Neuritis optica: diagnose en classificatie

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Disclosures

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Overview

- Background
- Cases
- Pearls and Oysters
- Diagnostic Criteria
- Classification
- Summary

Background

THE LANCET Neurology

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Optic Neuropathies

Published: September 22, 2022

Executive Summary

Optic neuropathies can reflect a wide range of pathophysiologies, both acquired and inherited. This Series provides an update on the clinical, imaging, and laboratory findings that differentiate these disorders, allowing clinicians to focus their diagnostic studies and optimise treatments. Multimodality optic nerve imaging—including fundus photography, optical coherence tomography, and MRI—has greatly advanced the diagnosis and follow-up of patients with optic neuropathies. Also reviewed in this Series, new evidence shows that optic neuritis can frequently indicate autoimmune neurological disorders, including multiple sclerosis and the recently recognised disease categories of aquaporin-4 antibody-associated neuromyelitis optica spectrum disorder and myelin-oligodendrocyte glycoprotein antibody-associated disease. Early clinical recognition of optic neuritis is, therefore, important for prognosis and treatment. Also reviewed in the Series, a unifying feature in the pathophysiology of hereditary disorders of the optic nerve is mitochondrial dysfunction. Treatments are emerging for optic neuropathies, including immunotherapies and genetic therapies.

Series

Imaging of the optic nerve: technological advances and future prospects

Valérie Biousse, Helen V Danesh-Meyer, Amit M Saindane, Cédric Lamirel, Nancy J Newman

The Lancet Neurology

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Optic neuritis and autoimmune optic neuropathies: advances in diagnosis and treatment

Jeffrey L Bennett, Fiona Costello, John J Chen, Axel Petzold, Valérie Biousse, Nancy J Newman, Steven L Galetta

The Lancet Neurology

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Understanding the molecular basis and pathogenesis of hereditary optic neuropathies: towards improved diagnosis and management

Nancy J Newman, Patrick Yu-Wai-Man, Valérie Biousse, Valerio Carelli

The Lancet Neurology

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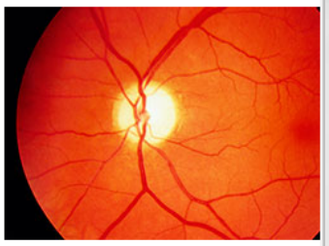

Related Content

POSITION PAPER

Diagnosis and classification of optic neuritis

Axel Petzold, Clare L Fraser, Mathias Abegg, Raed Alroughani, Daniah Alshowaeir, Regina Alvarenga, and others

The Lancet Neurology

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PERSONAL VIEW

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Romain Marignier, Yael Hacohen, Alvaro Cobo-Calvo, Anne-Katrin Pröbstel, Orhan Aktas, Harry Alexopoulos, and others

The Lancet Neurology, Vol. 20, No. 9

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REVIEW

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Yi Shiau Ng, Laurence A Bindoff, Gráinne S Gorman, Thomas Klopstock, Cornelia Kornblum, Michelangelo Mancuso, and others

The Lancet Neurology, Vol. 20, No. 7

Published: July, 2021

Free download Link:

1st Case

- 34 year old Caucasian female patient
- 7 day history of pain in the right eye which worsens on eye movements
- Reduced colour vision
- VA RE: 6/9, left eye LE: 6/5
- Right RAPD
- Reports: fatigue, cognitive problems, urinary incontinence, depression
- PmHx: right sided numbness lasting 1m, 3y ago

1st Case

- Bloods all normal except for low Vitamin D at 22 nmol/L (normal 50-200 nmol/L)
- MRI: DIS & DIT
  three Gd+ non-symptomatic lesions
- CSF not done

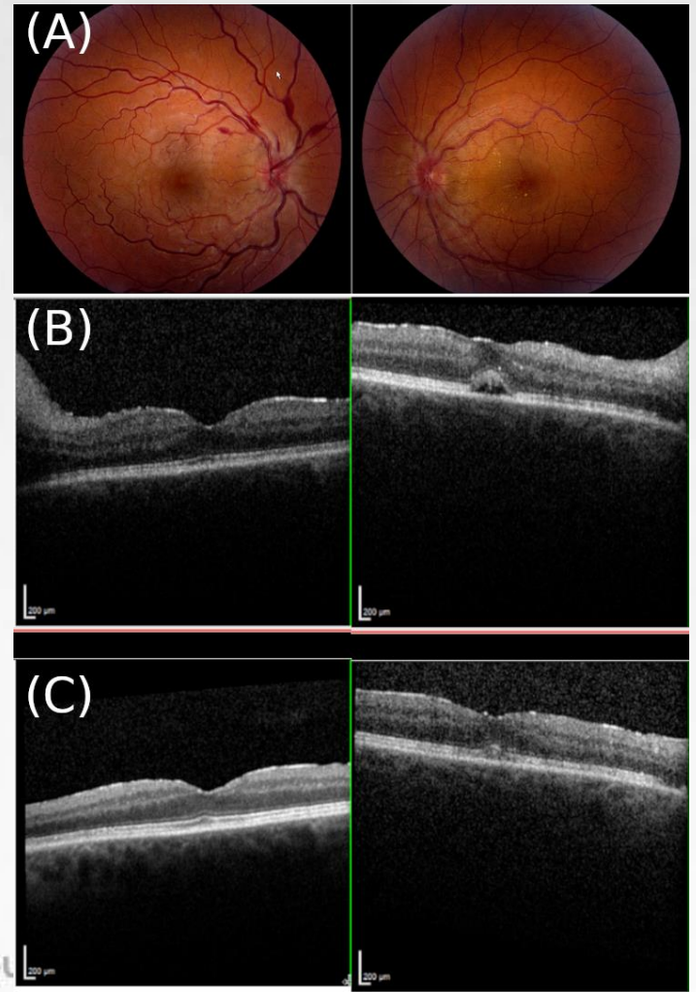
What is the most likely diagnosis?

2nd Case

- 28 year old, Afrocaribbean male
- Painless loss of vision LE (6/38)
- Dyschromatopsia
- L RAPD
- Several steroid responsive episodes over ~20 y fup
- OCT: pRNFL atrophy LE (IEPD >5%)
- MRI a swollen, Gd+, left optic nerve. No lesions elsewhere
- AQP4 seropositive

3rd Case

- 72 year old male develops febrile illness in Vietnam
- 2-3 weeks later bilateral, sequential, painless loss of vision (PL)
- no RAPD (but both pupils constrict with accomodation)
- Fundus (next slide):
  - Bilateral disc edema
  - RE hemorrhages
  - LE macular scar, CMO
- No recovery @ 6m fup (IVMP given ~6w after onset)



Cases summary

- Case 1: is this MS ?

  Scenario A: painful, monocular, subacute LOV, dyschromatopsia, RAPD

- Case 2: is this NMO ?

  Scenario B: no pain, monocular, subacute LOV, dyschromatopsia, RAPD

- Case 3: what is this ?

