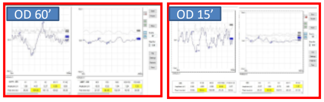
Si rileva ritardo della conduzione nervosa post-retinica sia lungo gli assoni di grosso calibro (OD=OS) che lungo gli assoni di piccolo calibro (OD=OS).

Applicazioni cliniche

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

1

IPERTENSIONE OCULARE:

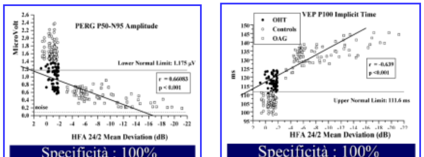


Considerazioni neurofunzionali

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 %



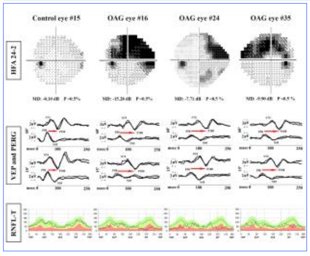
Specificità : 100%
Sensibilità: OHT 69.2%

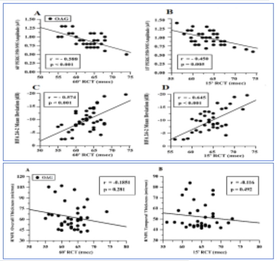
Specificità : 100%
Sensibilità: OHT 85.3%

**PERG RIDOTTO, VEP RITARDATO
E TRC NELLA NORMA**

2

GLAUCOMA

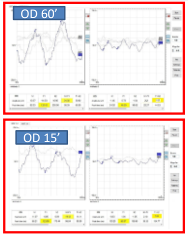


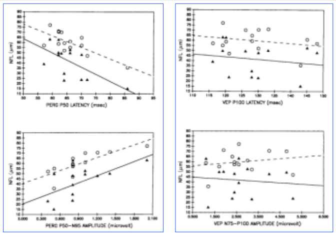


**PERG RIDOTTO, VEP RITARDATO
TRC: AUMENTATO IN PROPORZIONE ALLA RIDUZIONE DEL PERG, CORRELATO CON LA MD, NON CORRELATO CON RNFL**

3

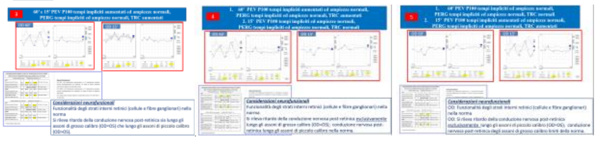
SCLEROSI MULTIPLA CON NORB





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

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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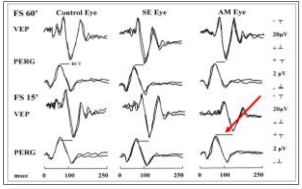
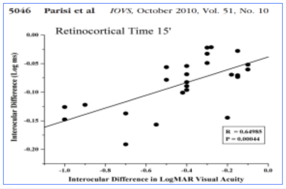
5 AMBLIOPIA





**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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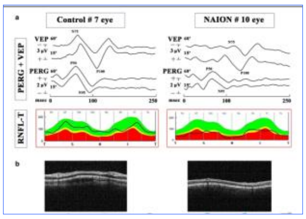
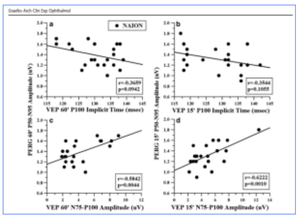
6 NOIA





PERG RIDOTTO, VEP RITARDATO

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

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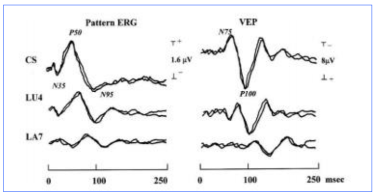
7 NEURITE OTTICA DI LEBER E CARRIER



**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**

Evidenze Scientifiche

Electrophysiological assessment of visual function in IDDM patients
Vincenzo Parisi, Luigi Uccioli, Giovanna Monticone, Leoluca Parisi, Gianluca Manni, Daniela Ippoliti, Guido Menzinger, Massimo G. Bucci

