



OFTALMOPATIA DI GRAVES: PERCORSO MULTIDISCIPLINARE

La neuropatia ottica e lo studio neurofisiologico

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Neuropatia ottica distiroidea (DON)

Dysthyroid optic neuropathy (DON) is a condition associated with Graves' hyperthyroidism that affects the optic nerve, leading to visual impairment

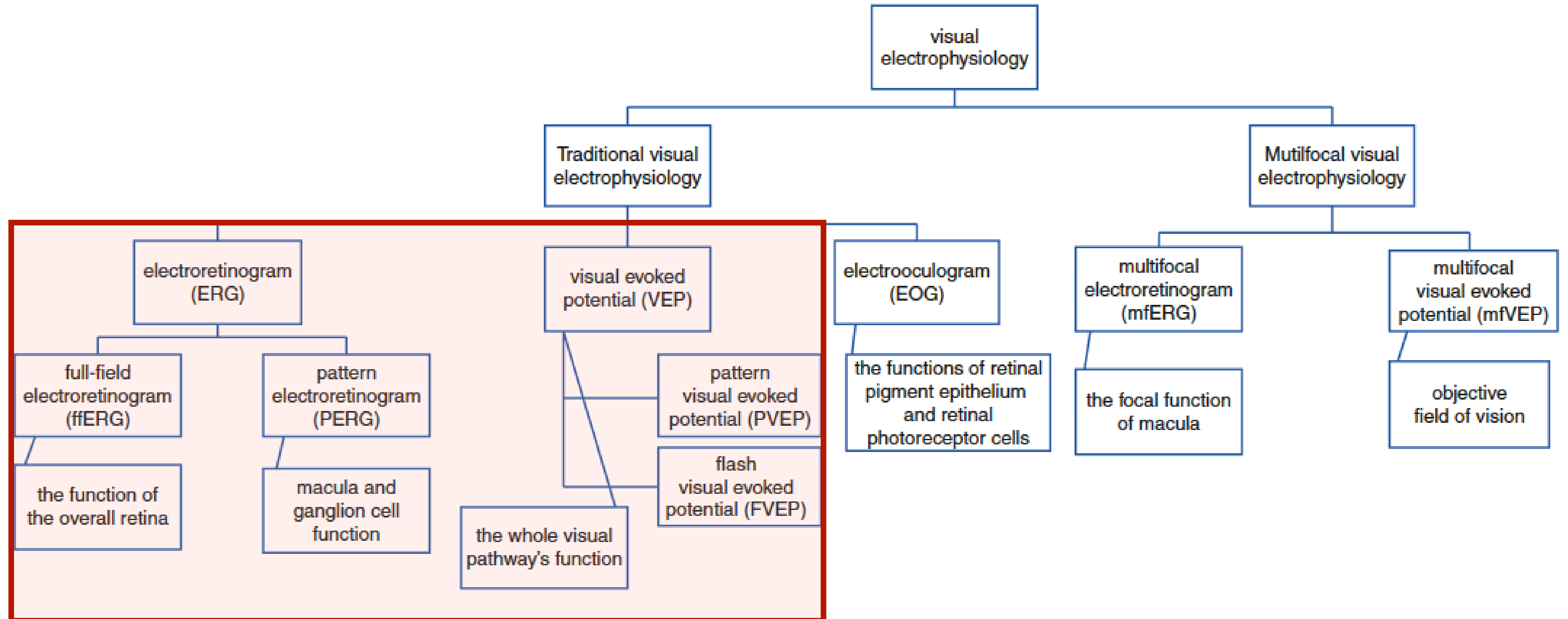
Dysthyroid optic neuropathy (DON) is a severe complication of thyroid eye disease (TED)

DON in 4-8% of TED

A large survey by the European Group on Graves' Orbitopathy (EUGOGO) collaboration reported that patients with Graves' orbitopathy (GO) are assumed to have DON if they exhibit at least one of the following:

- impaired colour vision,*
- optic disc swelling or atrophy,*
- abnormal visual acuity (VA), relative afferent pupillary defect (RAPD),*
- **abnormal visual evoked potential,***
- apical crowding on radiology*
- abnormal visual field (VF)*

Visual Electrophysiology



Indicazioni PEV

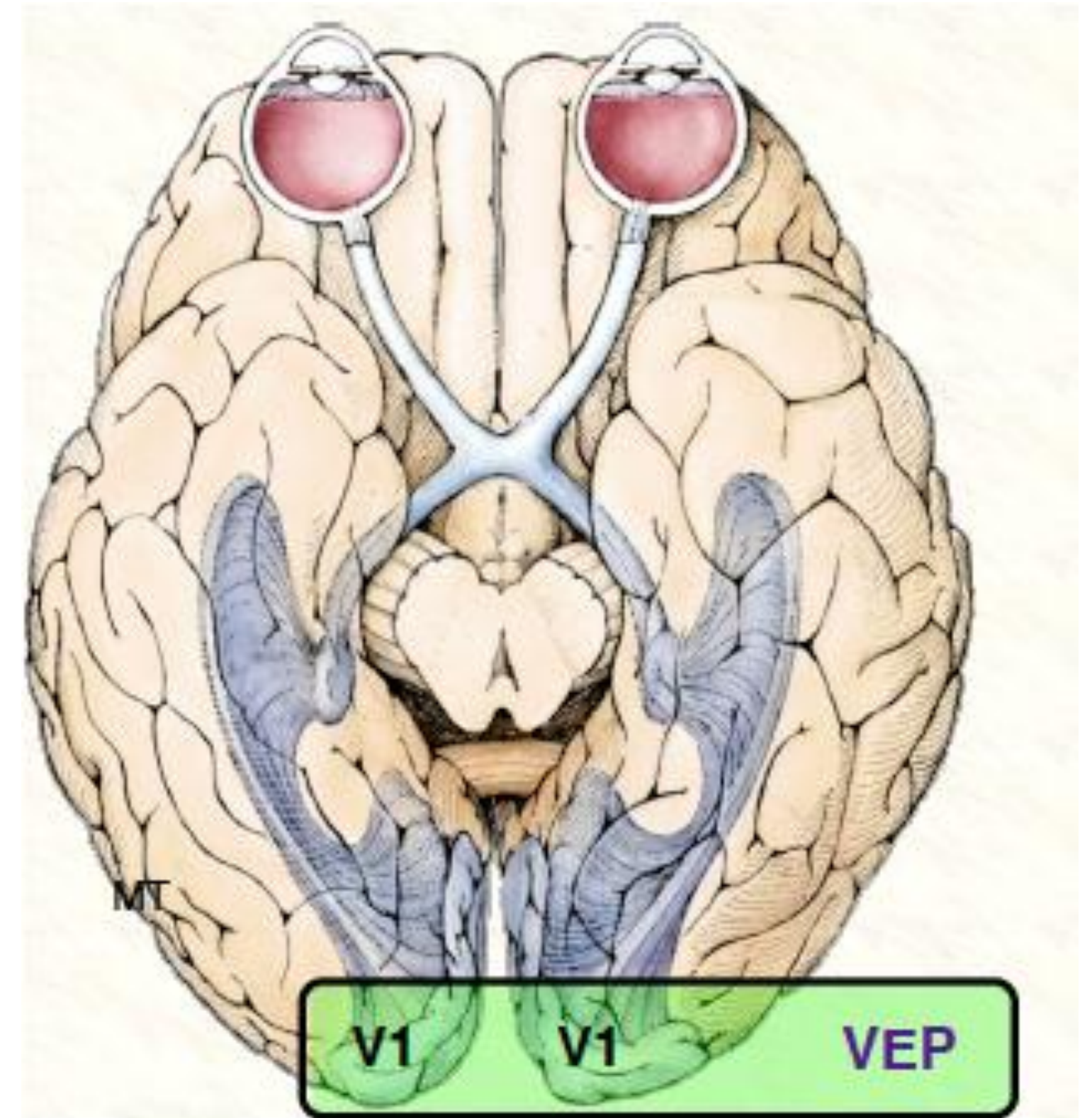
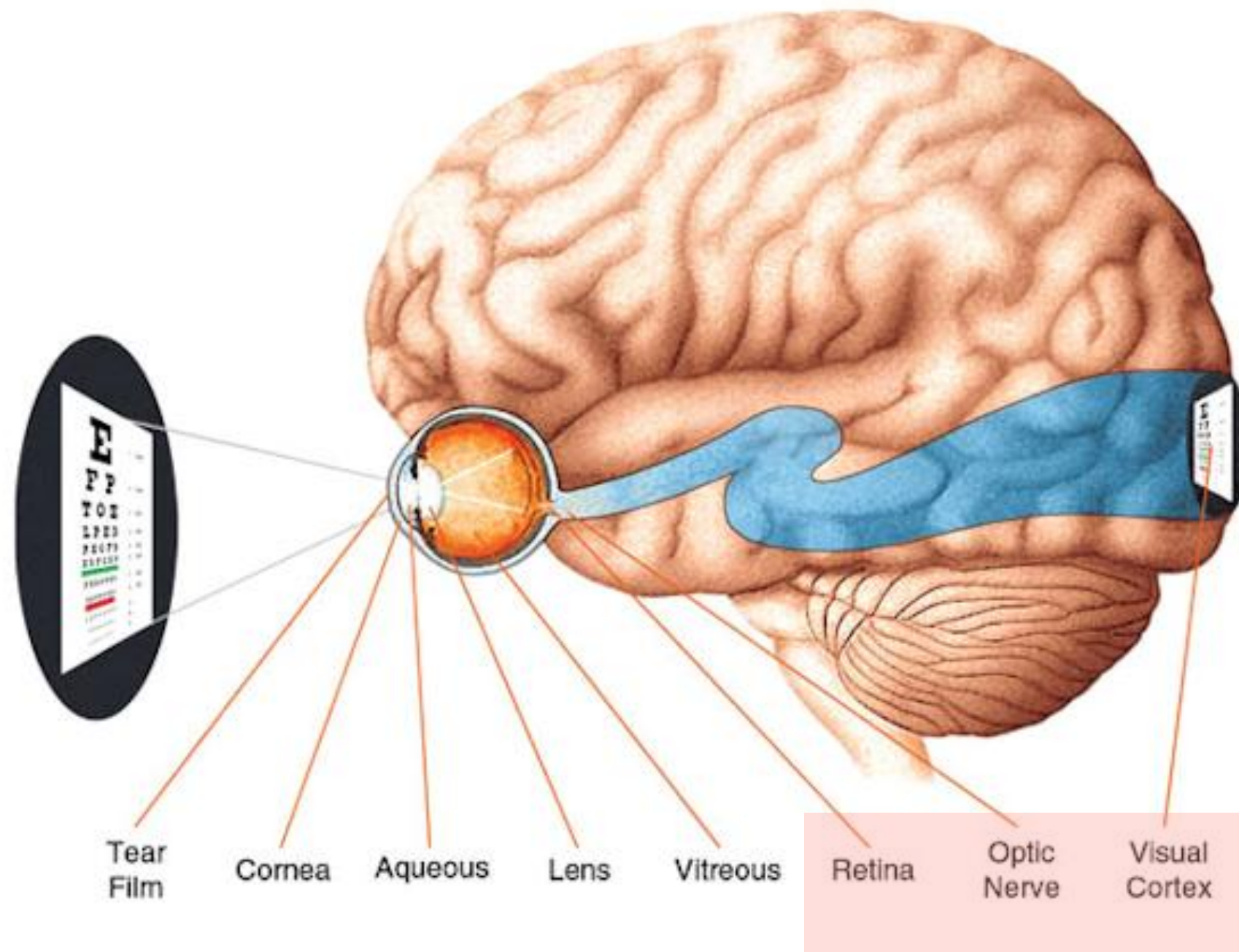
Clinical use of Pattern VEP