  Scenario C: binocular, subacute LOV, dyschromatopsia, no pain, no RAPD

Pearls & Oysters

- Key elements from Hx: Scenarios A-C
- Ethnicity is important:
  - MOG and AQP4 seropositivity more prevalent in African, Afrocaribbean and Asian background
- Examination: if you cannot demonstrate an afferent deficit, test the efferent pupil response

RAPD video

Link to video on Lancet website

Doi: https://doi.org/10.1016/S1474-4422(23)00110-2

https://www.thelancet.com/cms/10.1016/S1474-4422(23)00110-2/attachment/db63b5ad-7590-4103-bb7b-9a9635c26674/mmc2.mp4

How to harvest more pearls

Panel 3: Signs and symptoms aiding the clinical classification of optic neuritis and exclusion of alternative pathologies

Clinical presentation*:

- Sequence of symptoms over time
- Preceding infection or vaccination
- Ethnic background or location
- Progression of pain or visual loss (>2 weeks)
- Absence of pain
- Associated epilepsy†
- Simultaneous bilateral ON
- Evidence of retinitis or retinal dysfunction from OCT or electrophysiology
- Presence of severe optic disc oedema
- Absence of optic disc oedema
- Unexplained optic atrophy in either eye at onset
- Fever or other systemic symptoms and signs‡
- Other focal neurological signs

Disease course§:

- Progressive loss of vision
- Progressive retinal layer atrophy for more than 12 months
- Sequential bilateral optic neuritis
- Absence of spontaneous recovery (>3 months)
- Corticosteroid dependence

Medical history:

- Medical history of cancer or diseases listed in panel 4
- Family history of a suspected hereditary optic neuropathy
- Family history of other mitochondrial cytopathy

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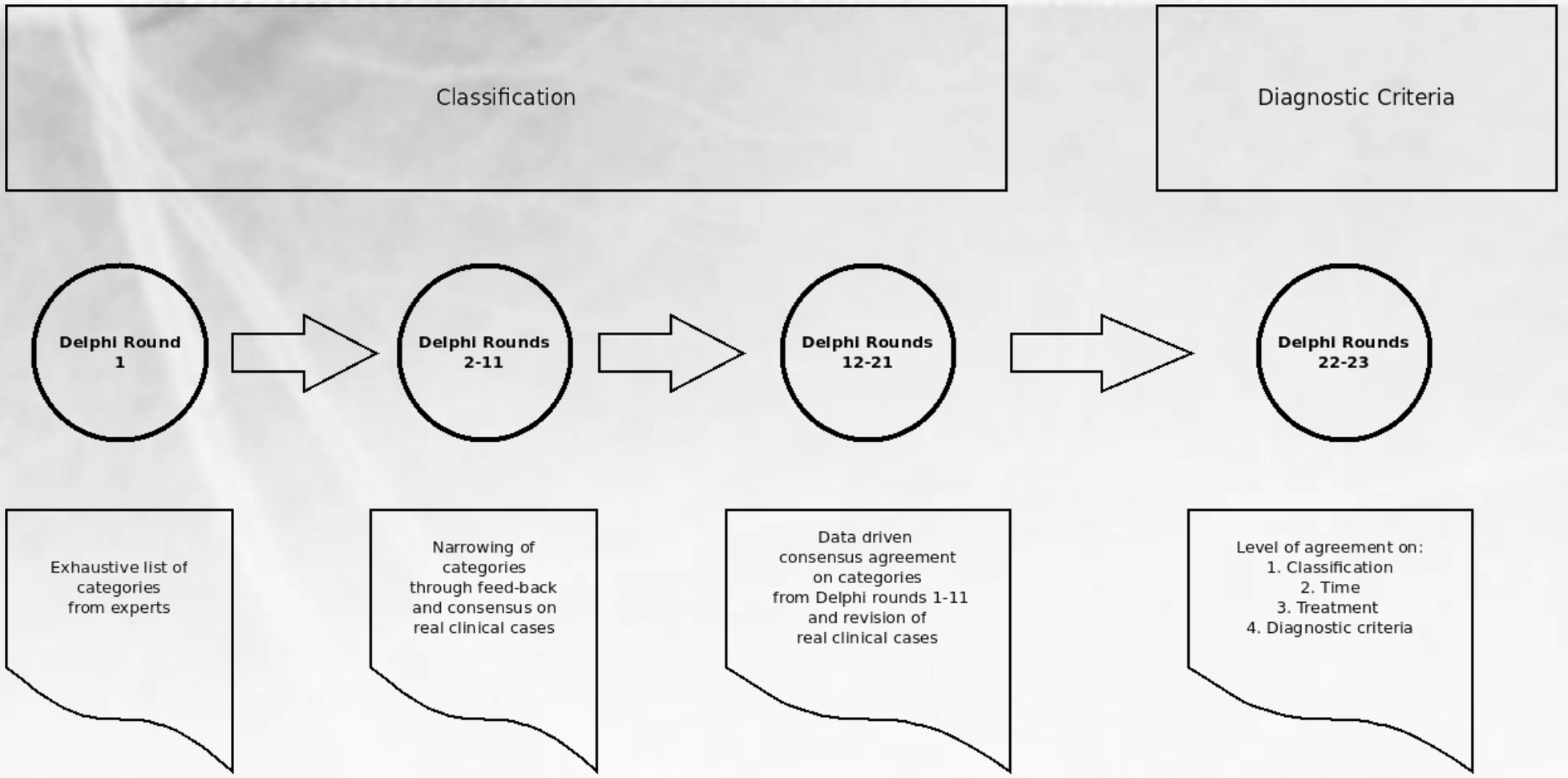
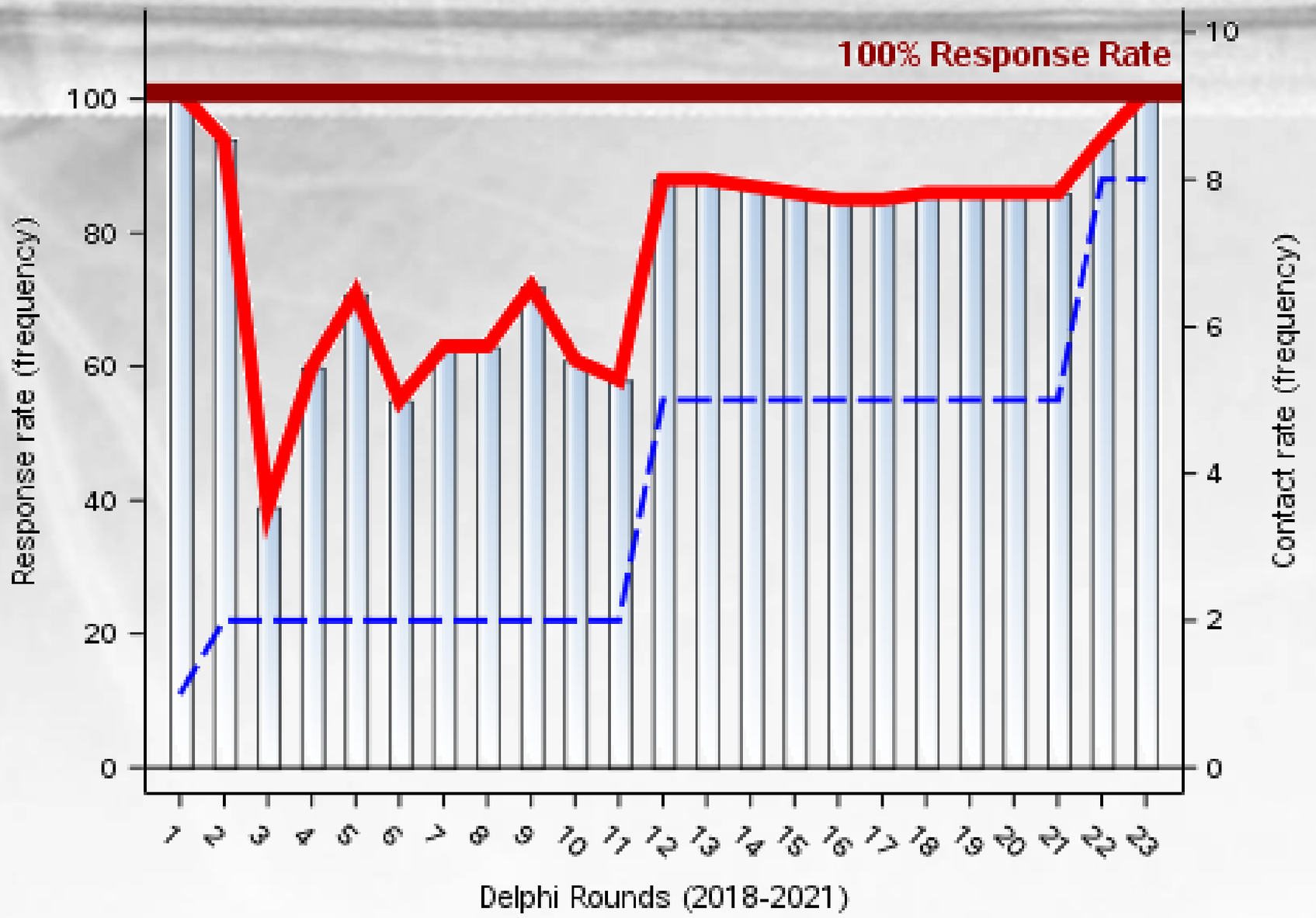
Delphi Process