Neural conduction in visual pathways in newly-diagnosed IDDM patients
Vincenzo Parisi, Luigi Uccioli, Leoluca Parisi, Gaspare Colacino, Gianluca Manni, Guido Menzinger, Massimo G. Bucci

CLINICAL INVESTIGATION
Vincenzo Parisi
Neural conduction in the visual pathways in ocular hypertension and glaucoma

ACTA OPHTHALMOLOGICA SCANDINAVICA 1997
Delayed postretinal neural conduction in glaucoma patients: Correlations between electrophysiological and computerized static perimetry parameters
V. Parisi, G. L. Manni, R. Sgrulletta, G. Colacino, M. Centofanti, M. G. Bucci

Electrophysiological assessment of visual pathways in glaucoma
V. PARISI, C. PERNINI, C. GUINETTI, R. NEUSCHULER, M.G. BUCCI

Ophthalmology 1999;106:1126–1134
Cytidine-5′-Diphosphocholine (Citicoline) Improves Retinal and Cortical Responses in Patients with Glaucoma
Vincenzo Parisi, MD, Gianluca Manni, MD, Gaspare Colacino, MD, Massimo G. Bucci, MD

ACTA OPHTHALMOLOGICA SCANDINAVICA 1999
Correlations between optical coherence tomography, pattern ERG and visual evoked potentials in patients with ocular hypertension and open angle glaucoma
G. L. Manni, V. Parisi, S. A. Gandolfi, M. Centofanti, G. Colacino, S. Marchi, M. G. Bucci

Pharmacological Research, Vol. 40, No. 3, 1999
EFFECTS OF NICERGOLINE ON THE RETINAL AND CORTICAL ELECTROPHYSIOLOGICAL RESPONSES IN GLAUCOMA PATIENTS: A PRELIMINARY OPEN STUDY
VINCENZO PARISI, GASPARE COLACINO, GIOVANNI MILAZZO, ANNA CLAUDIA SCUDERI and GIANLUCA MANNI

IOVS, July 1999, Vol. 40, No. 8
Visual Function Correlates with Nerve Fiber Layer Thickness in Eyes Affected by Ocular Hypertension
Vincenzo Parisi, Gianluca Manni, Stefano A. Gandolfi, Marco Centofanti, Gaspare Colacino, and Massimo G. Bucci

Visual electrophysiological responses in subjects with cerebral autosomal arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
Vincenzo Parisi, Francesco Pierelli, Alessandro Malandrini, Paola Carera, Diego Olzi, Daniela Gregori, Rita Restuccia, Leoluca Parisi, Francesco Fattapposta

Invest Ophthalmol Vis Sci. 1999;40:2520–2527
Correlation between Morphological and Functional Retinal Impairment in Multiple Sclerosis Patients
Vincenzo Parisi, Gianluca Manni, Maria Spadaro, Gaspare Colacino, Rita Restuccia, Stefano Marchi, Massimo G. Bucci, and Francesco Pierelli

Electrophysiological assessment of glaucomatous visual dysfunction during treatment with cytidine-5′-diphosphocholine (citicoline): a study of 8 years of follow-up
Vincenzo Parisi

Clinical Neurophysiology 112 (2001) 351–358
Impaired visual function in glaucoma
Vincenzo Parisi

Ophthalmology 2001;108:905–912
Correlation between Optical Coherence Tomography, Pattern Electroretinogram, and Visual Evoked Potentials in Open-angle Glaucoma Patients
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Clinical Ability of Pattern Electroretinograms and Visual Evoked Potentials in Detecting Visual Dysfunction in Ocular Hypertension and Glaucoma
Vincenzo Parisi, MD, Stefano Miglior, MD, Gianluca Manni, MD, Marco Centofanti, MD, Massimo G. Bucci, MD

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Vincenzo Parisi, Maria Elisa Scarale, Nicola Balducci, Michele Fresina, and Emilio C. Campos