- Optic nerve dysfunction
(demyelination, toxicity, compression)
- Chiasmal and retrochiasmal dysfunction
- Intracranial misrouting
(albinism)
- Objective VA assessment

Important! - the PVEP is usually abnormal in macular dysfunction

Clinical use of Flash VEP

- As a complement to the pattern VEP
- Media opacities / poor visual acuity
- Poor patient compliance
- Babies and infants



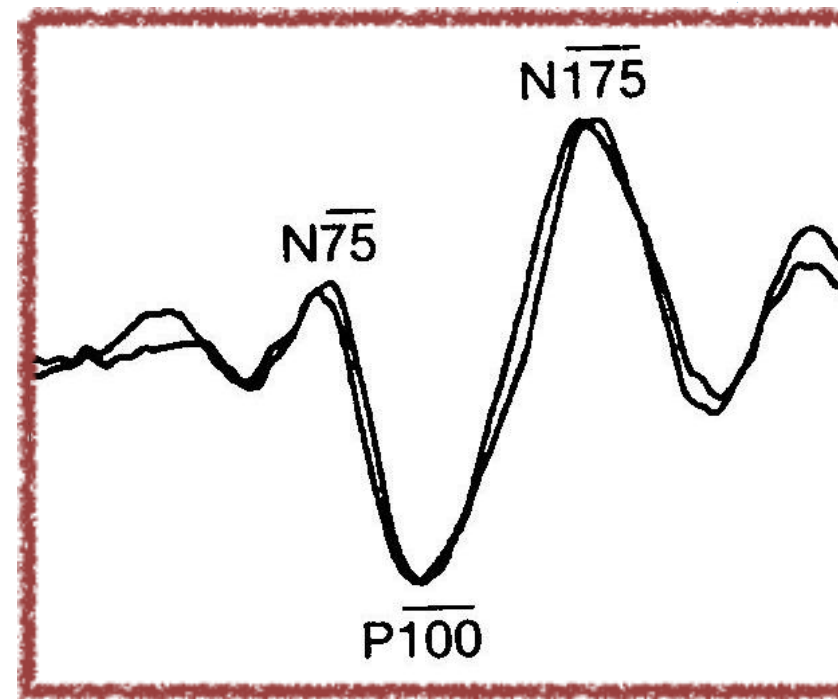
Potenziali evocati visivi - PEV

Potenziali Evocati Visivi (PEV):

Lo scopo è valutare la funzionalità della via nervosa visiva (retina, nervo ottico, corteccia), valutando la risposta corticale a stimoli visivi.

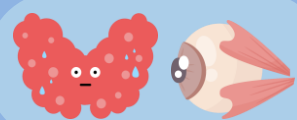
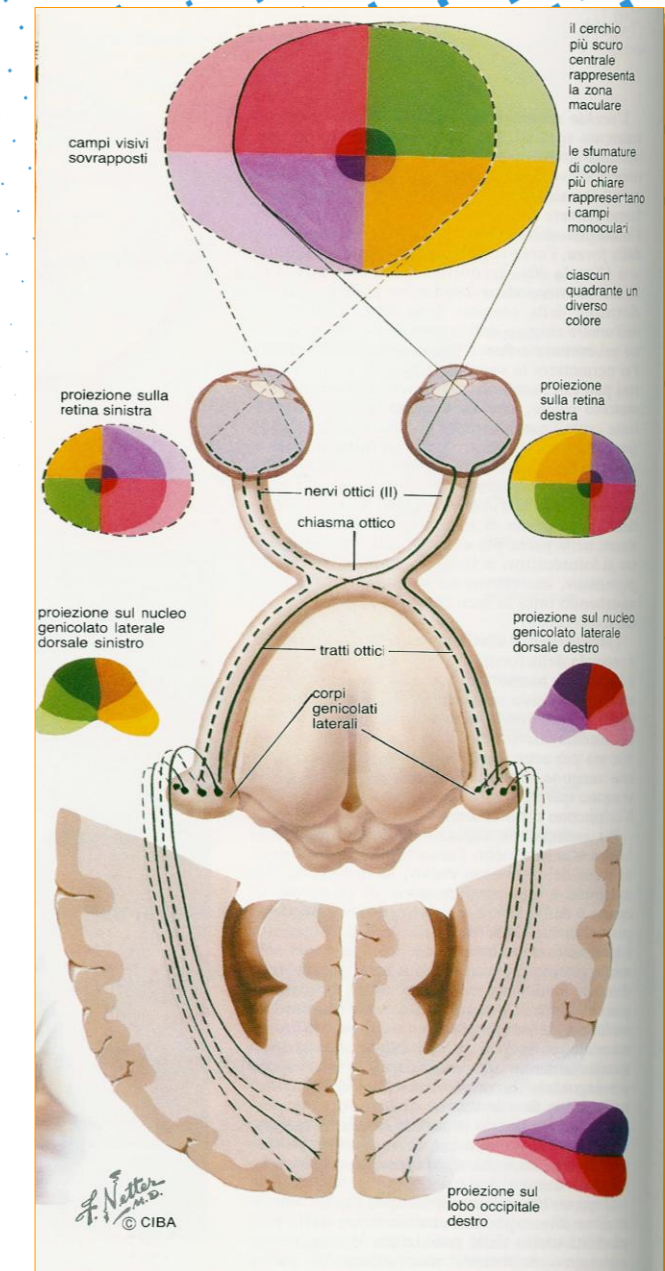
Registrazione

- Esame non invasivo
- Elettrodi registranti: O'z, + 7,5cm (dx/sx)
- Elettrodi a coppetta o cuffia (ago in casi particolari)
- Seduto, 1 m dal monitor
- Monoculare
- Almeno 2 Chexs (60' e 15')



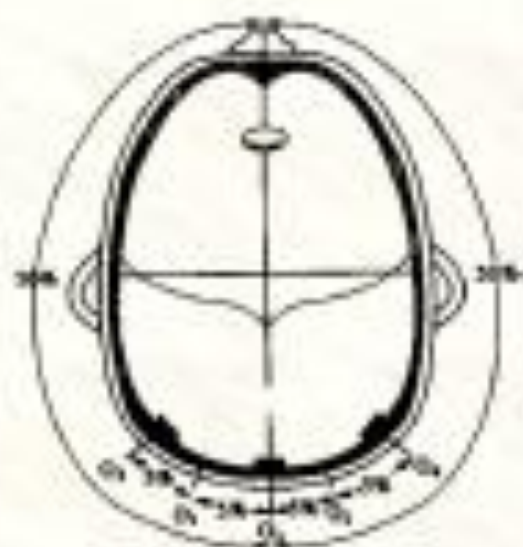
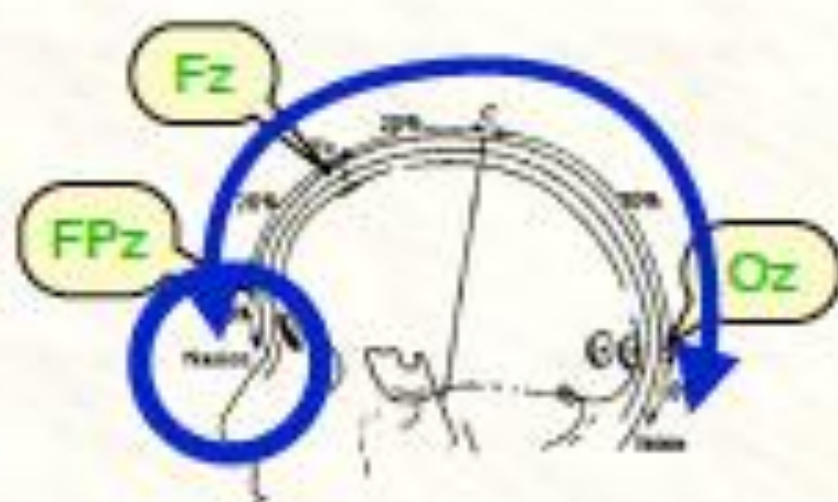
PEV = onda elettrica registrata dallo scalpo, elicitata da stimoli visivi

Il maggior contributo al PEV è dato dai quadranti centrali del CV relativi alla Corteccia del Polo Occipitale
P100 = 10° centrali (molto da 2° centrali)



Recording – Equipment related

- Amplifier bandwidth
 - 1–100 Hz (1 Hz Δ 0.16 s)
 - Artefact threshold $\approx 100 \mu\text{V}$
- Electrode positions
 - 10-20 System
 - for Pre-chiasmal assessment:
Oz (O3 + O4)
 - for Post-chiasmal:
Oz, O3, O4, (O1, O2)
 - Reference Fz (FPz)
- Impedance $< 5\text{k}\Omega$ and equal