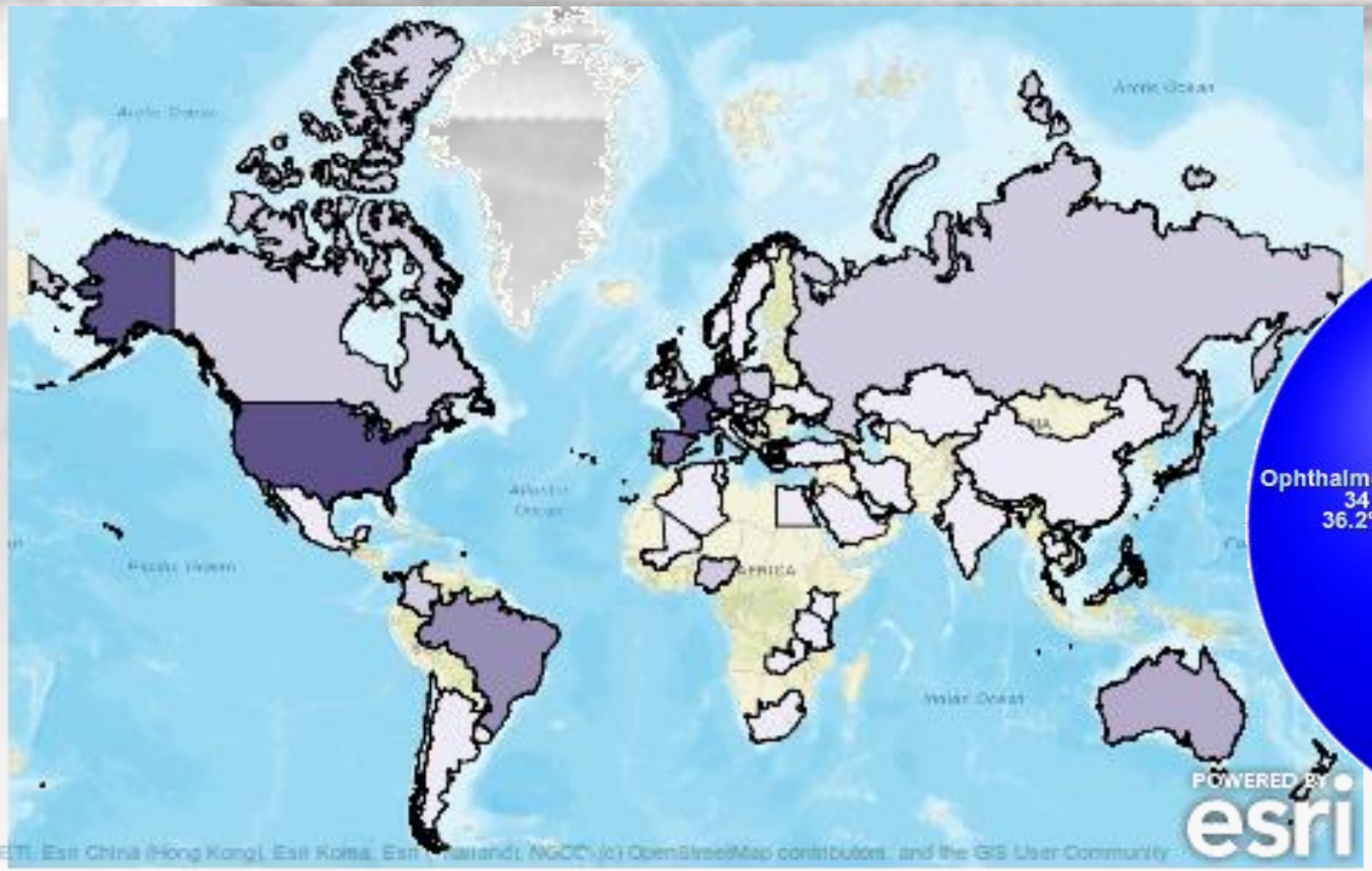


Definition of consensus >80%

Delphi (2018-2021)



The Panel


POWERED BY esri
1
2
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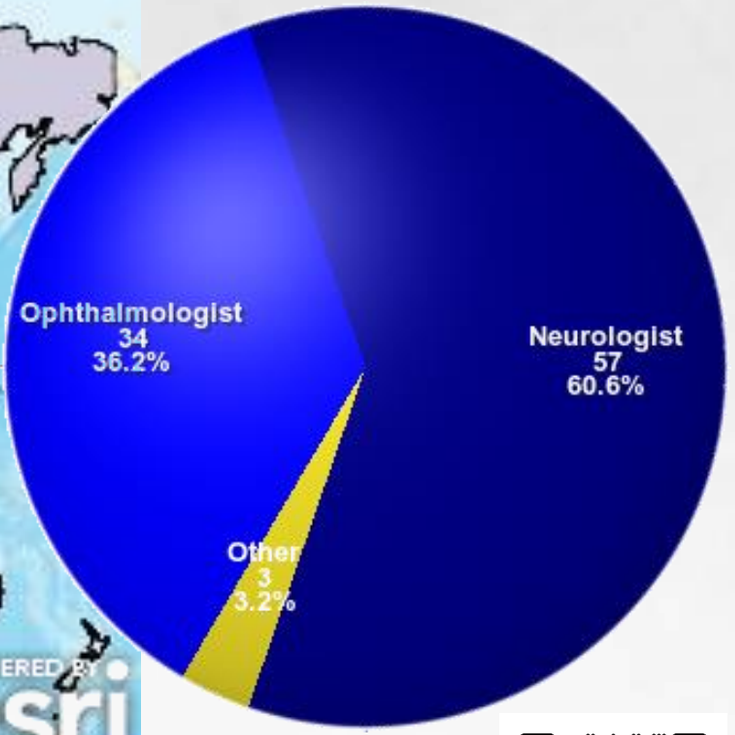
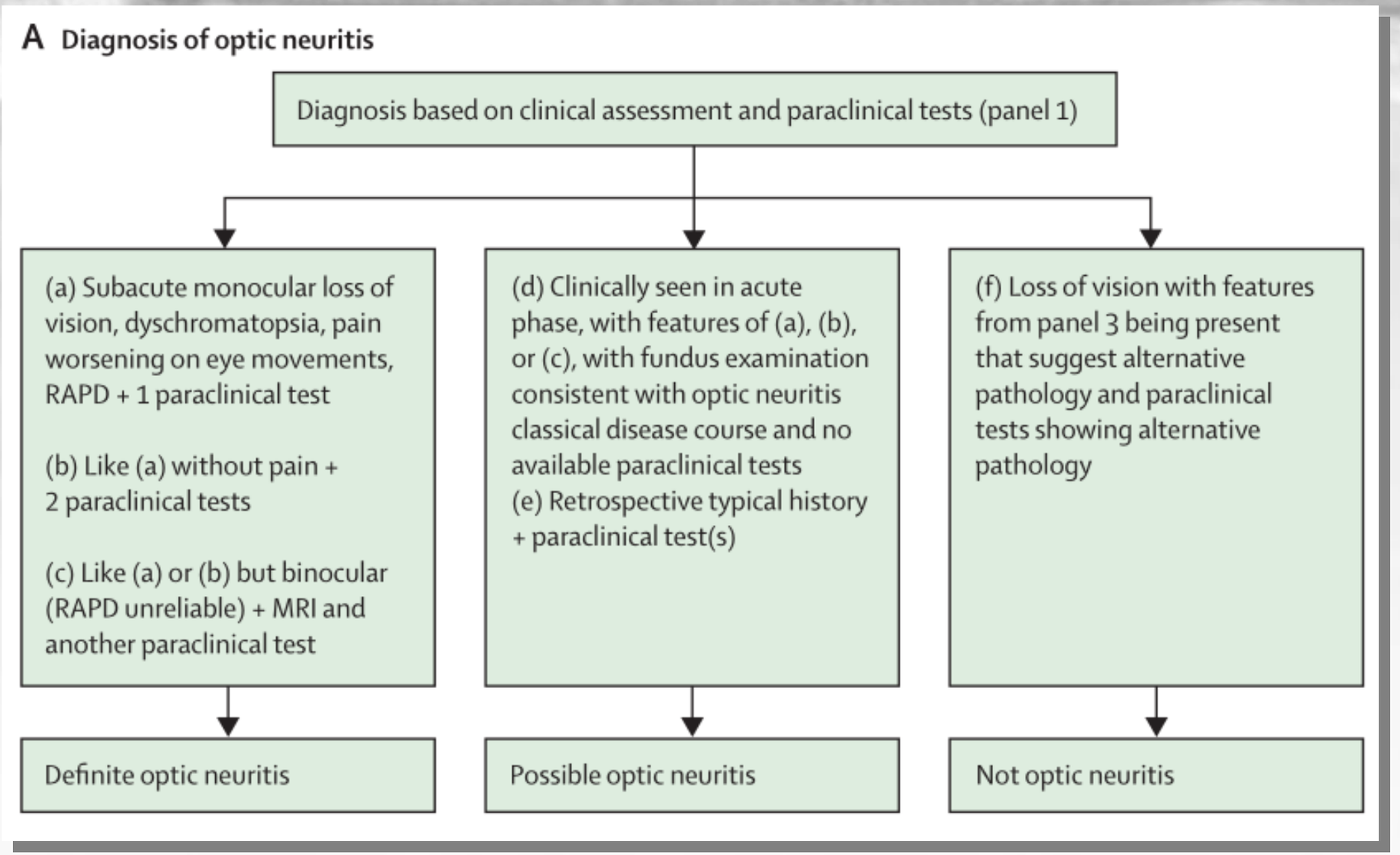
World wide distribution of number of experts