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Experimental and clinical evidence of neuroprotection by nerve growth factor eye drops: Implications for glaucoma
Alessandro Lambiase, Luigi Aloe, Marco Centofanti, Vincenzo Parisi, Flavio Mantelli, Valeria Colafrancesco, Gian Luca Manni, Massimo Gilberto Bucci, Stefano Bonini, and Rita Levi-Montalcini

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Retinal Function and Neural Conduction Along the Visual Pathways in Affected and Unaffected Carriers With Leber's Hereditary Optic Neuropathy
Lucia Ziccardi, Federico Sadun, Anna Maria De Negri, Piero Barboni, Giacomo Savini, Enrico Borrelli, Chiara La Morgia, Valerio Carelli and Vincenzo Parisi

A preliminary study of the neuroprotective role of citicoline eye drops in glaucomatous optic neuropathy
Gloria Roberti, Lucia Tanga, Vincenzo Parisi, Massimo Sampalmieri, Marco Centofanti, Gianluca Manni

Visual evoked potentials in subgroups of migraine with aura patients

Graefes Arch Clin Exp Ophthalmol Accepted 29 April 2015
Treatment with citicoline eye drops enhances retinal function and neural conduction along the visual pathways in open angle glaucoma
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J Glaucoma 2014;23:391–404
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Cytidine 5′-Diphosphocholine (Citicoline) in Glaucoma: Rationale of Its Use, Current Evidence and Future Perspectives
Gloria Roberti, Lucia Tanga, Manuele Michelessi, Luciano Quaranta, Vincenzo Parisi, Gianluca Manni and Francesco Oddone

Adv Ther (2018) 35:987–996
Enhancement of Retinal Function and of Neural Conduction Along the Visual Pathway Induced by Treatment with Citicoline Eye Drops in Liposomal Formulation in Open Angle Glaucoma: A Pilot Electrofunctional Study
Vincenzo Parisi · Francesco Oddone · Gloria Roberti · Lucia Tanga · Carmela Carnevale · Lucia Ziccardi · Gianluca Manni

Ophthalmology 2019;126:1033–1044
Functional Changes of Retinal Ganglion Cells and Visual Pathways in Patients with Chronic Leber's Hereditary Optic Neuropathy during One Year of Follow-up
Vincenzo Parisi, MD, Lucia Ziccardi, MD, PhD, Federico Sadun, MD, Anna Maria De Negri, MD, Chiara La Morgia, MD, PhD, Lucilla Barbano, MD, Valerio Carelli, MD, PhD, Piero Barboni, MD

Neuroenhancement and neuroprotection by oral solution citicoline in non-arteritic ischemic optic neuropathy as a model of neurodegeneration: A randomized pilot study
Vincenzo Parisi, Lucilla Barbano, Antonio Di Renzo, Gianluca Coppola, Lucia Ziccardi

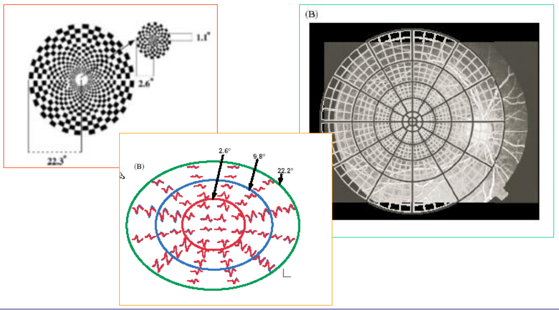
Adv Ther Accepted: October 14, 2020
Visual Evoked Potentials in Joubert Syndrome: A Suggested Useful Method for Evaluating Future Approaches Targeted to Improve Visual Pathways' Function
Giulio Ruberto · Vincenzo Parisi · Chiara Bertone · Sabrina Signorini · Luciano Quaranta

Graefe's Archive for Clinical and Experimental Ophthalmology Accepted: 19 November 2020
Correlations between visual morphological, electrophysiological, and acuity changes in chronic non-arteritic ischemic optic neuropathy
Lucilla Barbano · Lucia Ziccardi · Vincenzo Parisi

frontiers
Neural conduction along post-retinal visual pathways in glaucoma
Vincenzo Parisi, Lucia Ziccardi, Lucia Tanga, Gloria Roberti, Lucilla Barbano, Carmela Carnevale, Gianluca Manni and Francesco Oddone

