Optic neuritis
• The **optic nerve** (2nd pair of cranial nerves) is not a nerve in the common use of the term, but, morphologically and functionally, a diencephalic projection.

• It is made up of the **axons of retinal ganglion cells**, it extends from the retina to the optic chiasm enveloped in its sheath, the dura mater, arachnoid and pia mater, in continuation with the meningeal.

The **optic nerve** originates from the eyebulb, 1 mm below and 3-4 mm medially to its posterior pole; the length considerably varies (between 35 and 55 mm) even among the two eyes of the same individual; in the intraorbital tract its diameter is 3-4 mm and in the intracranial tract it is 4-7 mm.
Ganglion cells: ?

- They may receive information from 1 to 300 photoreceptors ✅ retinal sampling: 1/300 in the retinal periphery, 1/1 in the fovea ✅ visual acuity (maximum at the fovea)
- Center ON receptor fields ✅ activated by light and inhibited by darkness
- Center OFF receptor fields ✅ inhibited by light and activated by darkness
Ganglion cells:

in the retinal periphery:
- Large cell body (Magnocellular g.) and large caliber axon (high conduction speed)
- responsive to low spatial and temporal frequencies, to changes in luminance

in the macula:
- small cell body (Parvocellular g.) and small caliber axon (slow conduction speed)
- responsive to high temporal and spatial frequencies, to changes in chromatic contrast
Histology of the optic nerve
The optic nerve may be divided in 4 parts:

- **Intraocular (or optic nerve head):** inside the walls of the eyebulb (1 mm);
- **Intraorbital:** (20-25 mm);
- **Intracananicular:** in the optic canal (4-10 mm);
- **Intracranial:** (10-20 mm).
Blood supply of a normal optic disc
Histology of the optic disc
Vascularization of the optic nerve

- **Intraocular part:**
- **laminar portion** (lamina cribrosa):

  branches of the brief posterior ciliary arteries (**Zinn-Haller**): these do not constitute a precise anatomical structure, but when present, are a functional circular (incomplete) anastomosis between different posterior ciliary arteries which enter the sclera and supply the choroid and the optic nerve head.
Vascularization of the optic nerve

- **Intraorbital portion**: it may be divided in an anterior and a posterior tract in relation to the entrance of the central retinal artery; the anterior is double: axial (intraneural) derived by recurrent branches of the central retinal artery and superficial from branches of the pial plexus; the vascularization of the posterior tract is only of pial origin.

- **Intracanalicular and intracranial parts** supplied by the pial plexus (ophthalmic artery and collateral arteries for the first part; cerebral and anterior communicating arteries for the second part).

The **venous system** of the optic nerve repeats the arterious system (venous pial plexus).
Optic neuritis:

• Reduction of visual acuity in the absence of refractive defects or pathologies of the anterior segment or the retina

• The optic nerve may be involved as a result of ischemia, inflammation, demyelination, infection.
Optic neuritis: ophthalmoscopic aspects

- Papillitis or anterior optic neuritis: oedema of the optic disc

- Retrobulbar neuritis (intraorbital, canalicular or intracranial): absence of oedema or other signs of the optic disc

- Optic neuroretinitis: oedema of the optic disc and signs of inflammation (oedema, exudates and haemorrhages) of the peripapillary retina

- Optic perineuritis: oedema of the optic disc not associated to visual symptoms (d.d. with papilloedema)
Optic neuritis: functional aspects

- **Axial neuritis**: involvement of the papillo-macular bundle

- **Periaxial neuritis**: involvement of the extramacular portions of the nerve.
Optic neuritis

Functional aspects:

- Visual acuity
- Campimetry and Perimetry
- Pupil reflexes
- VISUAL EVOKED POTENTIALS
- ERG, PERG

Morphologic aspects:

- Ophthalmoscopy, Fluorangiography, OCT, HRT,
FUNCTIONAL EXPLORATION OF THE VISUAL PATHWAYS: VISUAL EVOKED POTENTIALS