Ophthalmologist
34
36.2%
Neurologist
57
60.6%
Other
3
3.2%

Diagnosis


A Diagnosis of optic neuritis
Diagnosis based on clinical assessment and paraclinical tests (panel 1)
(a) Subacute monocular loss of vision, dyschromatopsia, pain worsening on eye movements, RAPD + 1 paraclinical test
(b) Like (a) without pain + 2 paraclinical tests
(c) Like (a) or (b) but binocular (RAPD unreliable) + MRI and another paraclinical test
(d) Clinically seen in acute phase, with features of (a), (b), or (c), with fundus examination consistent with optic neuritis classical disease course and no available paraclinical tests
(e) Retrospective typical history + paraclinical test(s)
(f) Loss of vision with features from panel 3 being present that suggest alternative pathology and paraclinical tests showing alternative pathology
Definite optic neuritis
Possible optic neuritis
Not optic neuritis

Panel 1: Diagnostic criteria for optic neuritis

Clinical criteria

- A: Monocular, subacute loss of vision associated with orbital pain worsening on eye movements, reduced contrast and colour vision, and relative afferent pupillary deficit
- B: Painless with all other features of (A).
- C: Binocular loss of vision with all features of (A) or (B).

Paraclinical criteria

- OCT: Corresponding optic disc swelling acutely or an inter-eye difference in the mGCIPL of >4% or >4 µm or in the pRNFL of >5% or >5 µm within 3 months after onset.
- MRI: Contrast enhancement of the symptomatic optic nerve and sheaths acutely or an intrinsic signal (looking brighter) increase within 3 months.
- Biomarker: AQP4, MOG, or CRMP5 antibody seropositive, or intrathecal CSF IgG (oligoclonal bands).

Application of the clinical and paraclinical criteria

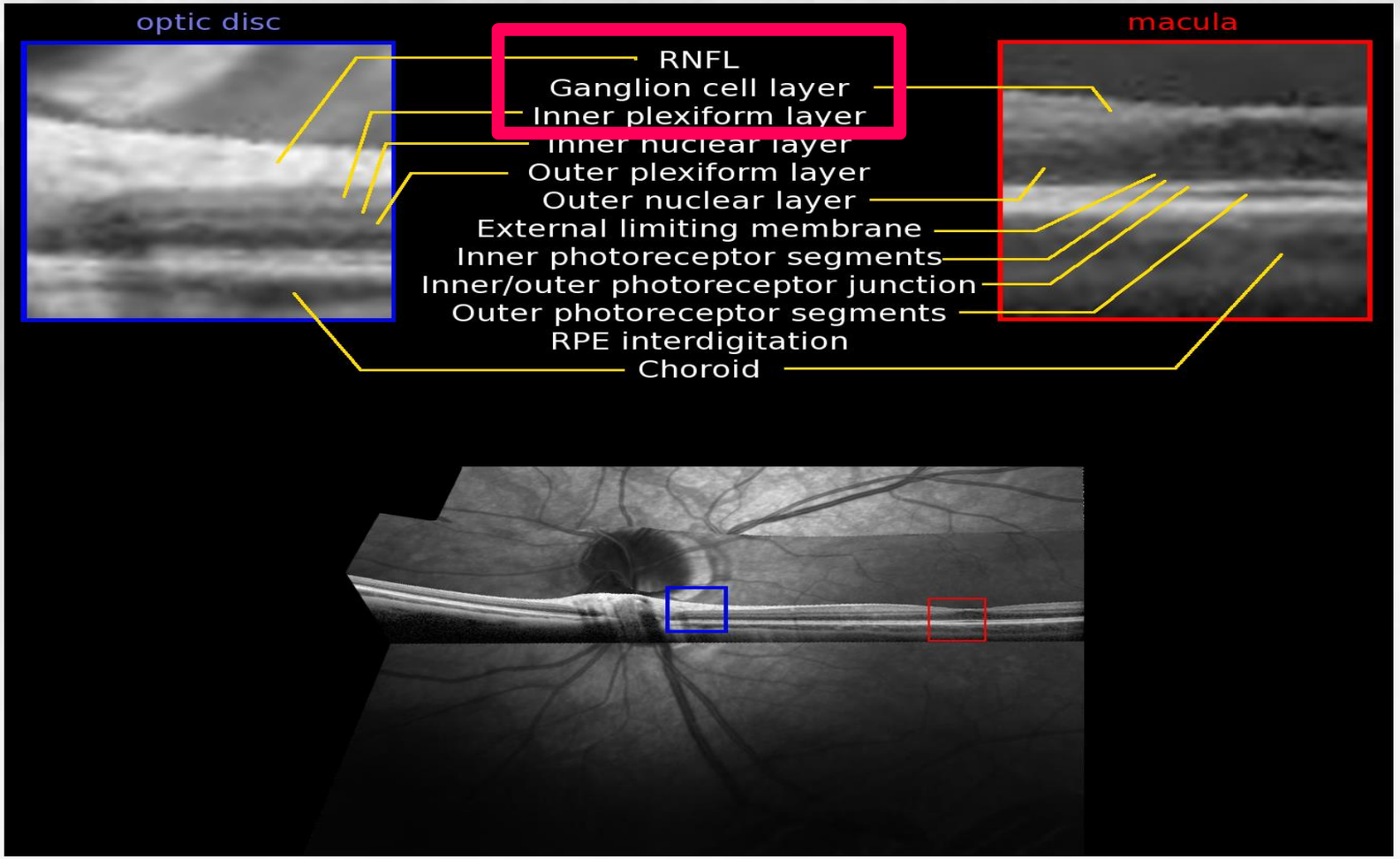
Definite optic neuritis

- (A) and one paraclinical test
- (B) and two paraclinical tests of different modality
- (C) and two different paraclinical tests of which one is MRI

