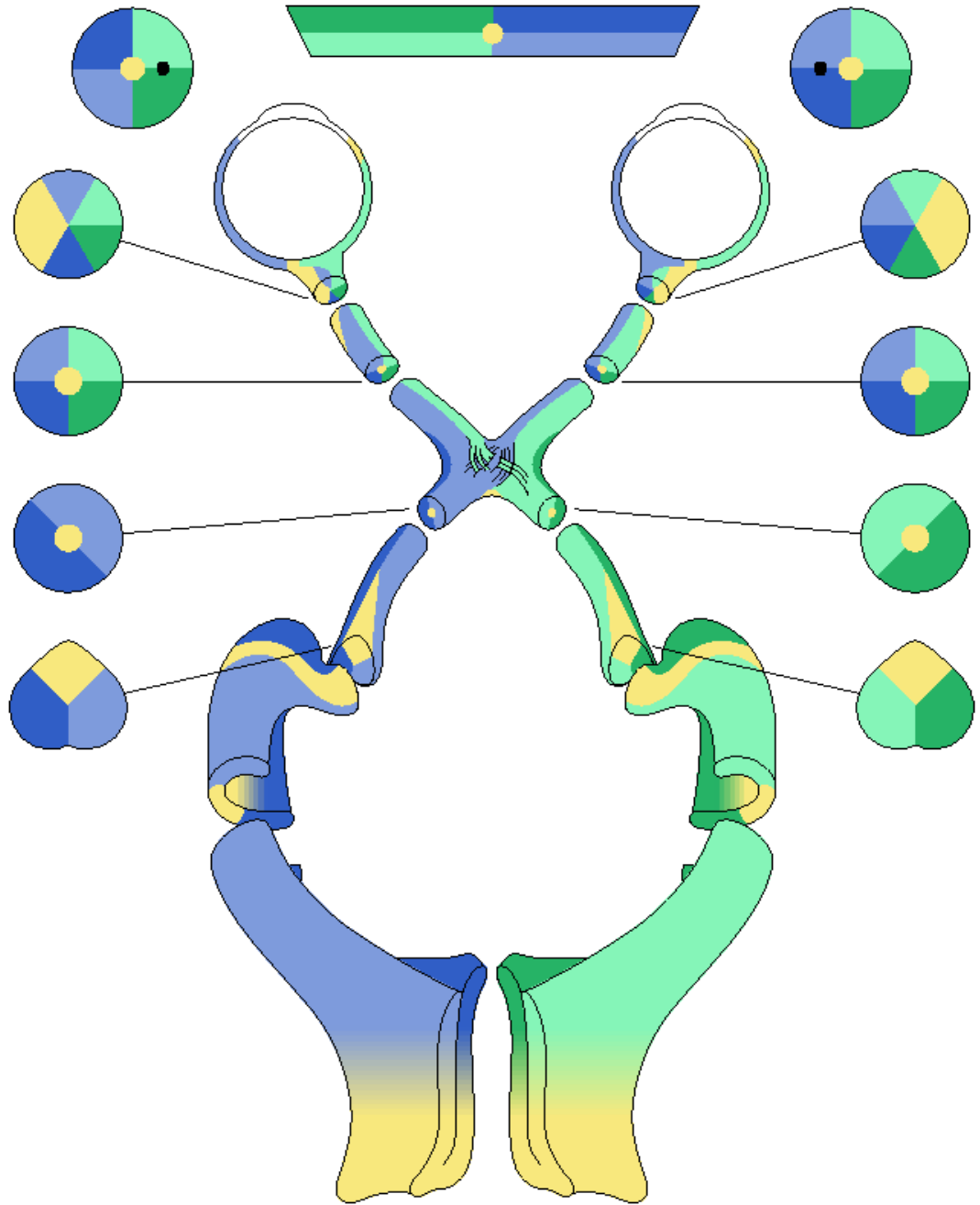