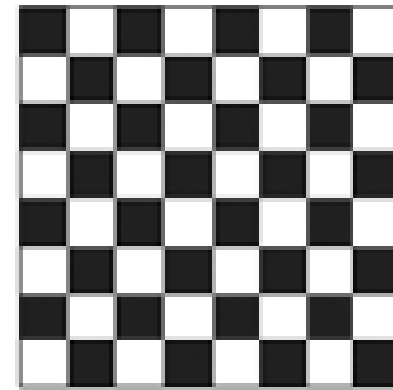


Tipi stimolo visivo

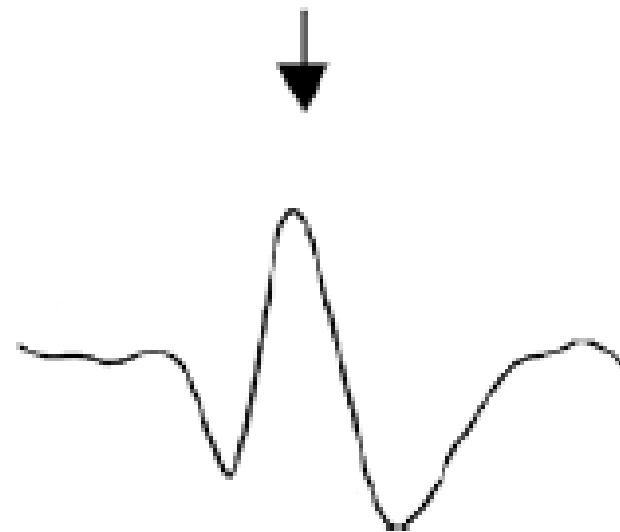
PEV

PE stimolo correlato

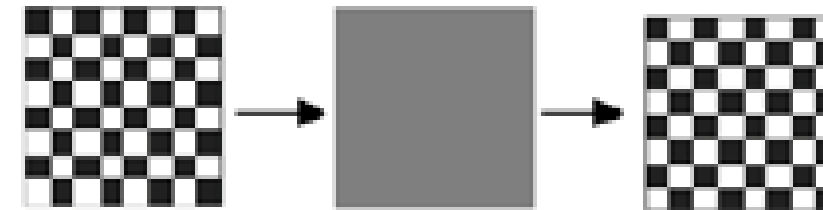
Pattern Reversal VEP



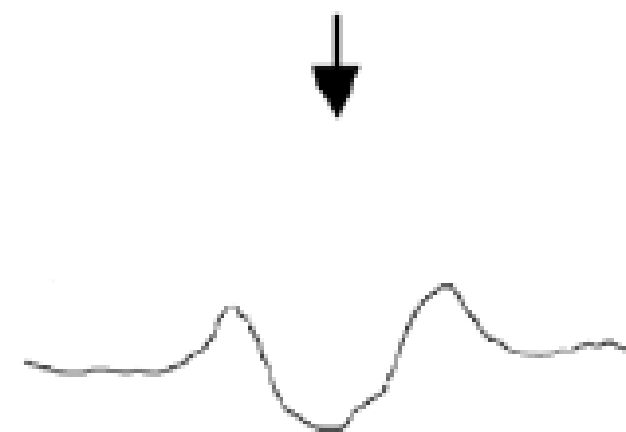
Reversing black & white checkerboard stimulus



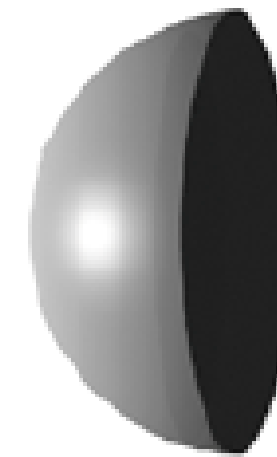
Pattern Onset/Offset VEP



Reversing black & white checkerboard stimulus with diffuse blank screen at regular intervals



Flash VEP



Flash stimulus $\geq 20^\circ$ delivered with monitor or full-field dome

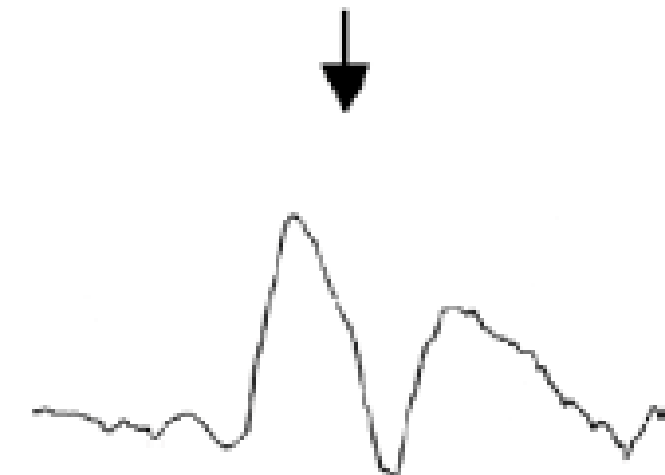


Figure 5.3 Clinical VEP responses. At least one of the three standard VEP responses should be included in clinical VEP assessment. In most cases, the pattern reversal VEP is the study of choice because it generates relatively consistent and vigorous responses from the visual cortex.

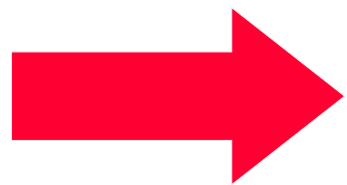
PEV - Stimolo

FLASH

- Stimolo non strutturato
- Luce bianca o filtri monocromatici per differenziare fotorecettori retinici
- Variazione di luminanza

PATTERN

- Stimolo strutturato (scacchi, grating...)
- Variazione di contrasto
- Luminanza costante
- Onset/offset, reversal



**CIRCUITI NEURONALI DIVERSI PER VARIAZIONE DI LUMINANZA
E VARIAZIONE DI CONTRASTO**

Waveform/Stimulus Pattern

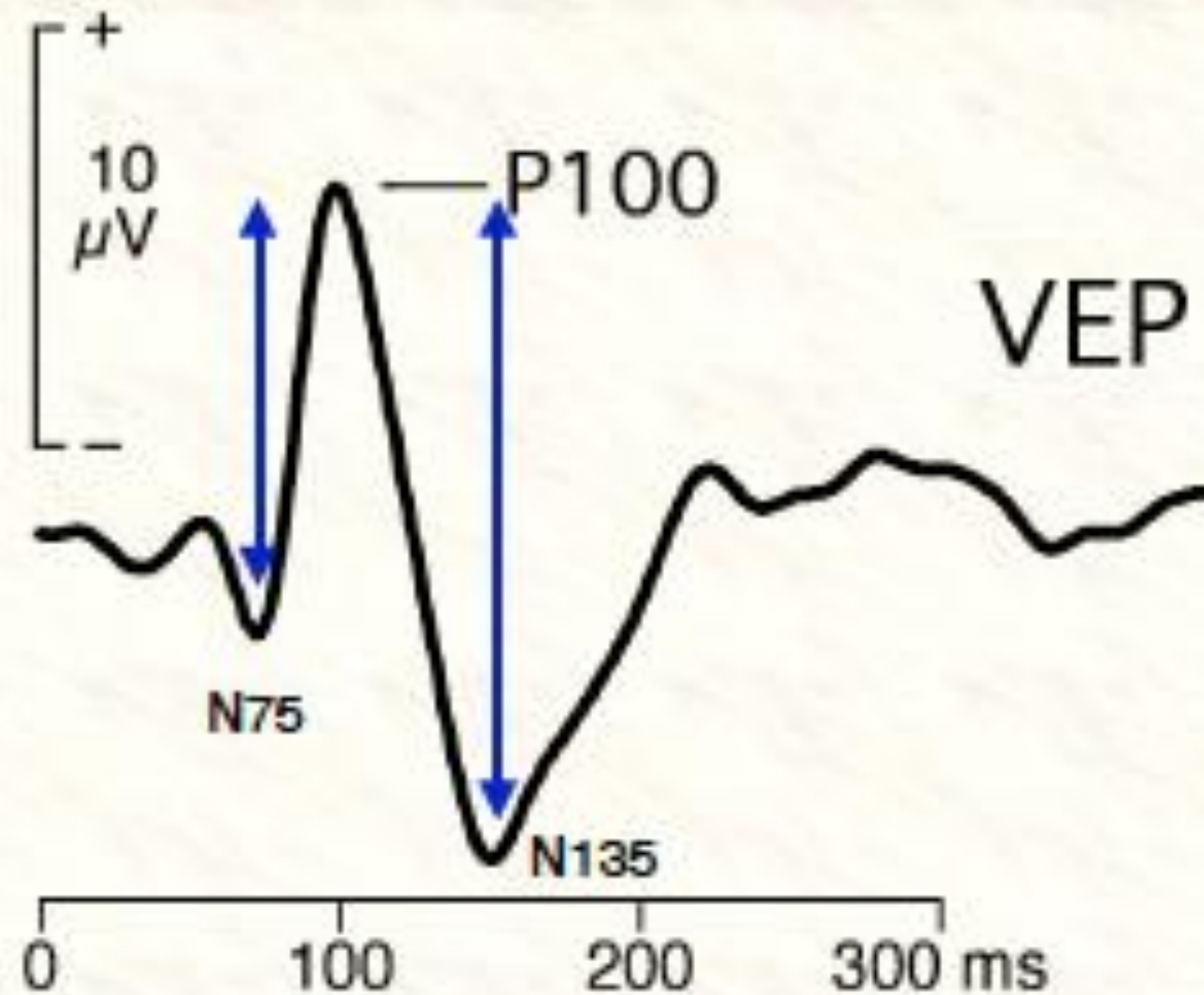


Fig. 2.4 LED backlit LCD graphic stimulator



Fig. 2.7 Handheld graphic stimulator

Normal transient pattern-reversal VEP



Peak time (= latency): P100

Amplitude: N75-P100
[or: average of
N75-P100 and P100-N135]

Traditional term: "Latency".

Misleading: there are always earlier deflections.

ERG's "implicit time" not any better.