Possible optic neuritis

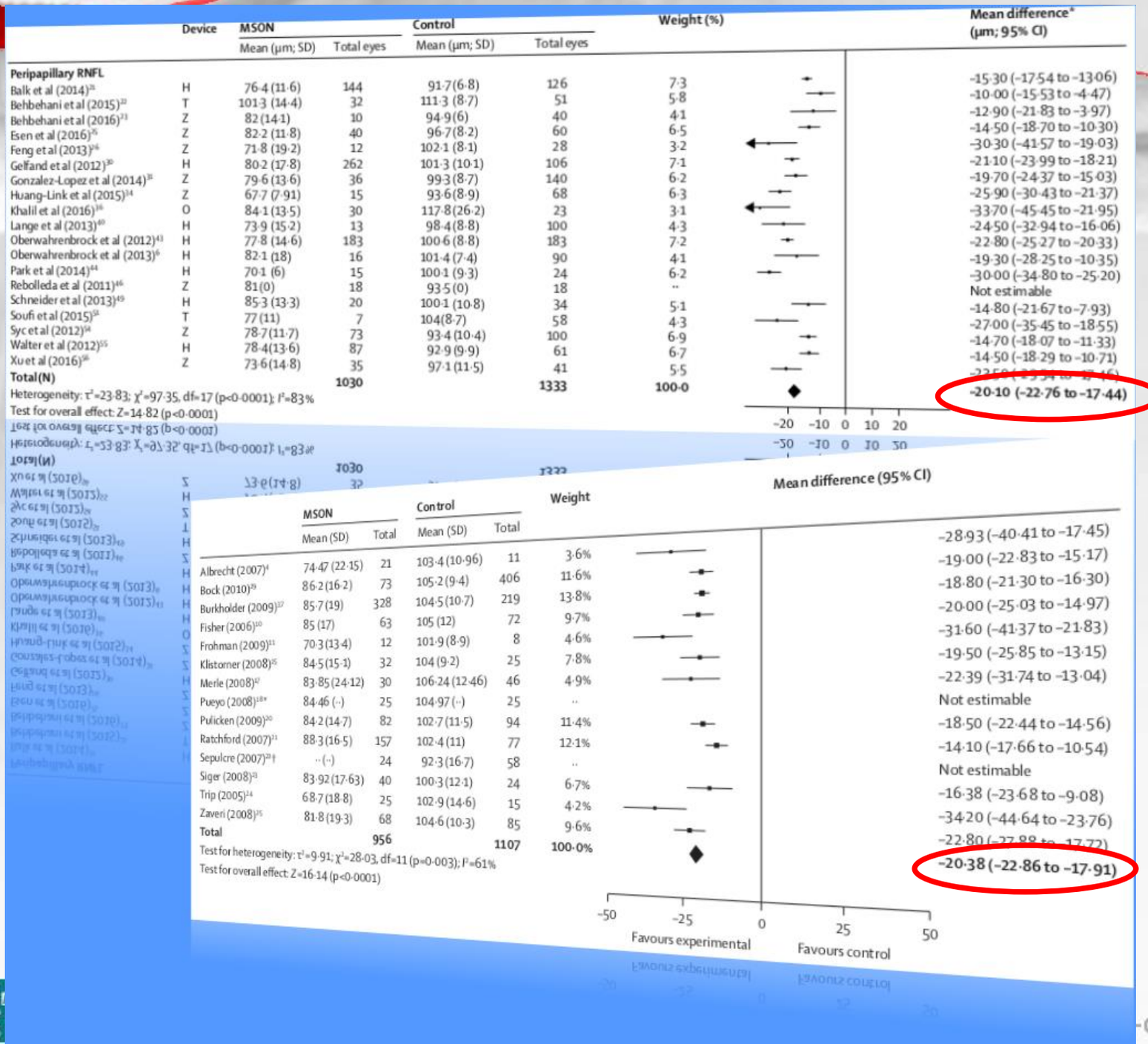
- (A), (B), or (C) if seen acutely but in absence of paraclinical tests, with fundus examination typical for optic neuritis and consistent with the natural history during follow-up
- Positive paraclinical test or tests, with a medical history suggestive of optic neuritis