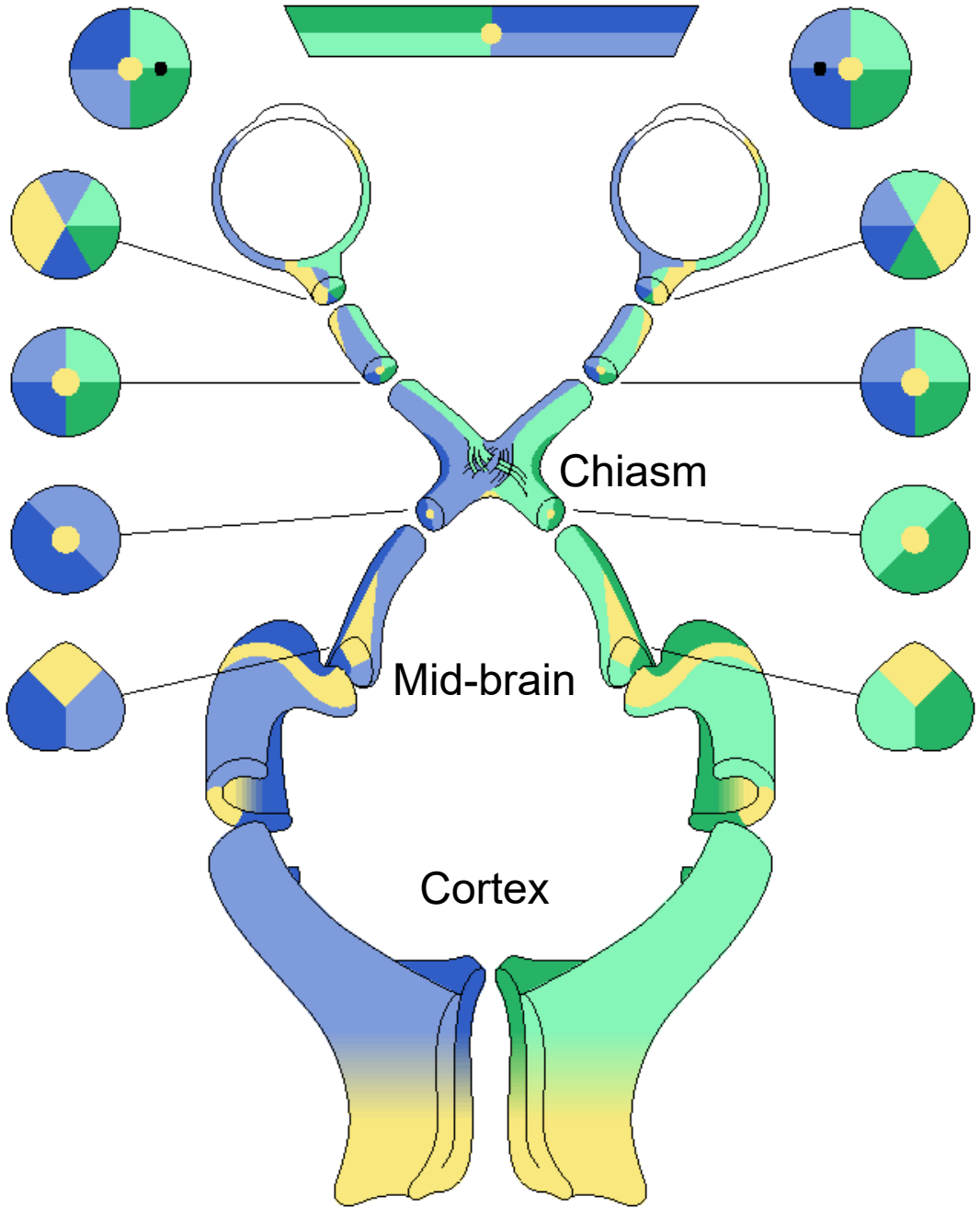
Multifocal Stimuli and MS