Generic term, intuitive & always correct: **"peak time"**

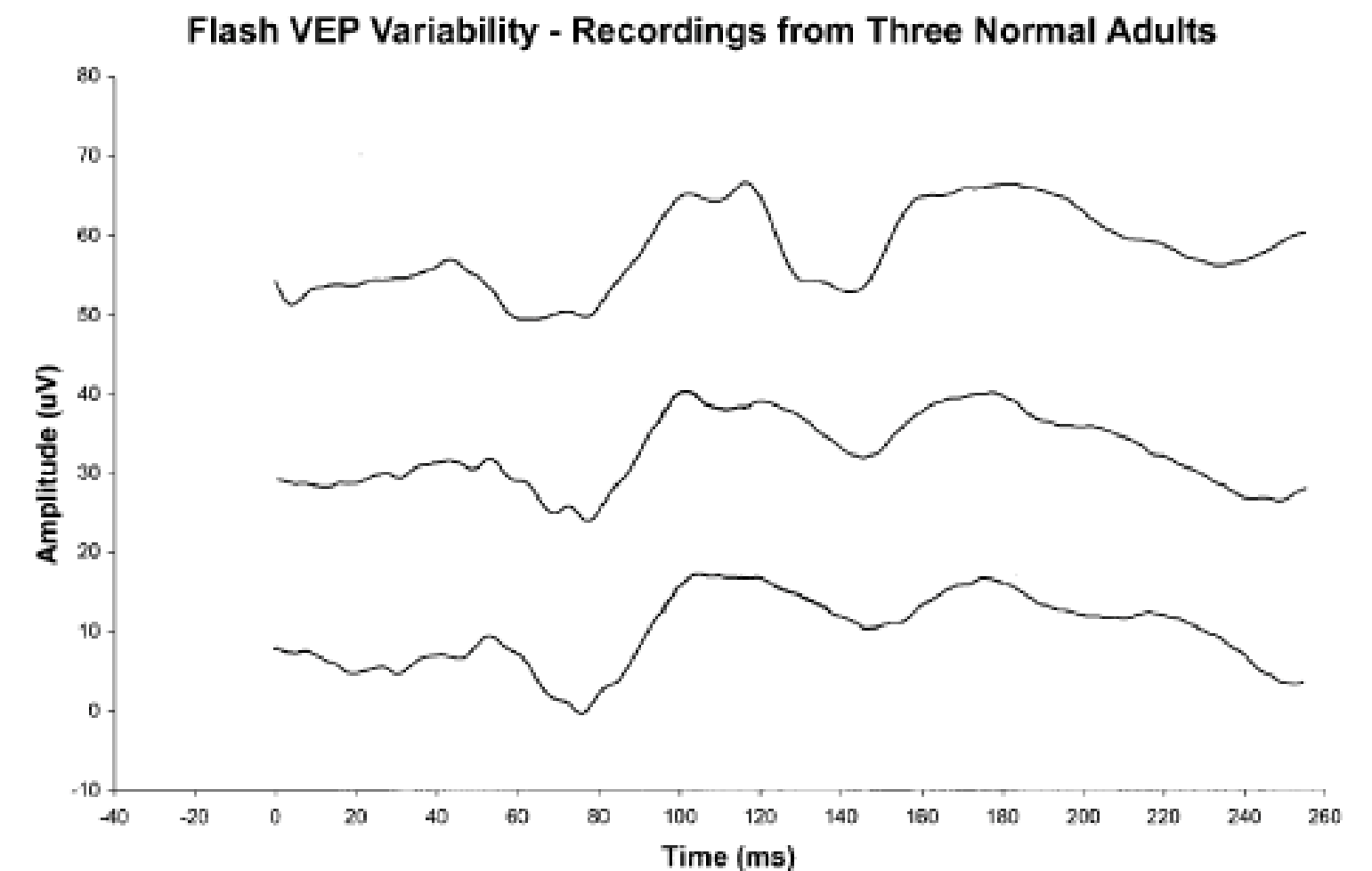
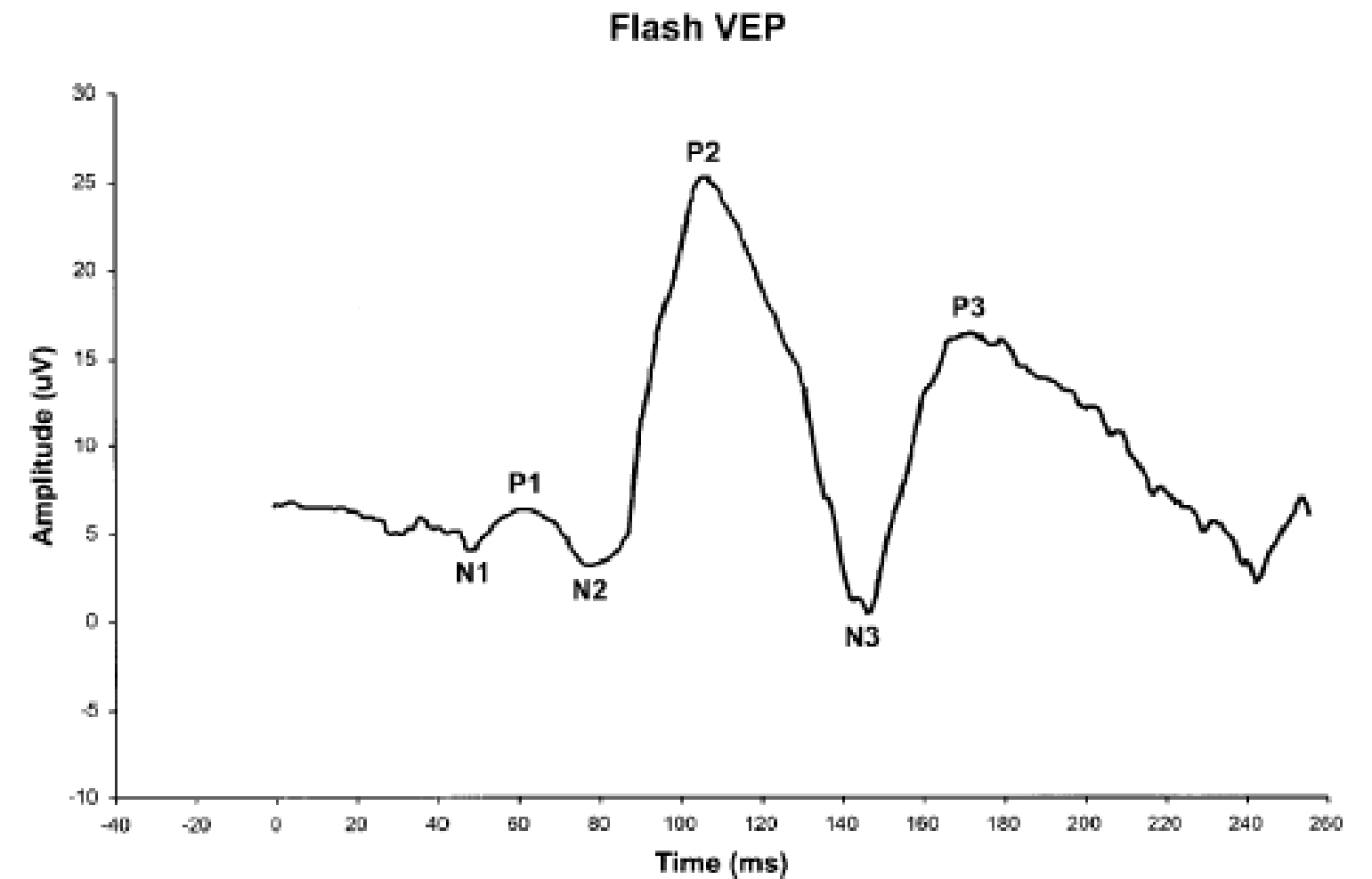
F-PEV Waveform

- Stimolo flash (non strutturato)
- Vantaggi: pz non collaborante (bambini, coma), scarsa acuità visiva
- Larga variabilità della risposta
- Scarsamente sensibile
- Interpretazione → presenza-assenza, asimmetria



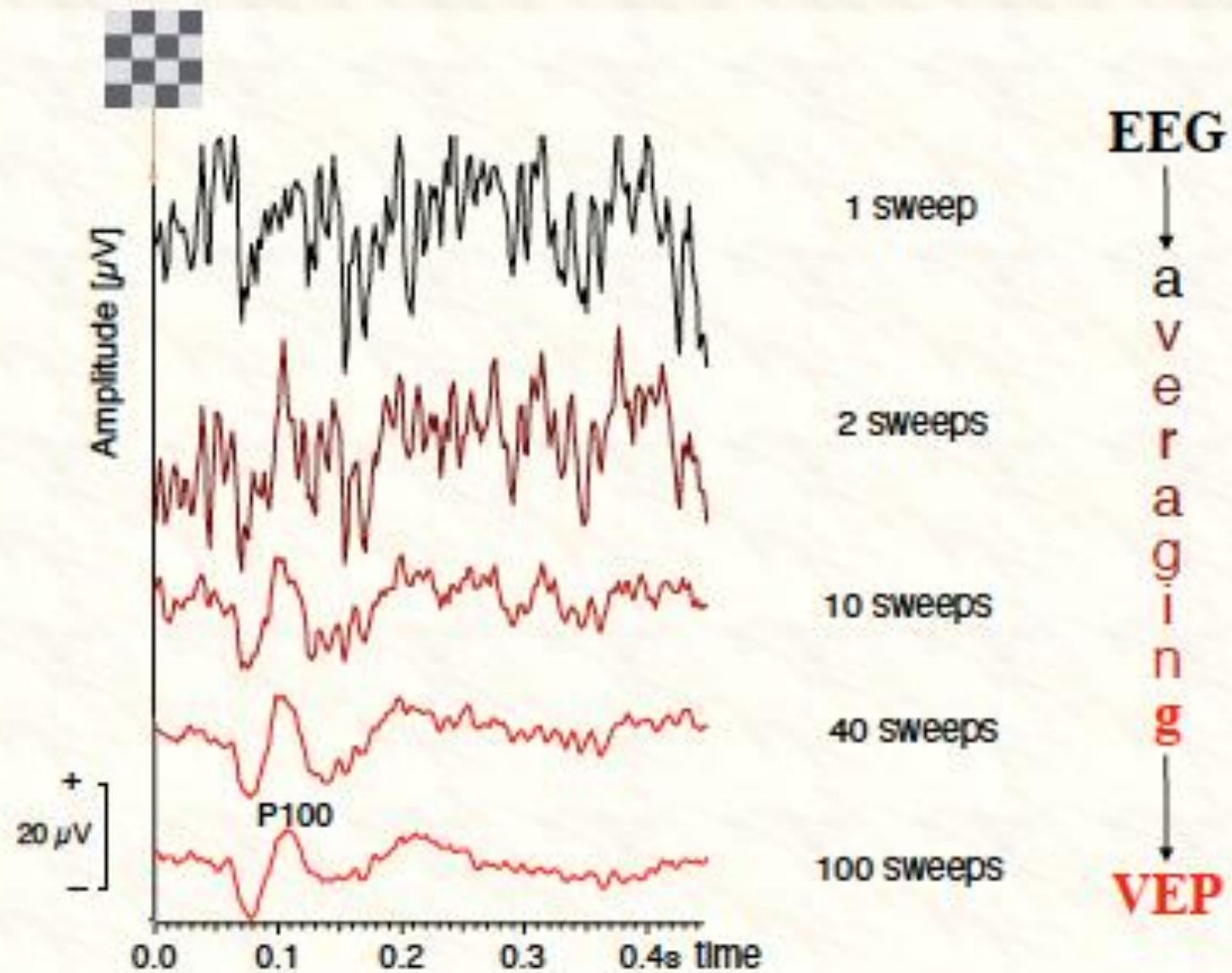
Fig. 2.8 Babyflash instant control flash stimulator