VISUAL EVOKED POTENTIALS (VEPs) are defined as the variations in bioelectrical potentials of the occipital cortex evoked by visual stimuli. They are, therefore, the manifestation of refined and complex neurosensorial events due to the transduction and transmission of the nervous impulse along the visual pathways, from the retinal photoreceptors to the occipital brain cortex.
VEP: visual stimulus and bioelectric cortical response

Flash
VEPs with increased latencies and reduced amplitude:

Normal

Pathologic

Glaucoma, RBON, AION, MS, diabetes, maculopathy, RP, papilloedema,.............
VEP with increased latency and reduced amplitude:

Differential diagnosis between:

- Retinal pathologies
- Post-retinal pathologies

It is necessary to associate:

VEP + ERG
VEP + PERG
VEP + focal ERG
VEP + ERG

Altered VEP + Normal ERG

post-photoreceptor pathology:
ganglion cells, optic nerve, visual pathways
Anterior optic neuritis
- Ischaemic (AION)
- Toxic
Anterior ischaemic optic neuritis (AION)

Pathogenesis

Infarction of the prelaminar (supplied by branches of the central retinal artery), laminar (supplied by posterior ciliary arteries) and immediately retrolaminar (supplied by the pial plexus) region of the optic n.

. Non arteritic form . Arteritic form

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Anterior ischaemic optic neuritis (AION)

- **Onset**: 50-70 years of age, prevalently female gender
- **Subjective symptoms**: reduction in visual acuity,
- *Non arteritic AION*: early hours of the morning/ abuse of antihypertensive drugs
- Contralateral eye in 25-50% of cases within 5 years
- *arteritic AION*: monolateral or bilateral severe loss of vision

- Campimetric defects
Anterior ischaemic optic neuritis (AION)

- **Ophthalmoscopic aspects:** oedema of the optic disc, haemorrhages, exudates. Evolution towards diffuse or localized whitening (atrophy or subatrophy)

- Changes in **chromatic sense**

- **VEP:** increased latency and reduced amplitude,

- **ERG:** normal.

- Reduction of **contrast sensitivity**
Ischaemic papillopathy
Ischaemic papillopatgy: visual fields
Resolving ischaemic papillopathy
Temporal arteritis
Ischaemic papillopathy due to temporal arteritis
Histology of temporal arteritis
Anterior ischaemic optic neuritis (AION)

**Therapy**

- **1-3 days:** Metilprednisolone 1-2g/die iv in 3-4 administrations
- **4-15 days:** prednisone 1mg/Kg/die
- **tapering** of prednisone: 10% every subsequent week
- **monitoring:** glycemia, blood pressure
- **Associate:** gastroprotectors, brain vasodilators, platelet antiaggregants
Anterior toxic optic neuritis (ATON)

Pathogenesis: Ingestion or absorption of various substances

Drugs:
- Amoproxan (vasodilator utilized in patients with coronary insufficiency)
- Barbiturates,
- chemotherapy, cloramphenicol, penicillin, sulphamidics
- emetin (for the treatment of amebiasis),
- ethambutol, isoniazide
- iodiophormium (topical antiseptic)
- iodopiracetum (radio-opaque contrast medium used in brain angiography)

Other substances:
- Dichlorodipheniltrichloroethanol (DDT, insecticide), methanol
- organophosphatic products, Lead, Trichloroethylene
Anterior toxic optic neuritis (ATON)

**Mechanism of action**

- **Inhibition of enzymatic activity (mitochondrial):**
  - e.g.: methanol

- **Tissue hypoxia for the direct action on arteries:**
  - e.g.: chinin

- **Induction of a state of deficiency,** e.g.: Chronic alcoholism and vitamin B1 deficiency
Anterior toxic optic neuritis (ATON)

- **Subjective symptoms**: reduction in visual acuity,
- gradual and bilateral
- absence of periocular pain
- **Campimetric defects**: central scotoma
Anterior toxic optic neuritis (ATON)