Ted Maddess[1] Josh van Kleef[1] Hanna Suominen[2] Anne Bruestle[3]
Corinne F Carle[1] Josh van Kleef[1] Emilie Rohan[1] Bhim Rai[1] Faran Sabeti[1]
Jo Lane[4] Rohan W Essex[5] Christian J Lueck[6] Christopher J Nolan[7]

[1]Eccels Institute of Neuroscience, The John Curtin School of Medical Research, ANU
[2]Department of Computer of Science, ANU
[3]Department of Immunology and Infectious Disease, The John Curtin School of Medical Research, ANU
[4]National Centre for Epidemiology and Population Health, ANU
[5]Department of Ophthalmology, The Canberra Hospital & ANU Medical School
[6]Department of Neurology, The Canberra Hospital & ANU Medical School
[7]Department of Endocrinology and Diabetes, The Canberra Hospital & ANU Medical School



4 quadrant stimulus on a TV

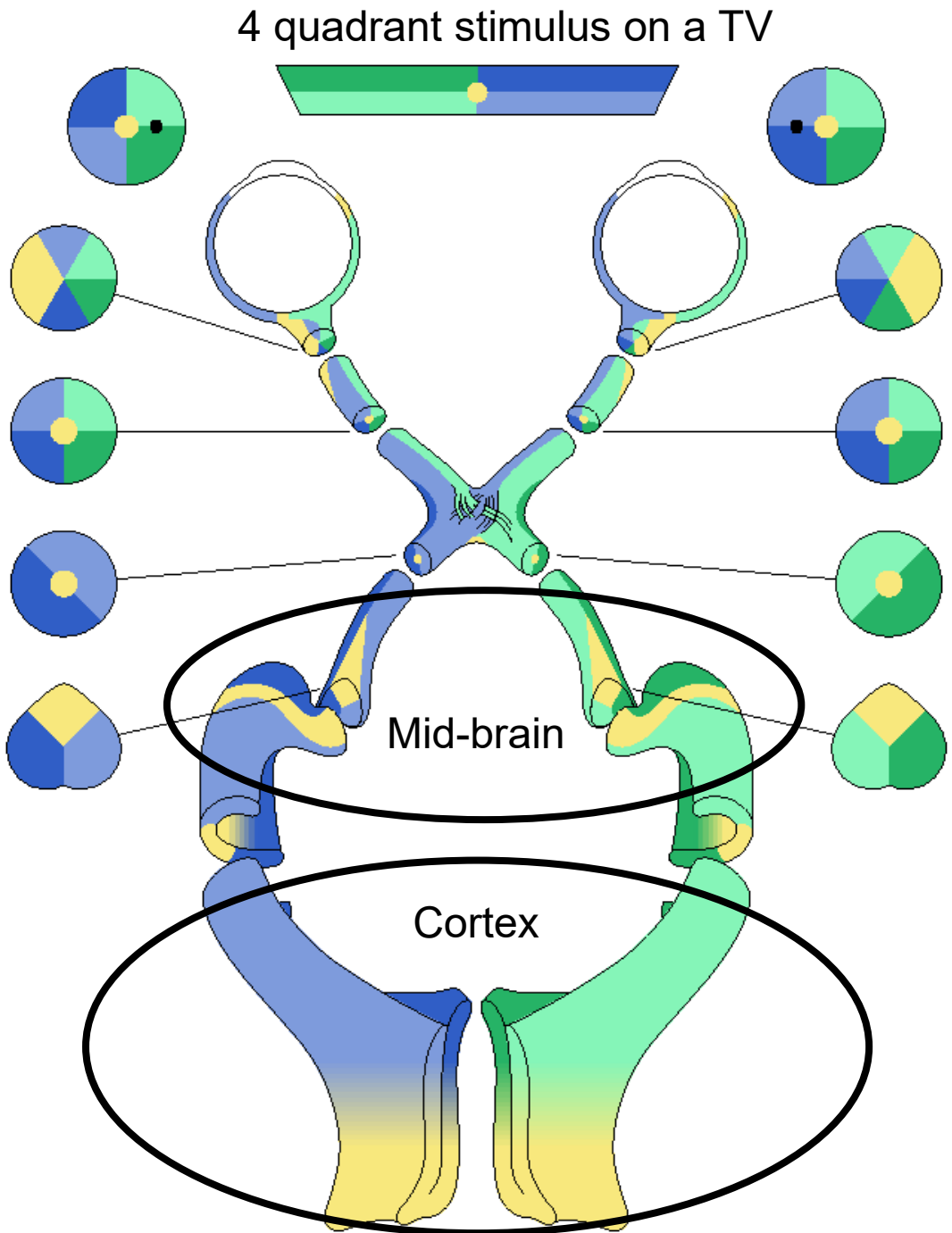


The map of visual space is somewhat preserved all along the pathways

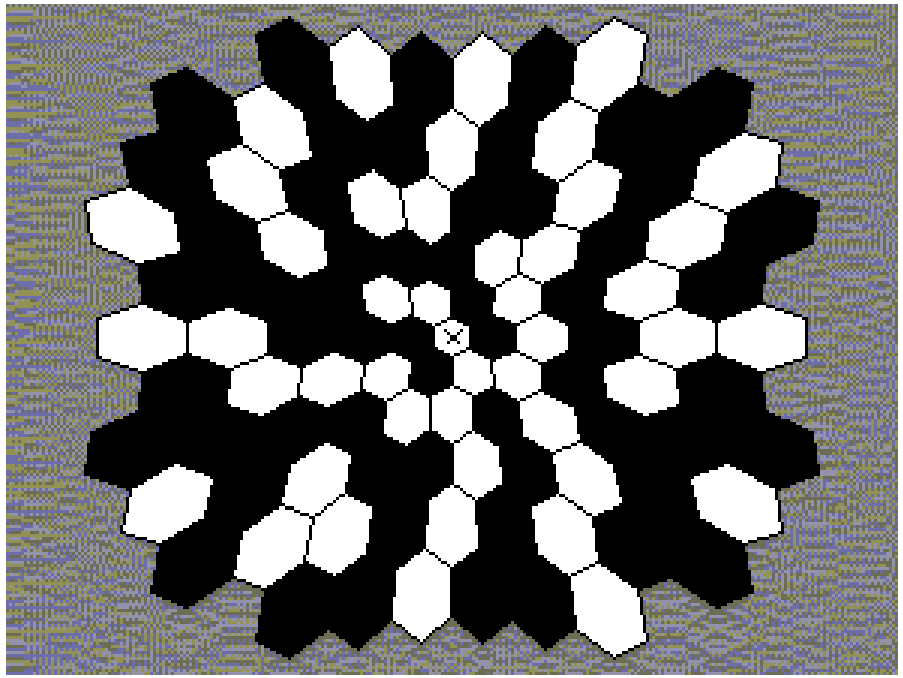
So testing a part of the visual field tests a part of the pathway