Forma tipica
N1-P1
N2-P2-N3
N3-P3

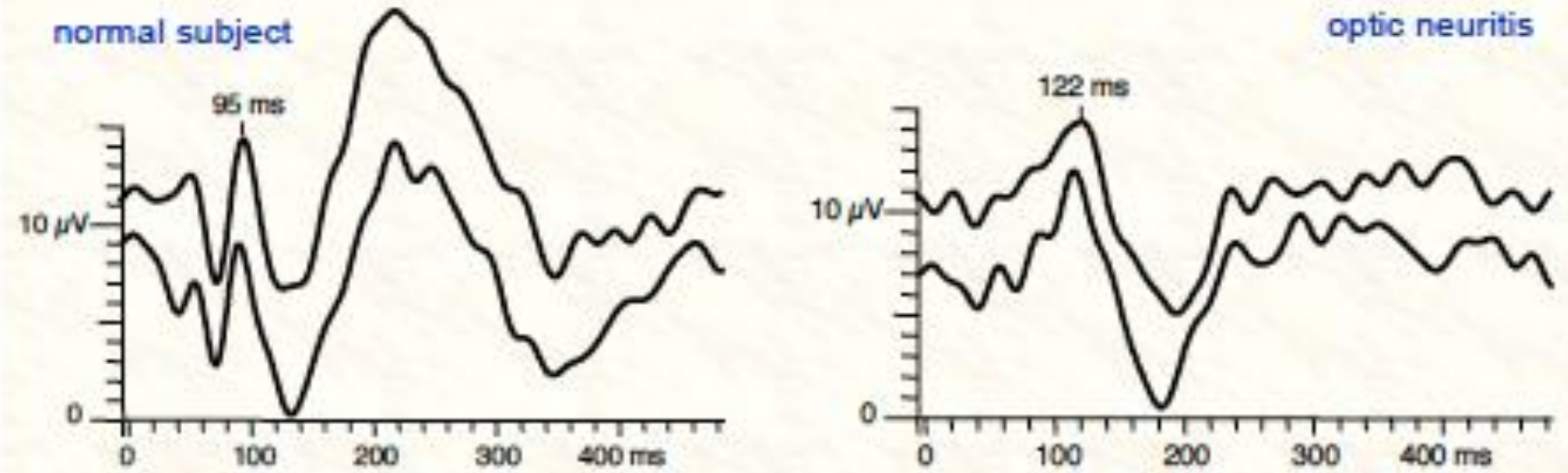


PEV note tecniche

Stimulus-synchronised averaging, EEG → VEP

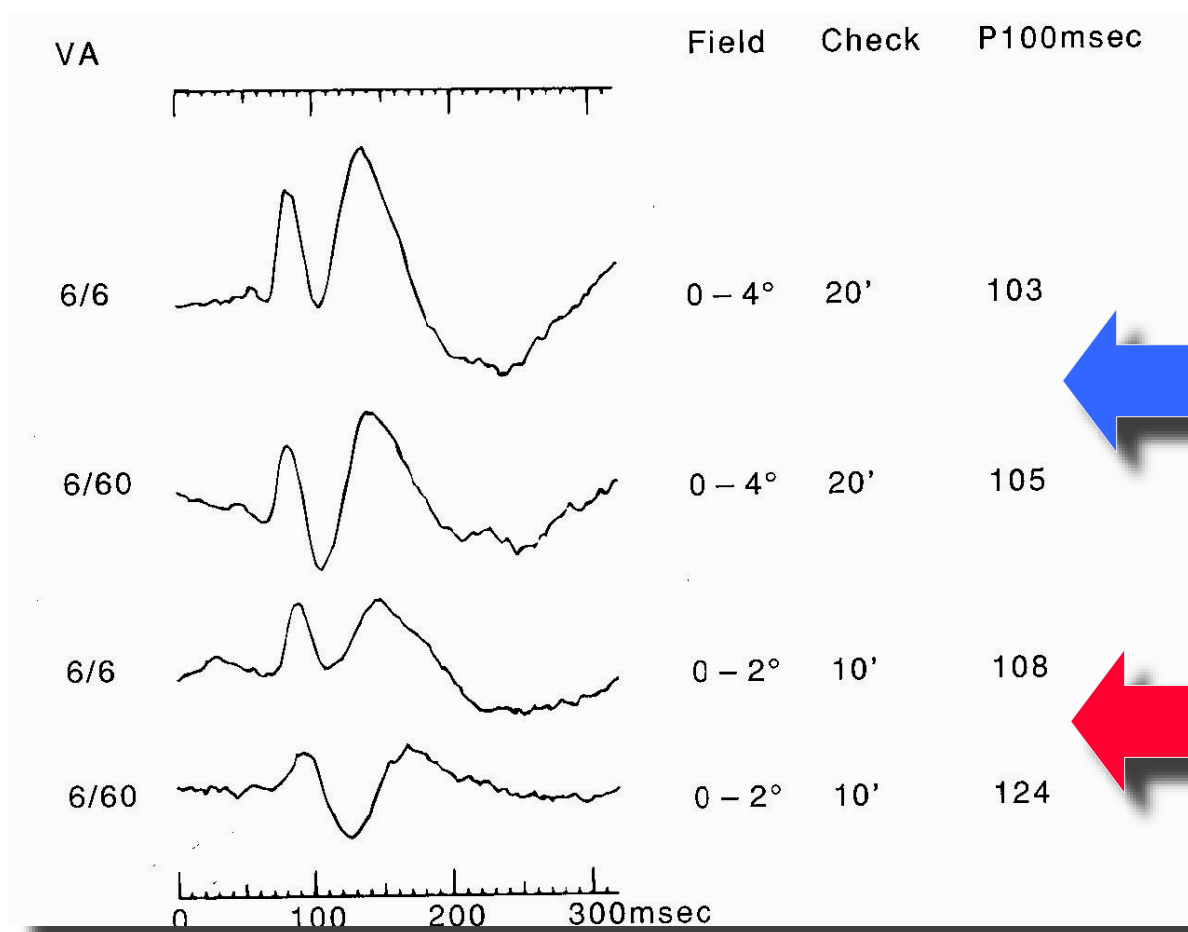


In electrophysiology, do everything twice (at least)



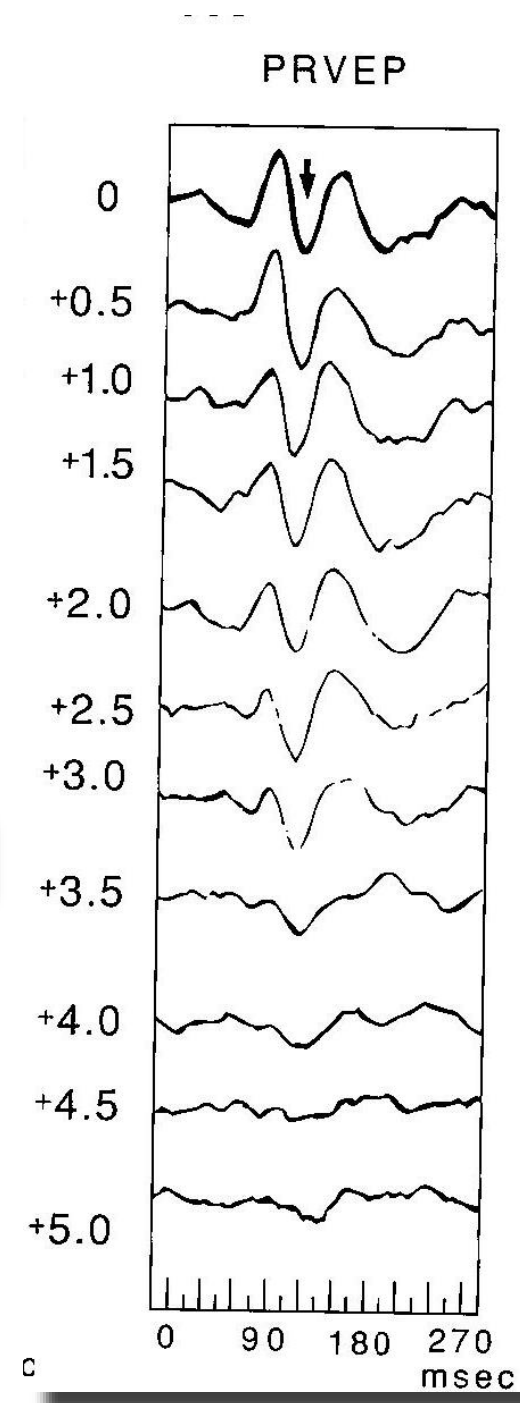
Almeno 2 tracciati riproducibili
Risposte mediate (50-100 risposte)
Almeno 2 scacchi di dimensioni diverse (60/15' - 0,25/1°)
Durata esame 40-60 min.

Fattori che influenzano l'esame PEV



Miopia

Ruolo della dimensione dello scacco nel differenziare l'occhio corretto 6/6 e non corretto 6/60



- Difetti di Rifrazione
- Cataratta
- Anisocoria/ Miosi serrate
- Colliri
- Ptosi palpebrale
- Collaborazione