OCT



Petzold *et al.* TLN 2010

OCT in MS-ON



pRNFL atrophy

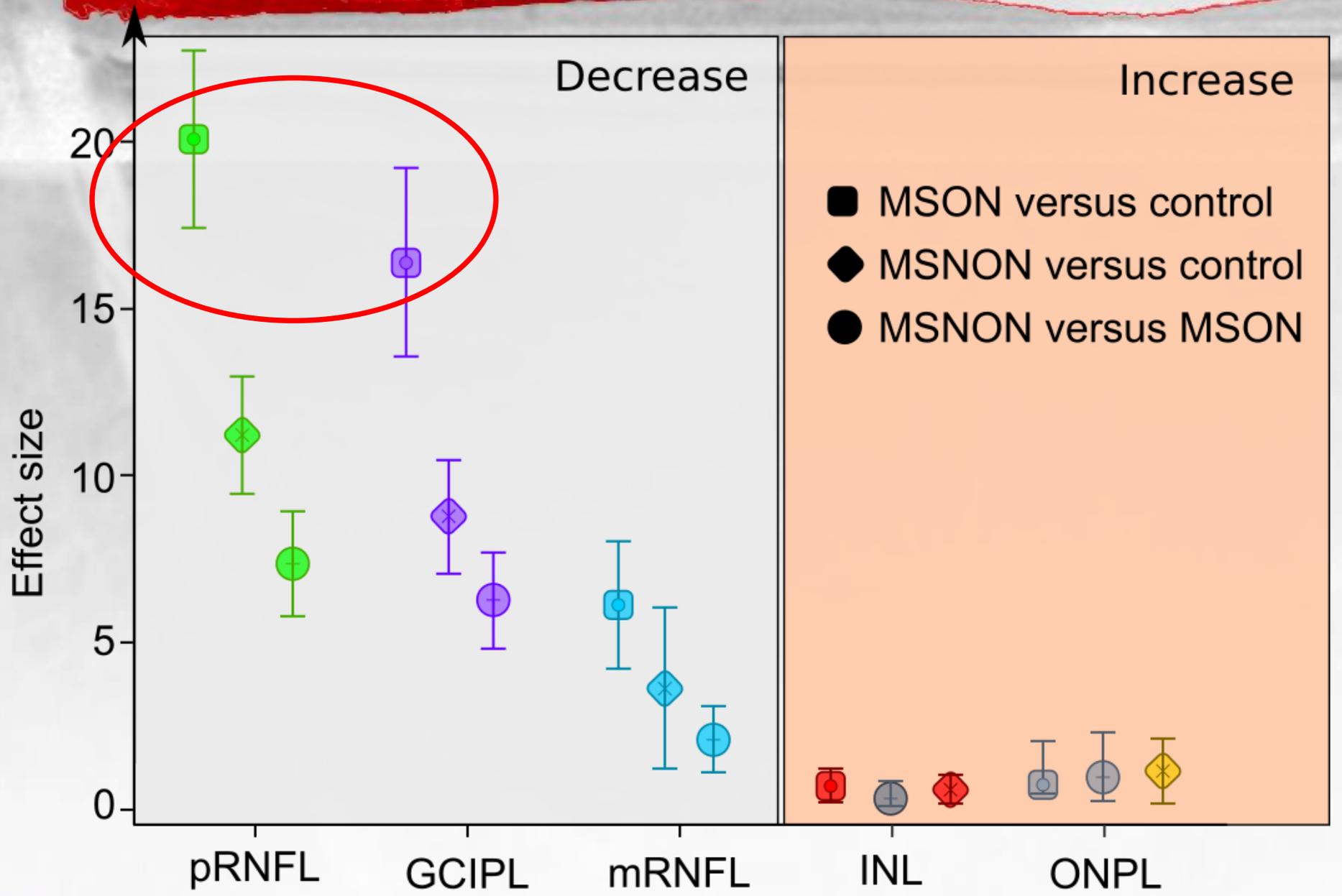
TLN 2010

20.10 (17.44-22.76) µm

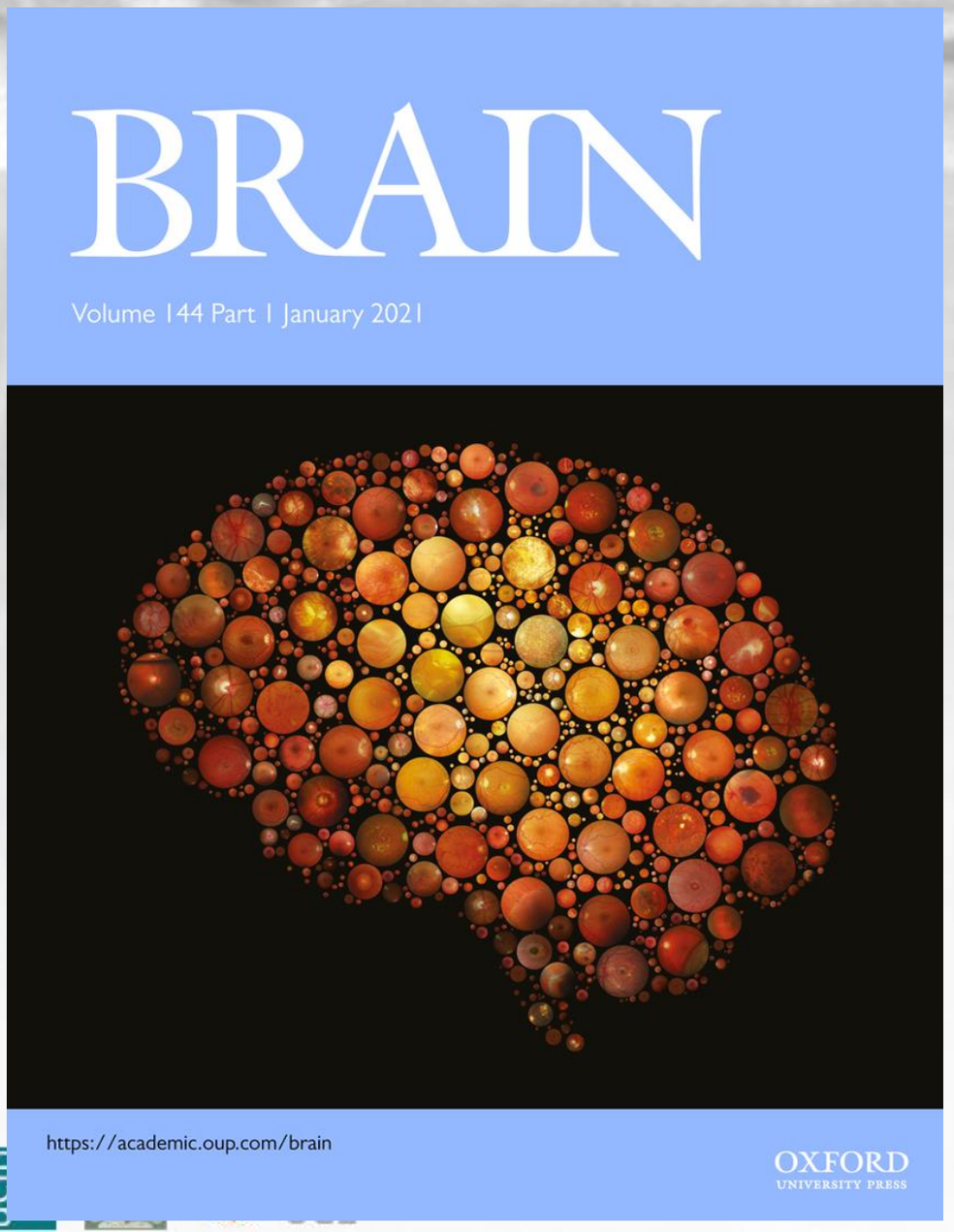
TLN 2017

20.38 (17.91-22.86) µm

What is relevant ?



Oysters



Inter-eye difference:

Percentage difference (IEPD): %

Absolute difference (IEAD): µm

Petzold *et al.* BRAIN 2021

High diagnostic accuracy

OCT measure	Optimized cut-off	Reference	Group comparison	Specificity	Sensitivity
IEPD mGCiPL	5 %	Coric et al. 2017	Symptomatic bilateral MSON vs. healthy controls	97 %	86 %
IEPD mGCIPL	6 %	Coric et al. 2017	Symptomatic unilateral MSON vs. healthy controls	97 %	70 %
IEAD mGCIPL	4.0 µm	Nolan-Kenney 2019	Symptomatic unilateral MSON vs. non-MSON	77 %	68 %
IEAD mGCIPL	3.5 µm	Behbehani 2020	Unilateral optic neuritis vs. healthy controls	98%	100 %
IEAD mGCIPL	2.83 µm	Davion 2020	Symptomatic unilateral or bilateral MSON vs. non-MSON[a]	67.4 %	67.3 %
IEPD/IEAD	4% / 4 µm	Petzold 2020	MS without MSON vs controls (n=72,120)	82.8% / 86.8%	51.7% / 43.5%
IEAD mGCIPL	1.42 µm	Outteryck 2020	CIS patients with vs. without an asymptomatic optic nerve lesion on 3D-DIR MRI	72.6 %	89.3 %
IEPD mGCIPL	2 %	Outteryck 2020	CIS patients with vs. without an asymptomatic optic nerve lesion on 3D-DIR MRI	69.4 %	89.3 %