- **ophthalmoscopic aspects**: negative in the initial phase, evolves towards pallor localized in the temporal sector (papillo-macular bundle)
- Changes in **chromatic sense**
- **VEP**: with increased latency and reduced amplitude,
- **ERG**: normal.
- Reduction in **contrast sensitivity**
Anterior toxic optic neuritis (ATON)

**Therapy**

- Immediate suspension of possible toxic substances
- CT and MRI to exclude compressive pathologies
- Liver function tests
  - polyvitaminic complexes
  - Vit. B1 in alcoholism
  - Vit. B6 in methanol intoxication
  - Vit. B12 in other forms.
Retrobulbar optic neuritis
(RBON)
Retrobulbar optic neuritis (RBON)  
“inexplicable acute or progressive loss of vision”

Characterized by:

Alterations of pupil reflexes
Visual field defects
Changes in chromatic sense, prevalently in the yellow-blue and red-green axes
Changes in contrast sensitivity
Pain during eye movements
Retrobulbar optic neuritis (RBON)

- **Clinical examination:** no sign of oedema, exudates, haemorrhage, changes in optic disc coloring. Pallor is subsequent.

- **Instrumental tests:**
  - **VEP** with increased latency and reduced amplitude (delay in conduction along visual pathways)
  - **ERG:** normal
  - **PERG:** if abnormal, it is an index of retrograde degeneration
Retrobulbar optic neuritis (RBON)

Etiology:

a) Ischaemic: arteriosclerotic or atherosclerotic alterations of the anterior cerebral arteries

b) Infective: tetanus, brucellosis, rosolia, influenza, chicken-pox, tubercolosis, syphilis. Isolated or associated to focal sepsis (tonsillitis, caries etc..)

c) Traumatic (direct compression, thrombotic phenomena, arterial spasm)

d) Radiations (after radiotherapy for intracranial or paranasal sinus tumors)

e) Optic-chiasmatic arachnoiditis: in association to: basal meningitis, head trauma, intracranial tumors, empty sell syndrome, due to: nerve tissue constriction, post-inflammatory necrosis of fibers, vascular occlusion
Retrobulbar optic neuritis (RBON)

Etiology:

f) Compressive lesions:
   - intracranial and intraorbital tumors, paranasal sinus inflammatory lesions, aneurisms, spontaneous or traumatic orbital haemorrhages
   - primary bone lesions (osteopetrosis, fibrous displasia, craniometaphisaric displasia)
   - congenital or acquired hydrocephaalus
   - meningioma of the anterior part of the brain
   - Pituitary tumors

g) Toxic deficiency forms
   - Nutritional amblyopia (Vitamine B1, B2, B6, B12, Nicotinic acid, Folic acid)
   - tropical amblyopia (associated to ataxia)
   - drugs

h) Infiltrating forms: leukaemia and lymphoma
Conditions associated to RBON

a) **Multiple sclerosis**

- Onset in 20-60% of subjects developing MS
- Age: 30-40 years of age
- Gender: prevalently female
- Pain: not correlated to MS
- Prevalently bilateral and recurrent
- Prevalent onset in April-October
- Not related to race or place of birth
- BT 101 (lymphocyte typification) in 34-70% of cases
- Oligoclonal IgG in the BSF
- Uhthoff’s sign
Multiple sclerosis
MORPHO-FUNCTIONAL CORRELATIONS:

- Evaluation of NFL thickness in patients with MS with and without RBON
- Comparison of the variability of amplitude and latency of PERG and VEP with nerve fiber layer thickness measured by OCT in patients with MS with and without retrobulbar optic neuritis

• Parisi, Manni et al, IOVS, 1999
Multiple Sclerosis

NORMAL SUBJECT

PERG

VEP O1

VEP O2

N35

N95

P100

N75

N145

DELAY IN POSTRETINAL VISUAL PATHWAYS

PERG

VEP O1

VEP O2

NORB + ASYMMETRICAL DELAY IN POSTRETINAL VISUAL PATHWAYS

PERG

VEP O1

VEP O2

NORB + SYMMETRICAL DELAY IN POSTRETINAL VISUAL PATHWAYS

PERG

VEP O1

VEP O2
Correlation between PERG and VEP and NFL thickness: MS

PERG

NFLO / P50 Implicit Time: $r: -0.866, P<0.001$
NFLO / P50- N95 Amplitude: $r: -0.842, P< 0.001$