**Eseguire sempre
valutazione oculistica prima!**



Generatori corticali PEV

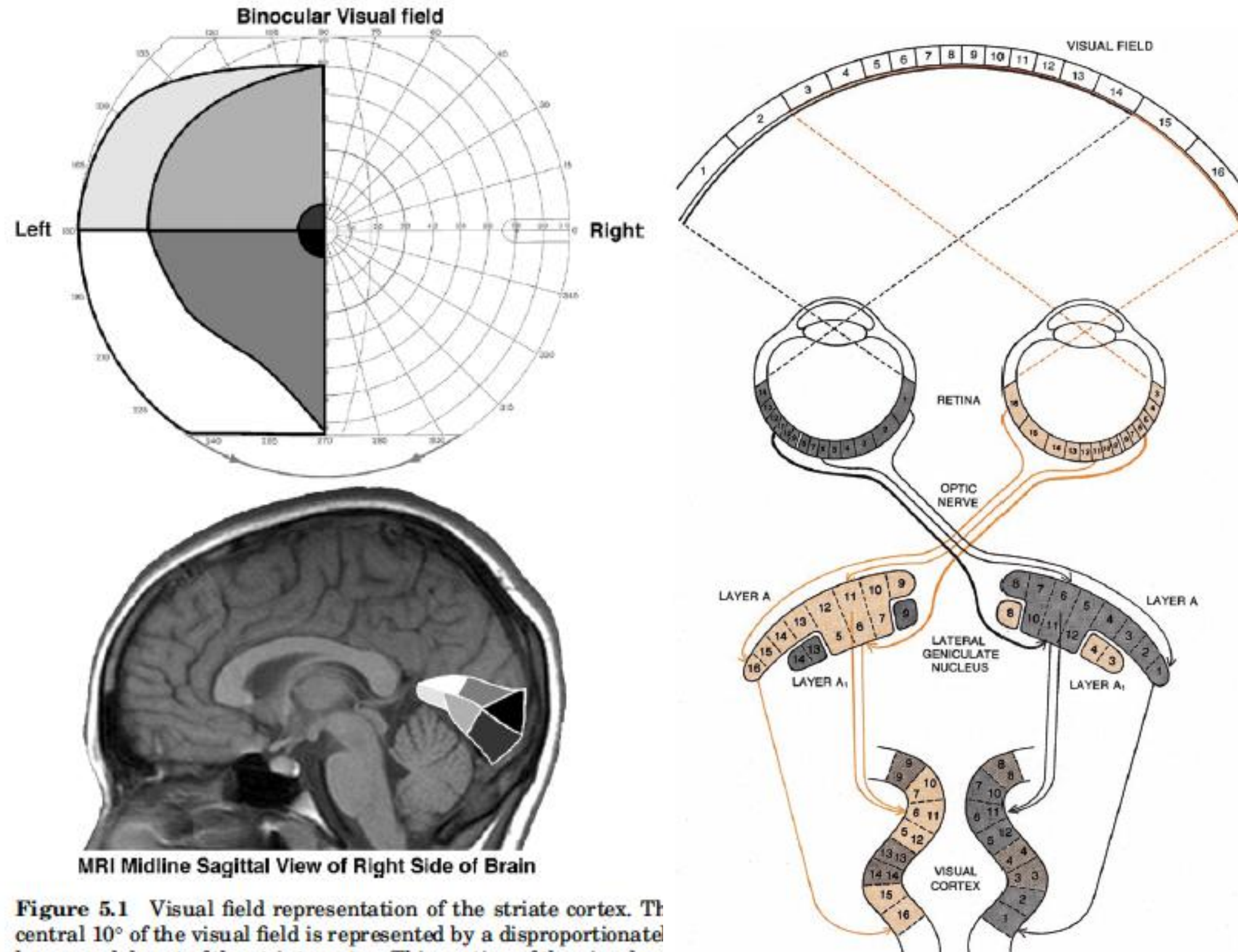
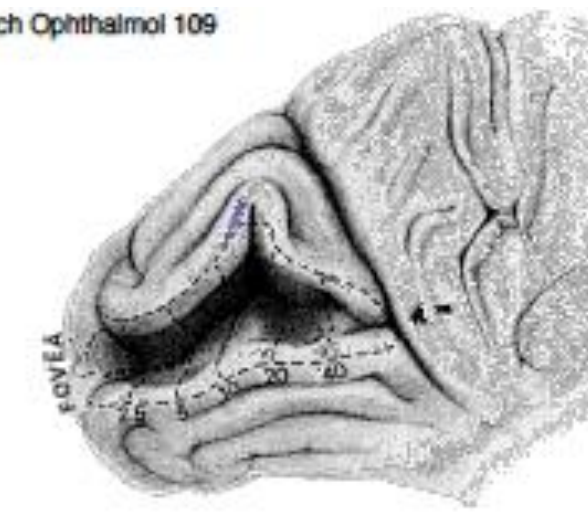


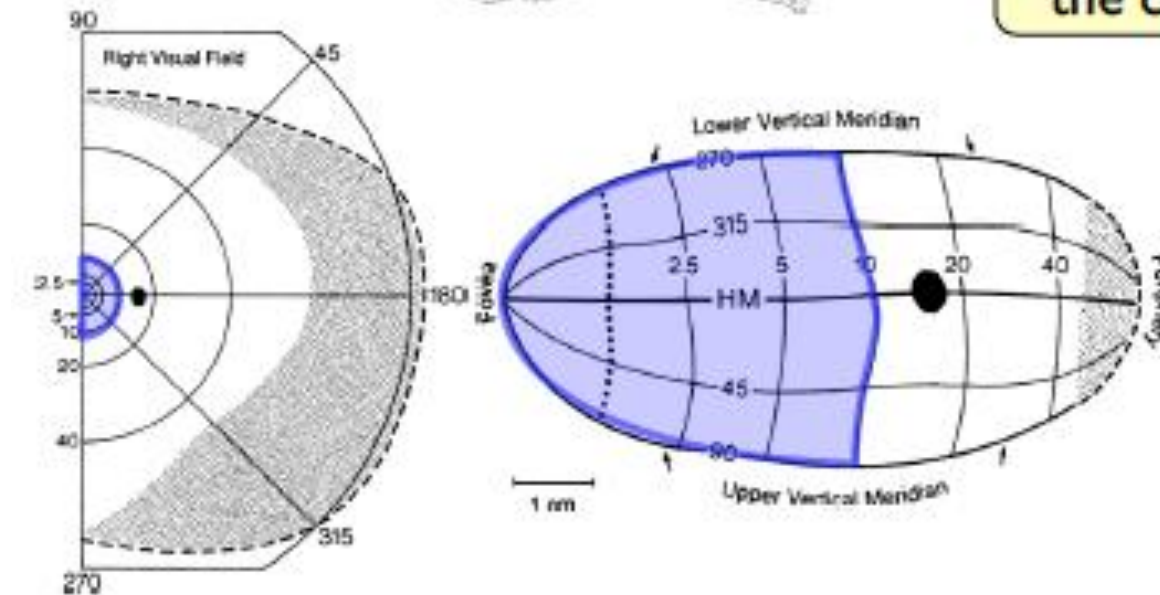
Figure 5.1 Visual field representation of the striate cortex. The central 10° of the visual field is represented by a disproportionately large caudal part of the striate cortex. This portion of the visual cortex is closest to the electrodes placed at the scalp for VEP recording, and therefore, VEP is dominated by the central visual field. In contrast, peripheral visual field is represented more anteriorly, further away from the VEP recording electrodes.

Horton & Hoyt (1991) Arch Ophthalmol 109



V1 Retinotopy

VEP is dominated by the central 10°Ø



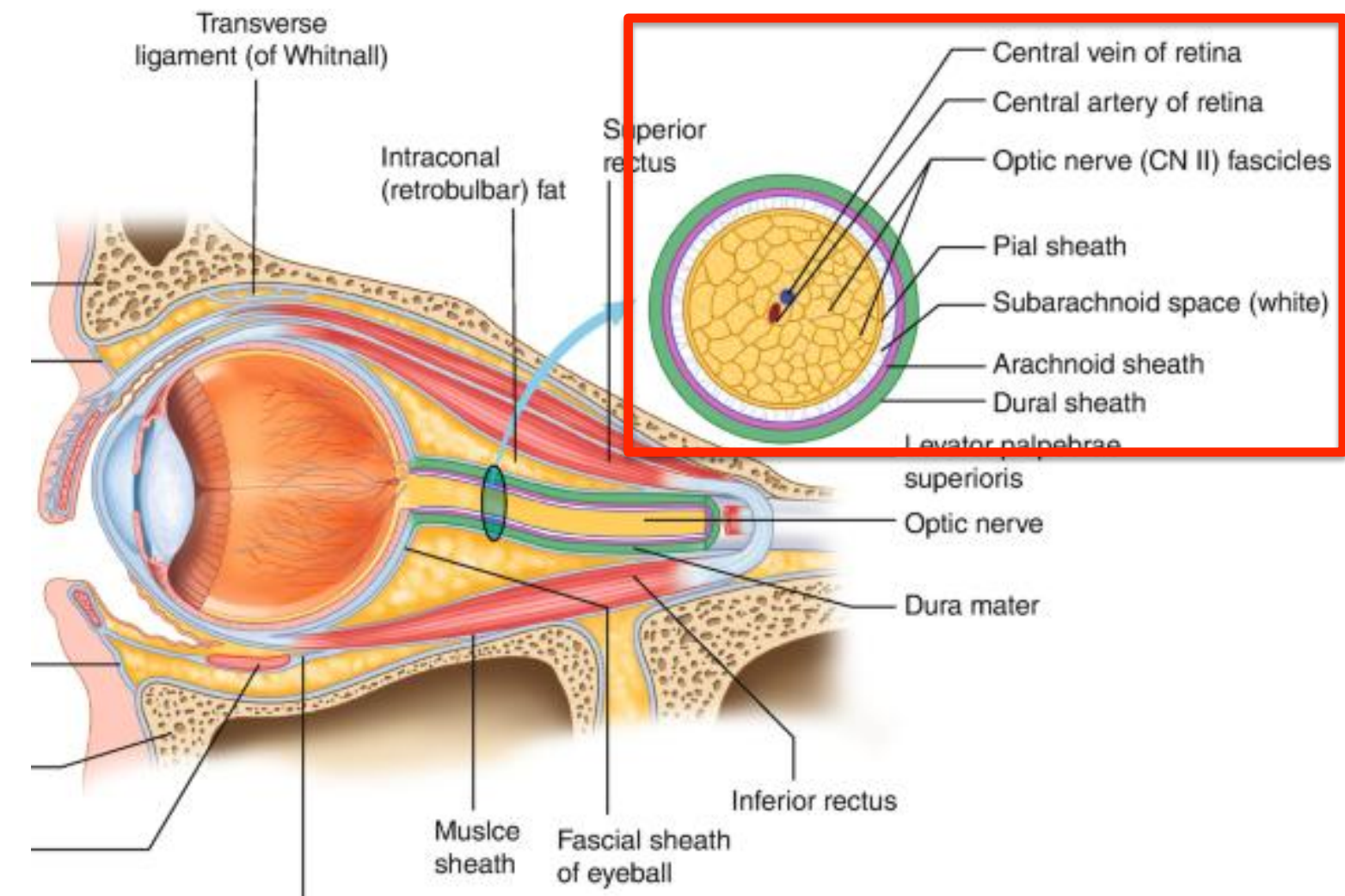
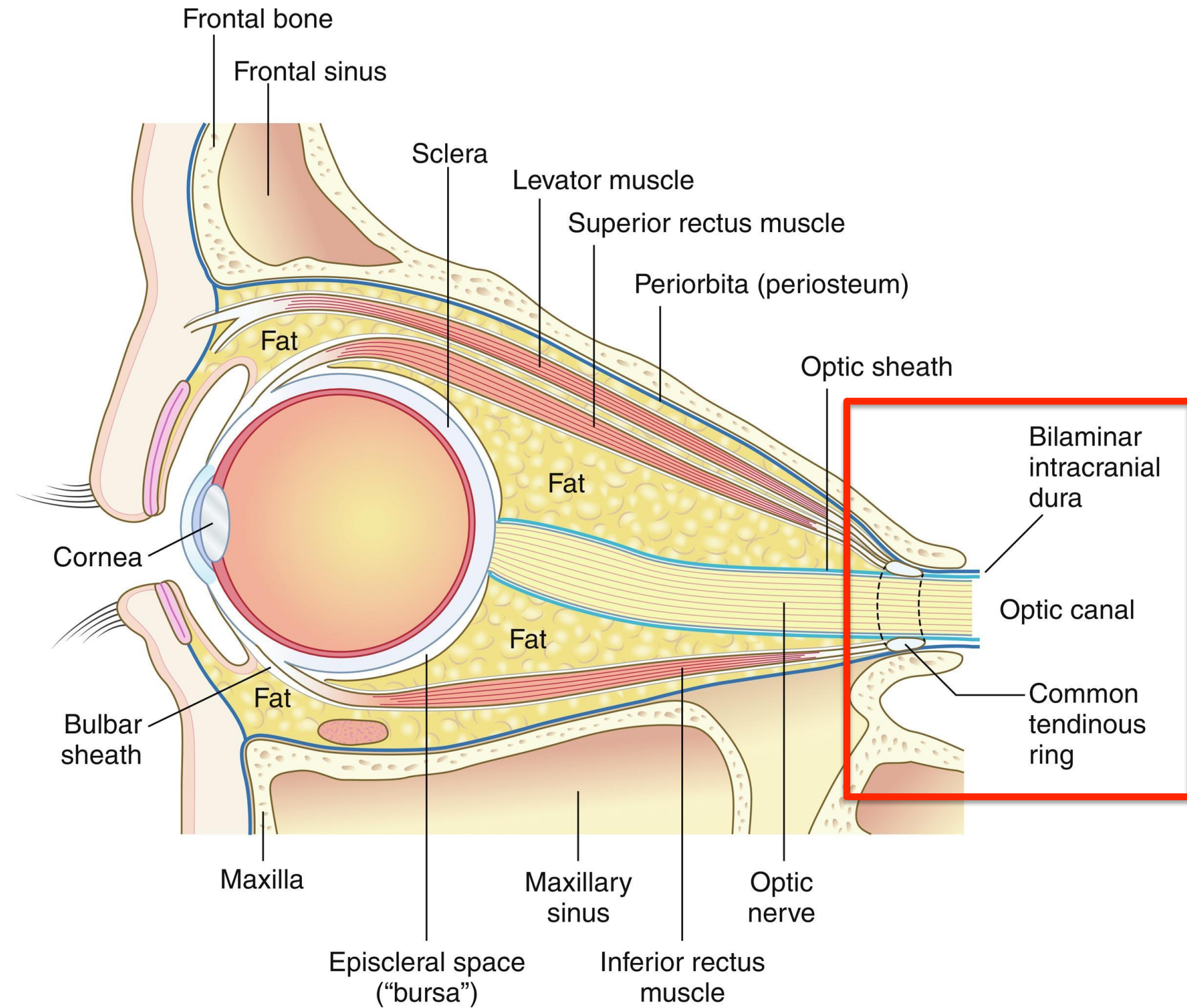
Magnificazione corticale =
mm corteccia / ° CV.