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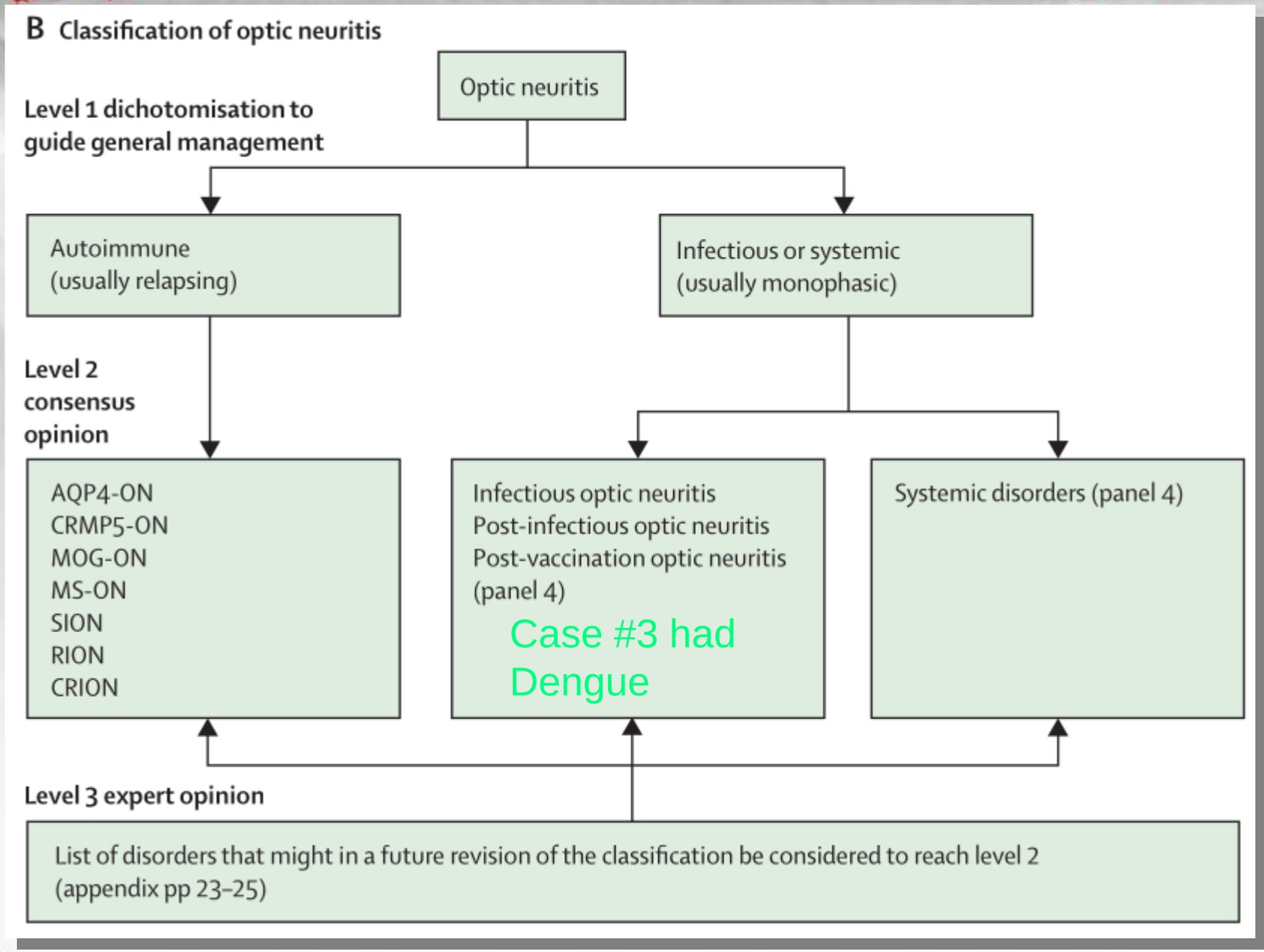
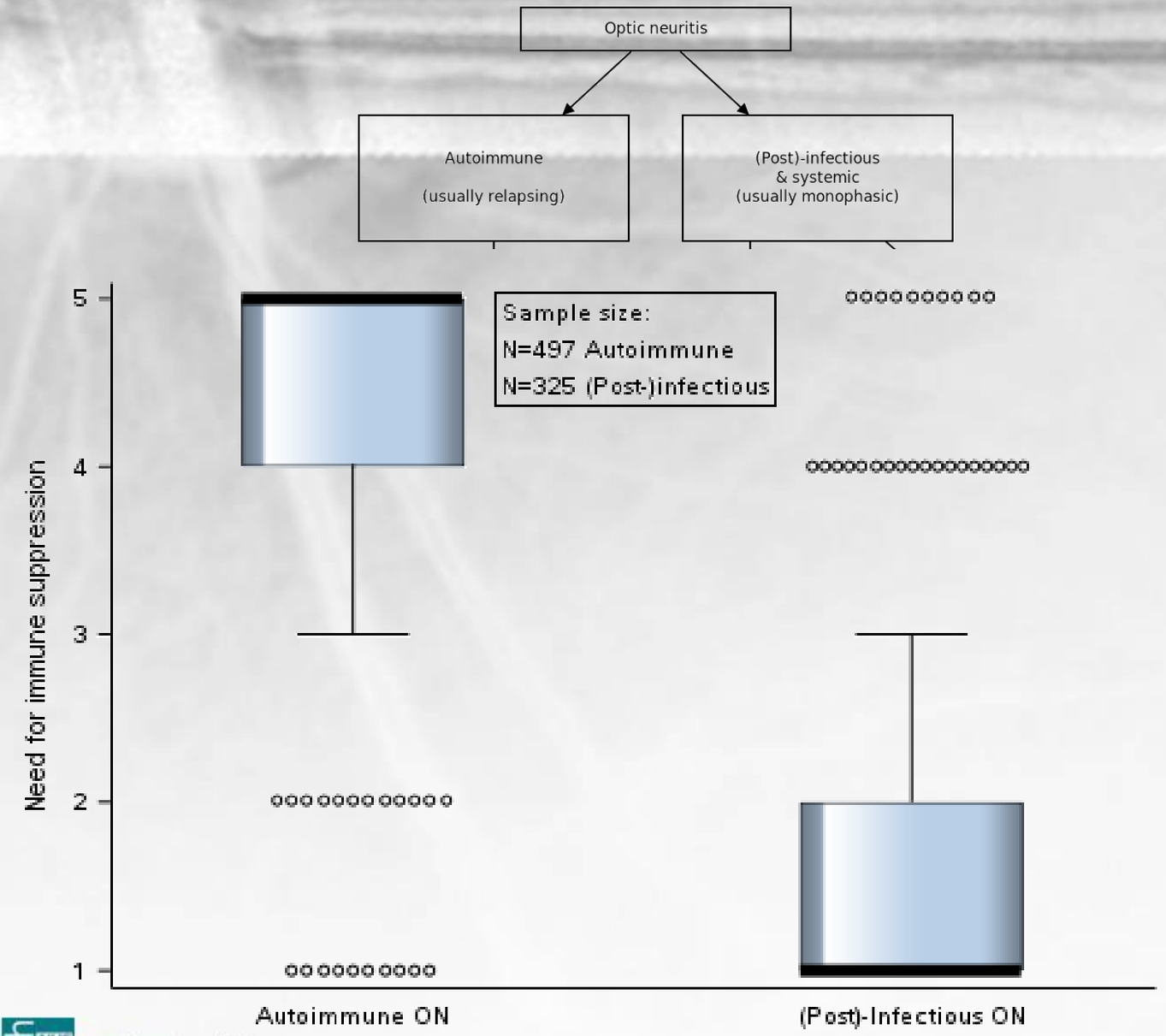
Classification



How did we get there?