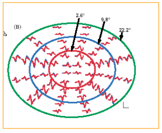
**1997-2021
32 lavori pubblicati**

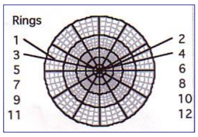
VEP Multifocale: stimolo visivo e risposta elettrofunzionale


1.1°
2.6°
22.3°
(B)
2.6°
9.8°
22.2°
(B)

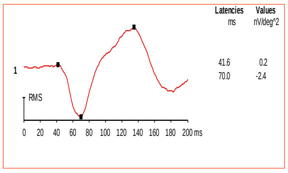
VEP Multifocale Normale

Rings

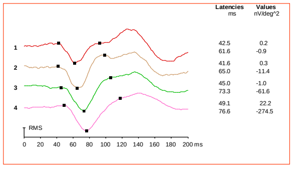



Rings
1
3
5
7
9
11
2
4
6
8
10
12

Absolute Response



Normalized Response

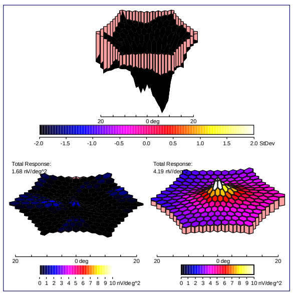


Applicazioni Cliniche

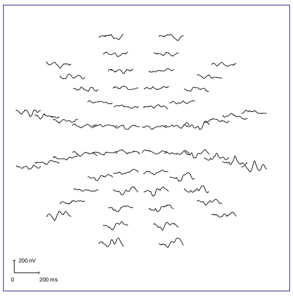
- Retinite Pigmentosa
- Maculopatie
- Glaucoma
- Neuriti Ottiche

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

Mf-ERG

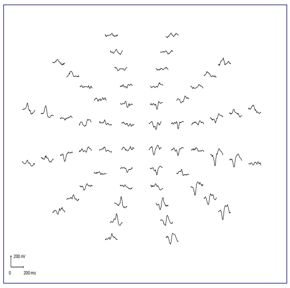

20
0 deg
20
-2.0
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0 StDev
Total Response:
1.68 nV/deg^2
Total Response:
4.19 nV/deg^2
0 deg
0 1 2 3 4 5 6 7 8 9 10 nV/deg^2

Mf-VEP

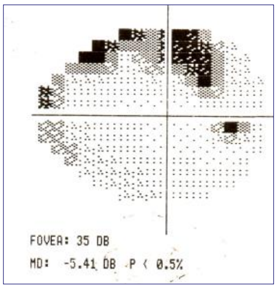

200 nV
0
200 ms

Subject C.A.: 56 years, Glaucoma

Mf-VEP


200 nV
0
200 ms

Visual Field

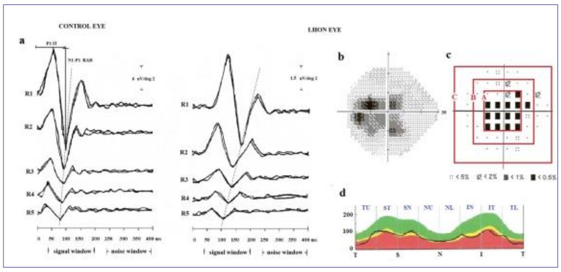

FOVEA: 35 DB
MD: -5.41 DB P < 0.5%

Leber's Optic Neuritis

Graefes Arch Clin Exp Ophthalmol. 2015 Mar 17. [Epub ahead of print]

Multifocal VEP provide electrophysiological evidence of predominant dysfunction of the optic nerve fibers derived from the central retina in Leber's hereditary optic neuropathy.

Ziccardi L[1], Parisi V, Giannini D, Sadun F, De Negri AM, Barboni P, La Morgia C, Sadun AA, Carelli V.