Scimmia: 6.4mm/vis.centrale;
5mm/vis. parafoveale; 0,5mm/20-
30° periferici

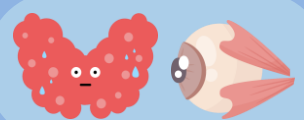
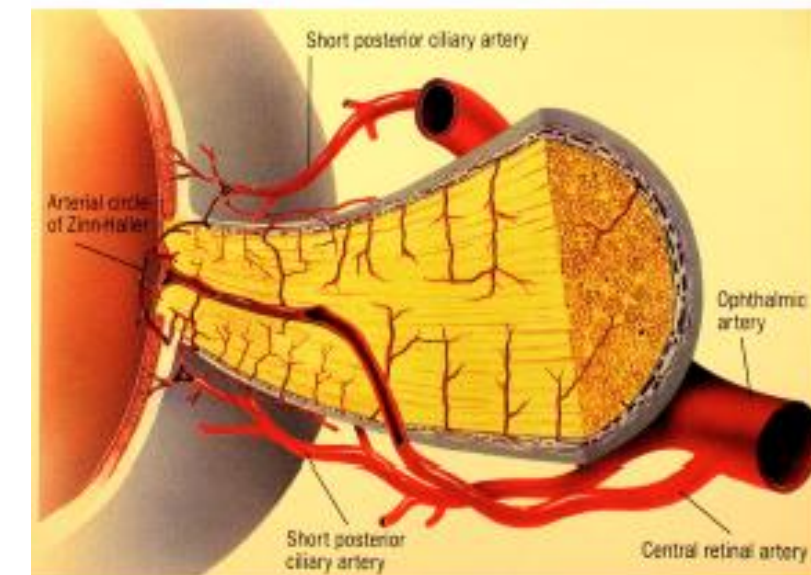
Il maggior contributo al PEV è dato dai
quadranti centrali del CV relativi
alla Corteccia del Polo Occipitale

P100 = 10° centrali (spt 2° centrali)

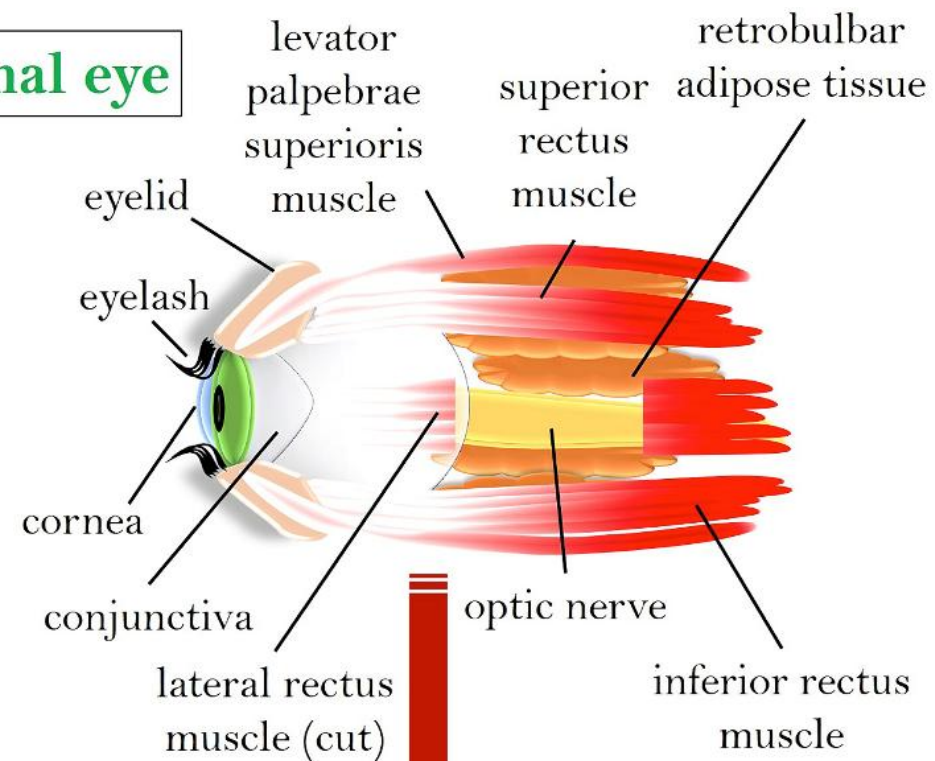
Neuropatia ottica distiroidea (DON)



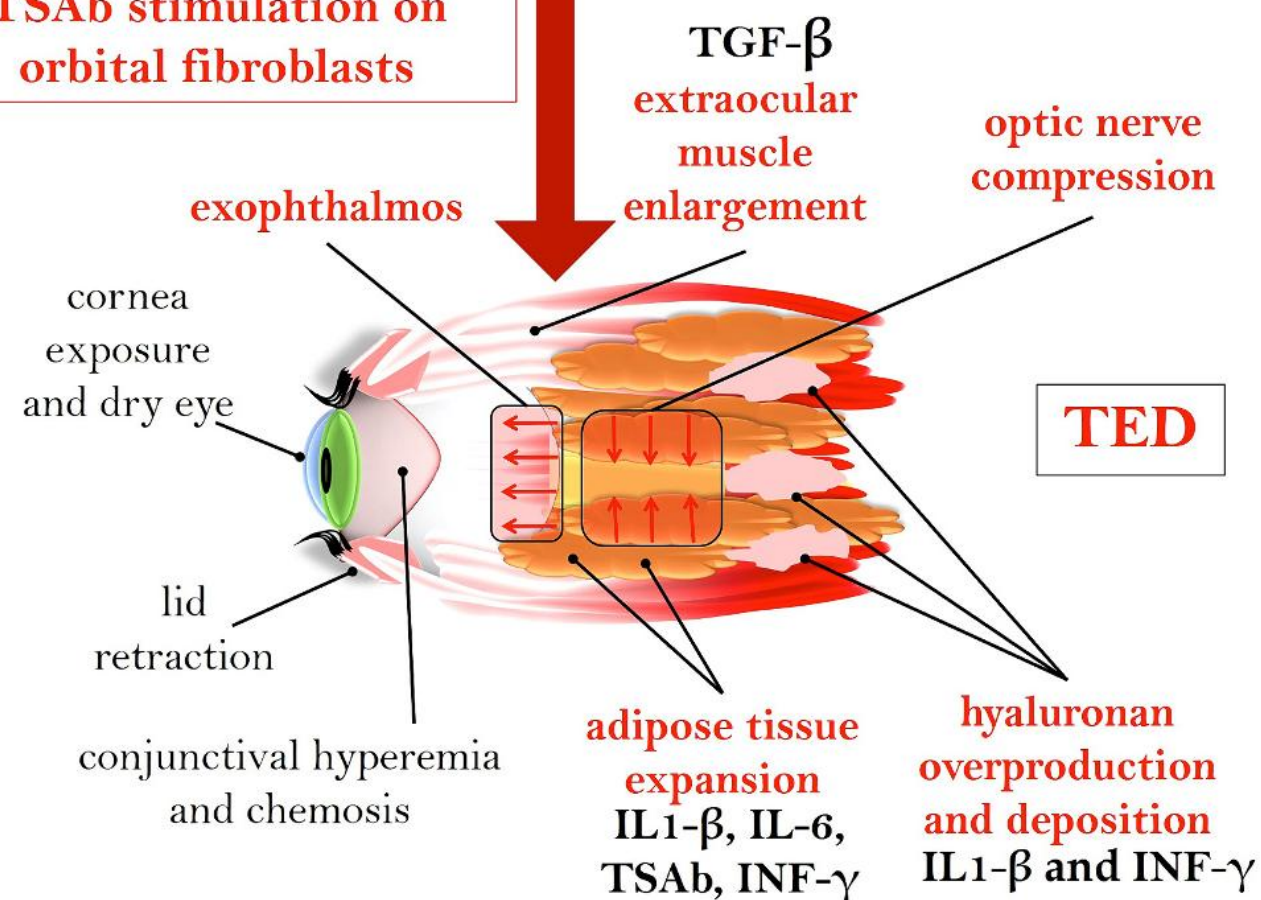
Blood Supply to Optic Nerve



Normal eye



TSAb stimulation on orbital fibroblasts

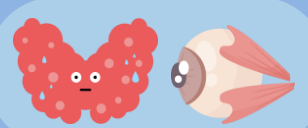


Neuropatia ottica distiroidea (DON)