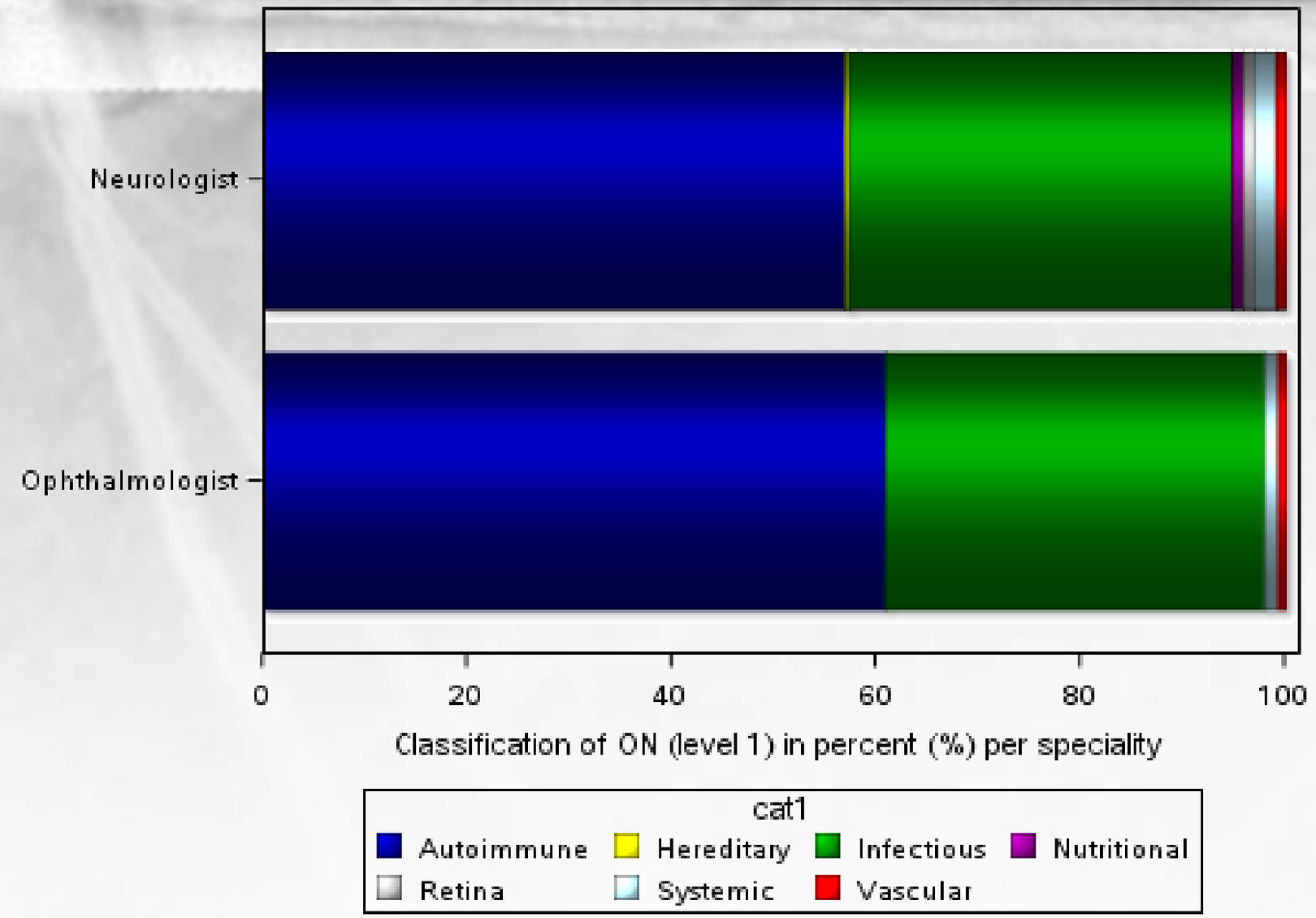


Level 1: 95% agreement

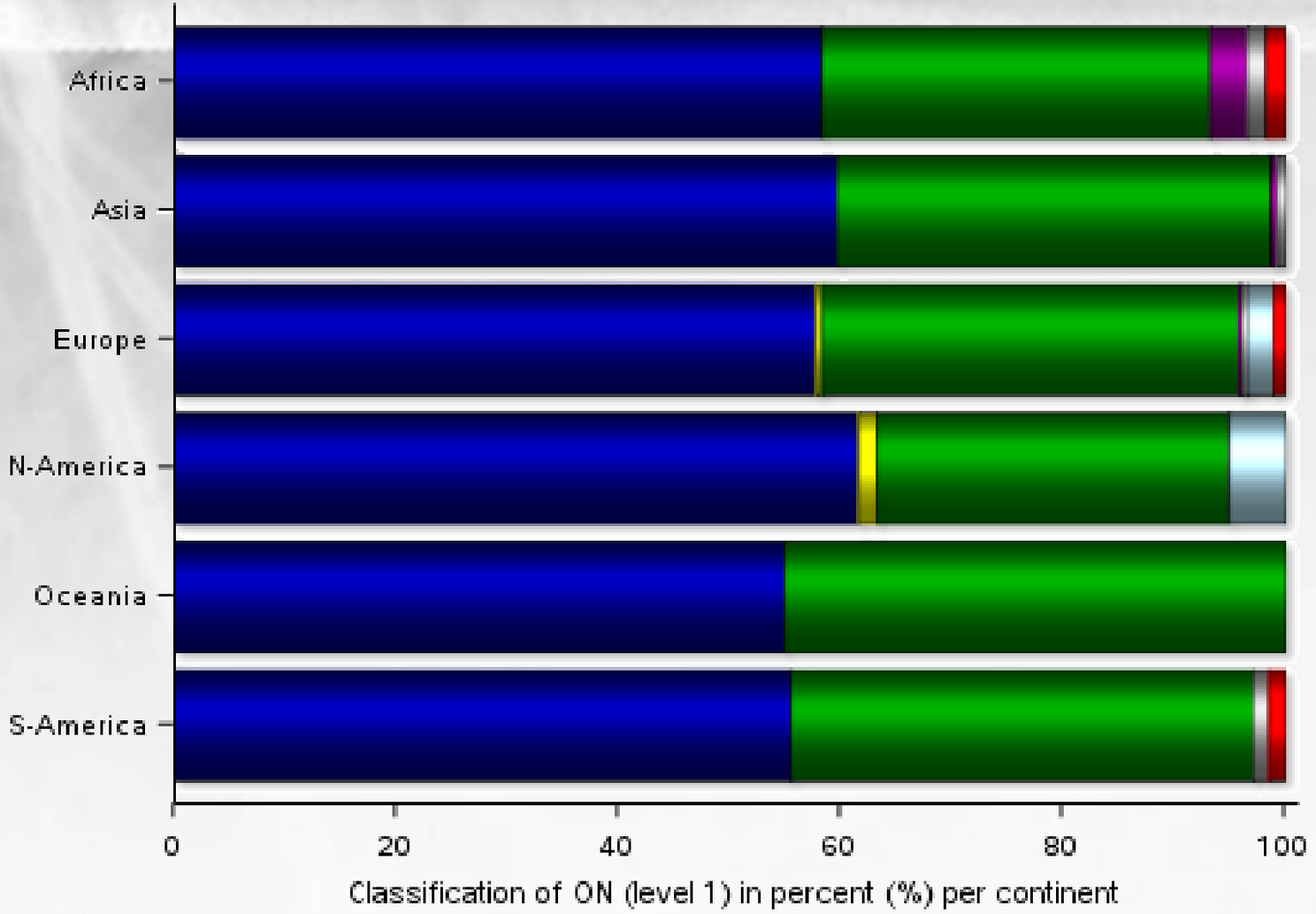
Based on iterative assessments from Delphi rounds 2-21

Relevant for patient management

Agreement: Speciality



Agreement: Continent



Cases summary

- Case 1: **MS-ON**

  Scenario A: painful, monocular, subacute LOV, dyschromatopsia, RAPD

- Case 2: **NMO-ON**

  Scenario B: no pain, monocular, subacute LOV, dyschromatopsia, RAPD

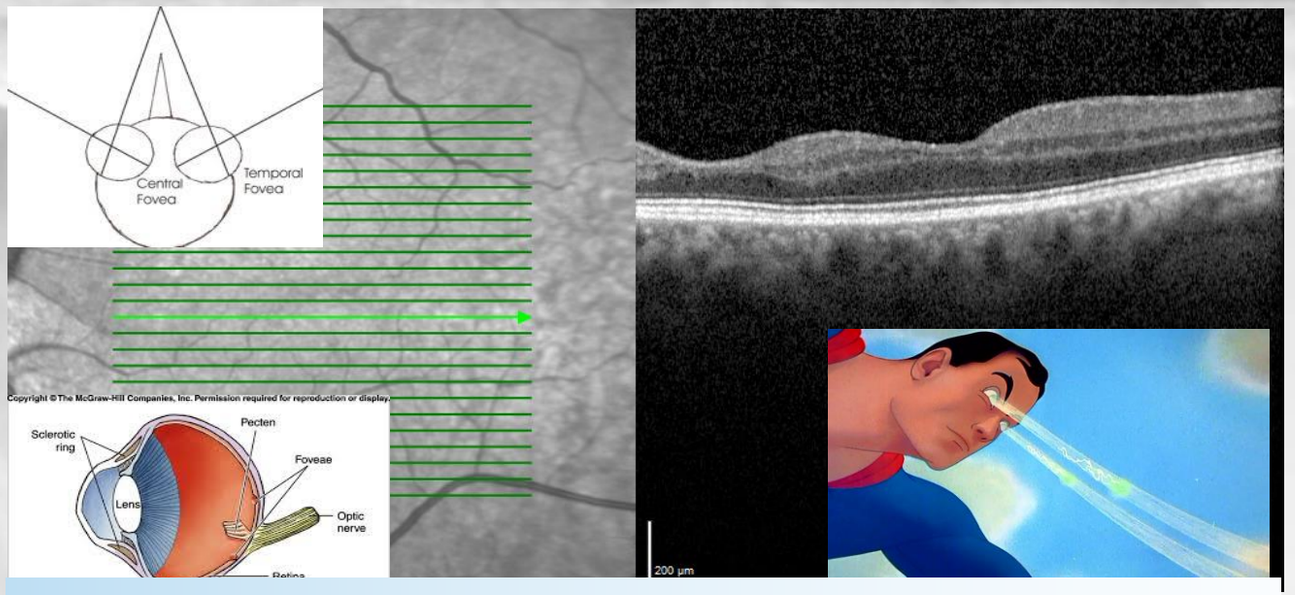
- Case 3: **post-infectious ON**

  Scenario C: binocular, subacute LOV, dyschromatopsia, no pain, no RAPD

Overall summary

- Optic Neuritis: Clinical approach
- Novel criteria incorporating OCT (sensitivity 61-100%), MRI (sensitivity 22-44%), biomarker (specificity >95%)
- Novel classification prioritising practical management
- Future revisions planned to optimise diagnostic sensitivity and broaden clinical spectrum

Dank voor toen en nu



MS Symposium 2016

Vrijdag 1 april |

```
Prima!
De volgende keer dat ik je op 1 april zie, zal ik heel erg goed uitkijken, met al mijn vier
foveae...

Groeten, Bob.
```

Give it a tweed