VEP

$A$

NFLO / P50 Implicit Time: $r: -0.263, P= 0.159$, $r: -0.161, P= 0.379$

$B$

NFLO / P50- N95 Amplitude: $r: 0.220, P= 0.240$, $r: 0.213, P= 0.257$
Conditions associated to RBON

b) Optic neuromyelitis (Devic’s disease)
- bilateral RBON associated to transverse myelitis
- Both genders, all ages
- slight edema of the optic disc
- Severe visual defects
- BSF: pleocytosis, polymorphonuclear cells, increased protein concentration

c) Diffuse periaxial encephalitis (Schilder’s disease)
d) Diseases of the sinus (sphenoidal and ethmoidal)
  e) Acute encephalomyelitis
  f) Creutzfeld-Jakob’s disease
  g) Guillain-Barrè syndrome
Retrobulbar optic neuritis (RBON)

**Therapy:**

Aims to accelerate recovery but does not affect entity of the disease

- **1-3 days:** Metilprednisolone 1-2d/die iv in 3-4 administrations
- **4-15 days:** Prednisone 1mg/Kg/die
- **tapering** of prednisone: 10% every subsequent week
- **monitor:** glycemia, blood pressure
- **Associate:** gastroprotectors
Hereditary optic neuropathies

a) Leber’s optic atrophy

? onset between 10 and 30 years of age
Prevalently males (sex-linked, women healthy carriers, not transmitted by males, or viral etiology due to slow viruses)
? Severe visual involvement up to blindness
? optic disc: normal or edematous with haemorrhage
? Campimetric defects and alterations of chromatic sense

? Associated to:
- spastic paresis, deafness, loss of consciousness, muscle atrophy
- tremors, ataxia, cardiac abnormalities
Acute and late stages of Leber’s optic atrophy
**Hereditary optic neuropathies**

b) Dominant optic atrophy

? Congenital or juvenile form (under 10 ys of age)

? Dominant transmission

? Associated to nystagmus

? Severe loss of vision

c) Recessive Optic atrophy

? Present at birth or before 4 years of age

? Severe loss of vision

d) Recessive optic atrophy ass. to diabetes insipidus and deafness

? Diabetes in the first and second decade of life

? Severe loss of vision
e) Dominant optic atrophy associated to congenital deafness with or without ataxia
   Severe deafness since birth
   Visual acuity 1/10 after 20 yrs of age

f) Dominant optic atrophy associated to progressive deafness and polineuropathy
   Severe deafness since birth
   Visual acuity 1/10 after 20 yrs of age

g) Dominant optic atrophy associated to progressive deafness, spastic tetraplegia, mental retardation (Optic-cliodentate degeneration)
   Severe progressive loss of vision and hearing since childhood
   Death in childhood
h) Childhood hereditary complicated optic atrophy (Behr’s syndrome)
   ? Onset during childhood
   ? Associated to mental retardation, pyramidal tract alterations, ataxia, bladder incontinence
   ? Diffuse cerebellar atrophy

i) Optic atrophy associated to Friedreich’s or Marie’s ataxia (spastic)
   l) Charcot-Marie-Tooth’s disease

**Optic atrophy**

? Diffuse or localized optic disc pallor
? Severe reduction of nerve fibers
? Absence of pupil reflexes
? Severe visual loss up to blindness
Destructured or severely altered VEPs
Conclusions:

“Reduction of visual acuity in the absence of refractive defects or pathologies of the anterior segment or retina”

- Medical history/ age/ gender
- Ocular fundus: AION/RBON
- Analyse: pupil reflexes, Visual field, Chromatic sense, ERG, VEP, PERG
- MRI, CAT, neurological examination, analysis of BSF
- Immediate therapy