- Reazione autoimmune contro i tessuti dell'orbita (muscoli/connettivo)
- Infiammazione cronica (proliferazione fibroblasti $\rightarrow$ adipociti, miofibroblasti)
- Edema e iperplasia dei tessuti (muscoli/grasso)

Compressione meccanica del nervo ottico

- i muscoli oculari ingrossati (in particolare RM) comprimono direttamente il nervo, spt nell'apice orbitario.
- Compromissione flusso assoplasmatico: rallentamento trasporto assonale nel nervo
- Ischemia: La pressione comprime i vasi sanguigni che irrora il nervo ottico, riducendo il flusso di sangue e causando ischemia



Neuropatia ottica distiroidea (DON)

Compressione meccanica del nervo ottico
(ridotto flusso assoplasmatico)
Si può associare una danno ischemico nervo
(arteriosa o da stasi venosa)

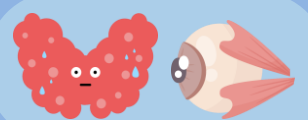
Danno di tutte le componenti del nervo
(assoni e guaina mielinica)

Può portare a grave calo del visus/cecità se
non identificata in fase precoce

Alterazioni Neurofisiologiche PEV:

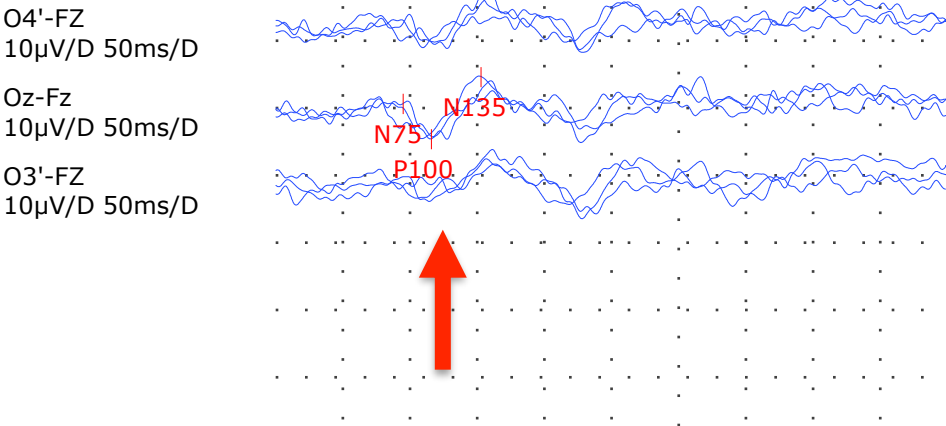
- danno alla mielina (rallentamento della conduzione → aumento latenza P100)
- danno assonale (riduzione di ampiezza)

Neuropatia con prevalente danno assonale

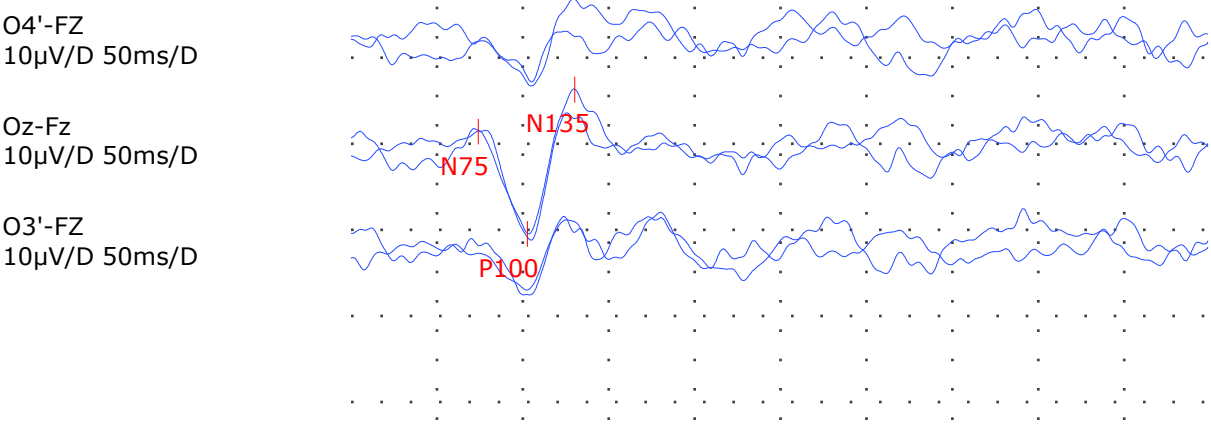


Caso: PEV patologico in OD

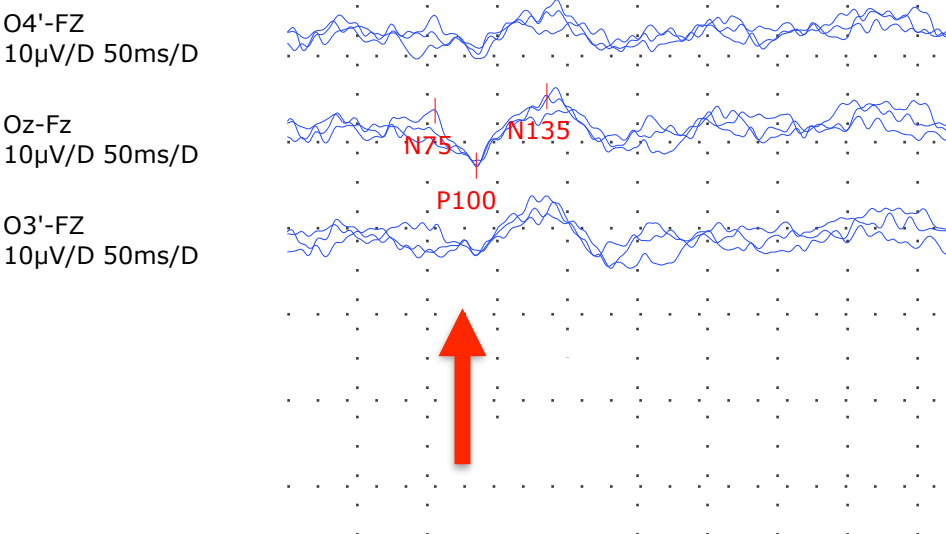
VEP: Destra Patt 60[-]



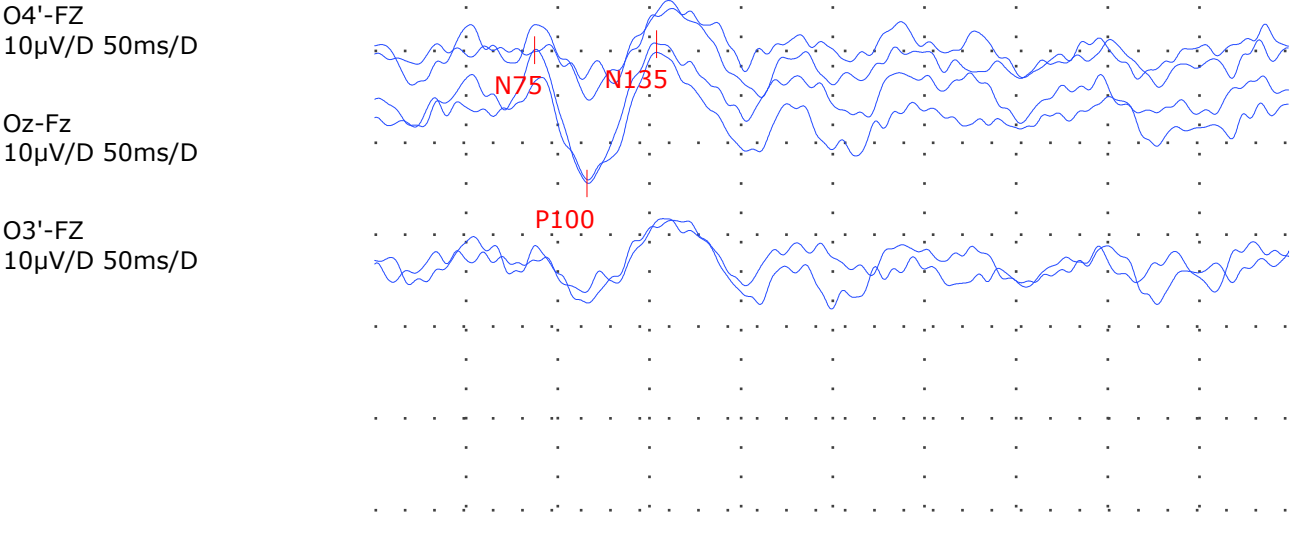
VEP: Sinistra Patt 60[-]



VEP: Destra Patt 15[-]

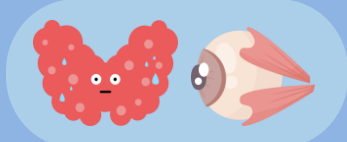


VEP: Sinistra Patt 15[-]



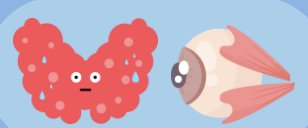
Lat P100 60' DX	Lat P100 60' SX
116 ms	103 ms
Amp 60' DX	Amp 60 SX'
3,2 uV	12,1 uV
Lat P100 15' DX	Lat P100 15' SX
135 ms	116 ms
Amp 15' DX	Amp 15' SX
4 uV	12 uV

Anomalie della conduzione della via visiva esaminata in OD con stimoli a variazione di contrasto.



Conclusioni

- PEV metodica semplice, non invasiva, veloce, economica
- Preceduto da Vs oculistica per escludere fattori oculari (correzione diottrica, ecc) che possono influenzare il segnale
- Informazioni sulla **funzione** del nervo ottico, indipendentemente dal dato morfologico, e del tipo di danno del nervo ottico (assonale/demielinizzante)
- Identificazione precoce di una danno del nervo ottico
- Utile per il monitoraggio longitudinale del danno con possibilità di quantificare modificazioni funzionali espressioni del danno del nervo ottico
- Va sempre interpretato e correlato ai dati clinici e strumentali



Grazie per l'attenzione