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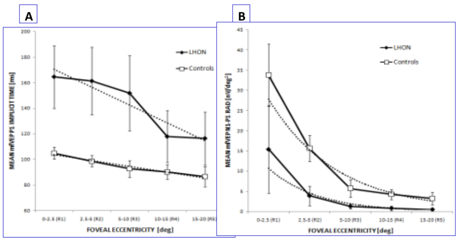


Greatest delay in the papillo-macular bundle

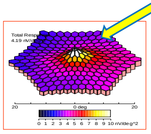
Quanto viene influenzata la risposta corticale da eventuali deficit localizzati retinici?

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

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

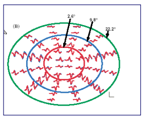
Metodo

RISPOSTE MULTIFOCALI

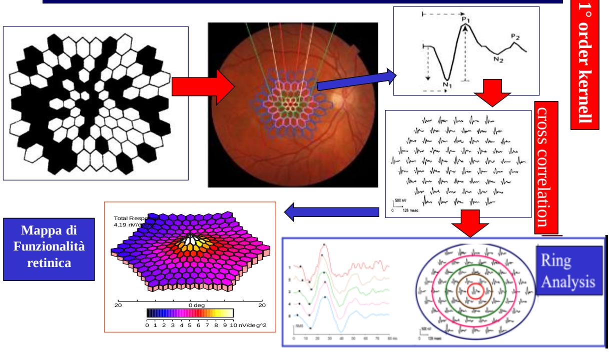


mfERG

mfVEP



ERG Multifocale: stimolo visivo e risposta elettrofunzionale



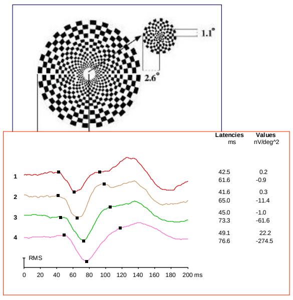
1° order kernell

cross correlation

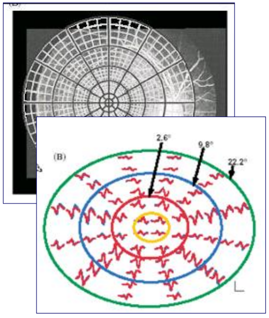
Mappa di Funzionalità retinica

Ring Analysis

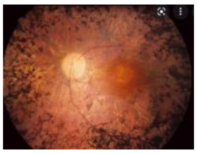
VEP Multifocale: stimolo visivo e risposta elettrofunzionale



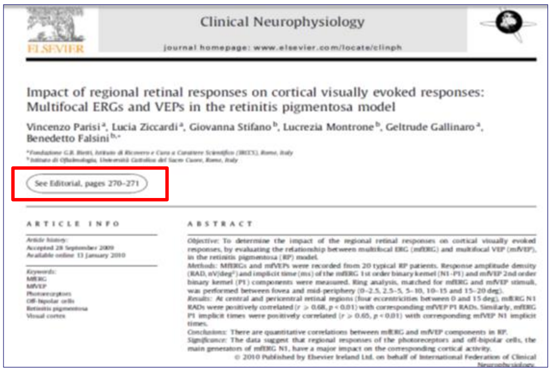
Latencies ms	Values nV/deg^2
42.5	0.2
61.6	-0.9
41.6	0.3
65.0	-11.4
45.0	-1.0
73.3	-61.6
49.1	22.2
76.6	-274.5



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



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,*]

[a] Fondazione G.B. Bietti, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Roma, Italy
[b] Istituto di Oftalmologia, Università Cattolica del Sacro Cuore, Roma, Italy

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MfVEP
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Off-bipolar cells
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

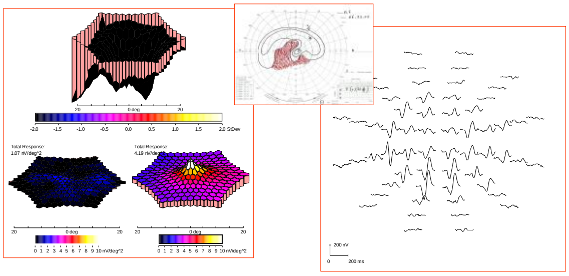
Ganzfeld ERG (ISCEV standard)

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

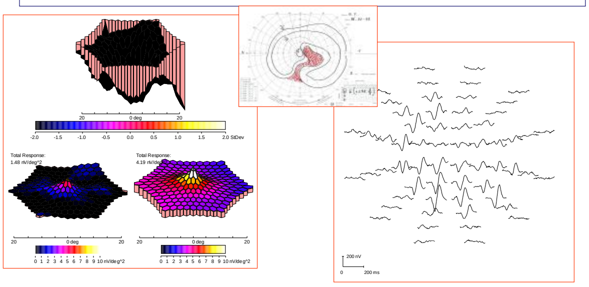
Soggetto B.A.: 34 anni, RP, OS

mfERG — Campo Visivo — mfVEP



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

mfERG — Campo Visivo — mfVEP



CORRELAZIONI TRA AREE RETINICHE E LE RELATIVE PROIEZIONI CORTICALI:

5 LIVELLI DI ECCENTRICITA'

MERG — MVEP

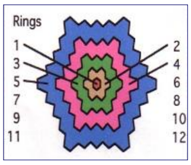
R1:0-2.5 gradi

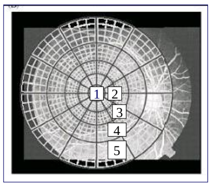
R2:2.5-5 gradi

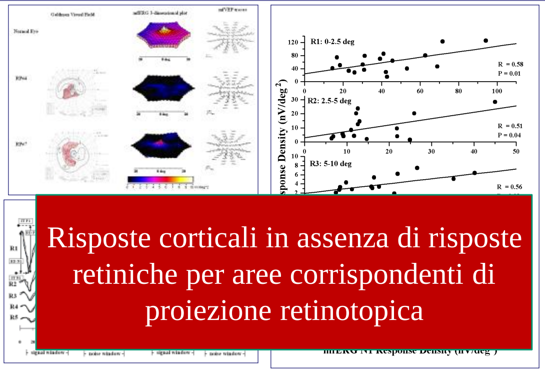
R3: 5-10 gradi

R4:10-15 gradi

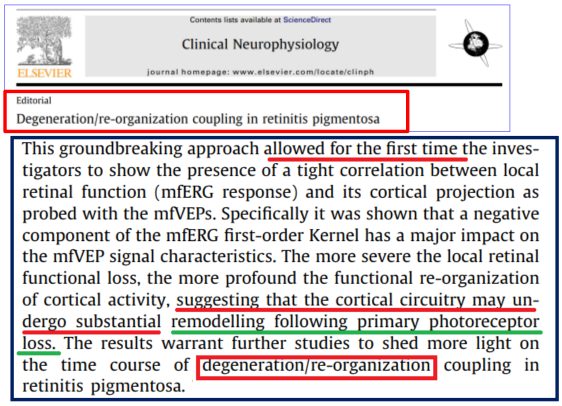
R5:15-20 gradi







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



Contents lists available at ScienceDirect

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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.

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

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

Coautori degli studi presentati

Retinite pigmentosa
Prof. Benedetto Falsini
Dott.ssa Lina Gallinaro
Dott.ssa Lucia Ziccardi
Dott.ssa Giovanna Stifano

Pucker Maculari
Dott.Guido Ripandelli
Dott.Andrea Coppè
Dott.ssa Lina Gallinaro
Prof. Mario Stirpe

Glaucoma
Prof. Gianluca Manni
Prof. Marco Centofanti
Dr.ssa Lina Gallinaro
Dr.ssa Lucia Tanga
Dr.ssa Lucia Ziccardi
Prof. Massimo G. Bucci

CNV miopica e AMD
Dott.ssa Monica Varano
Dott.ssa Lina Gallinaro
Dr.ssa Loredana Perillo
Dr.ssa Nicoletta Capaldo
Dr. Massimiliano Tedeschi

Neuroftalmologia
Prof. Francesco Pierelli
Prof. Leoluca Parisi
Prof. Francesco Fattapposta
Prof. Federico Bianco
Dr.ssa Rita Restuccia

Grazie dell'attenzione!!!