Can tease out small regions of damage

How to measure many parts of the fields?



Multifocal stimuli

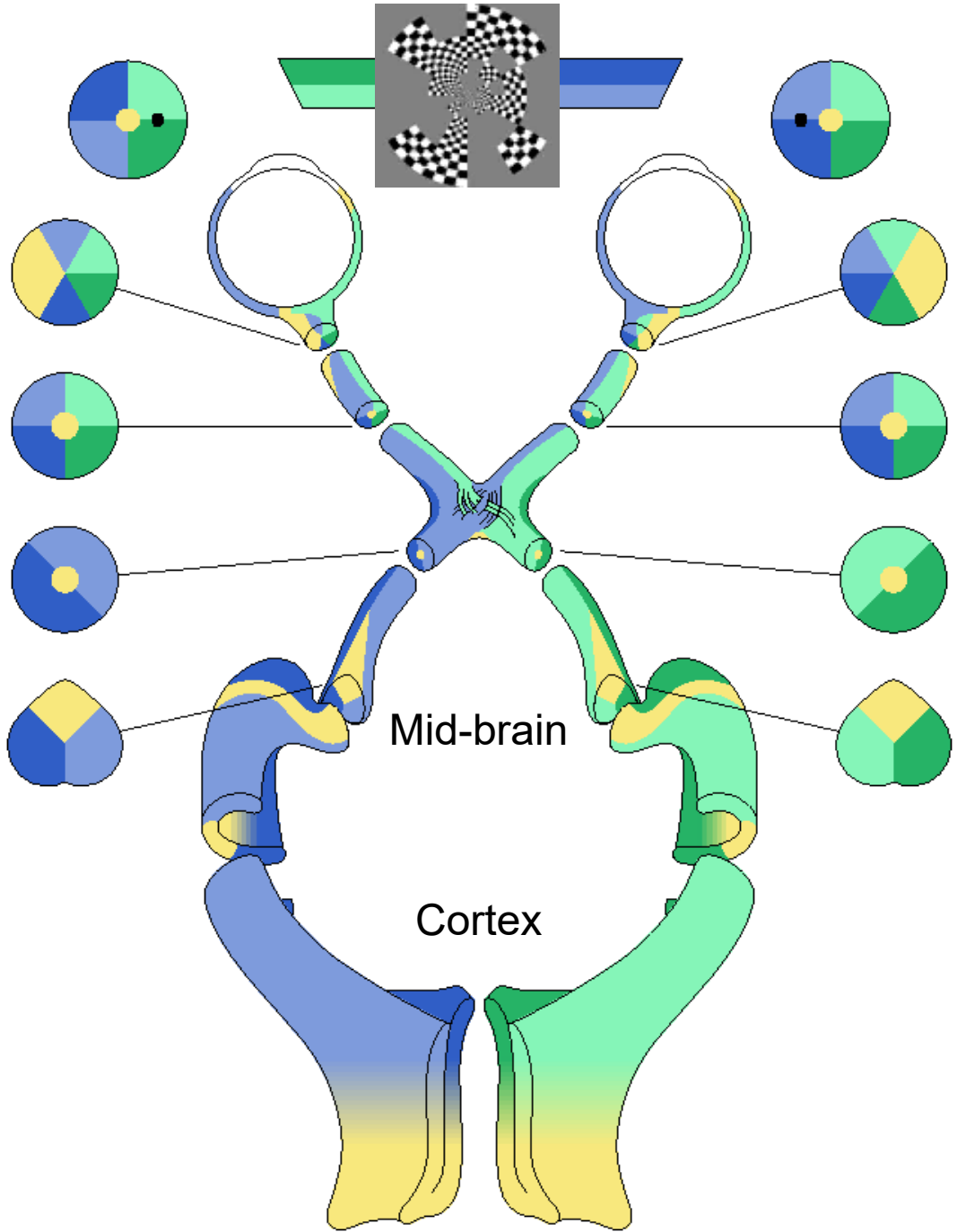


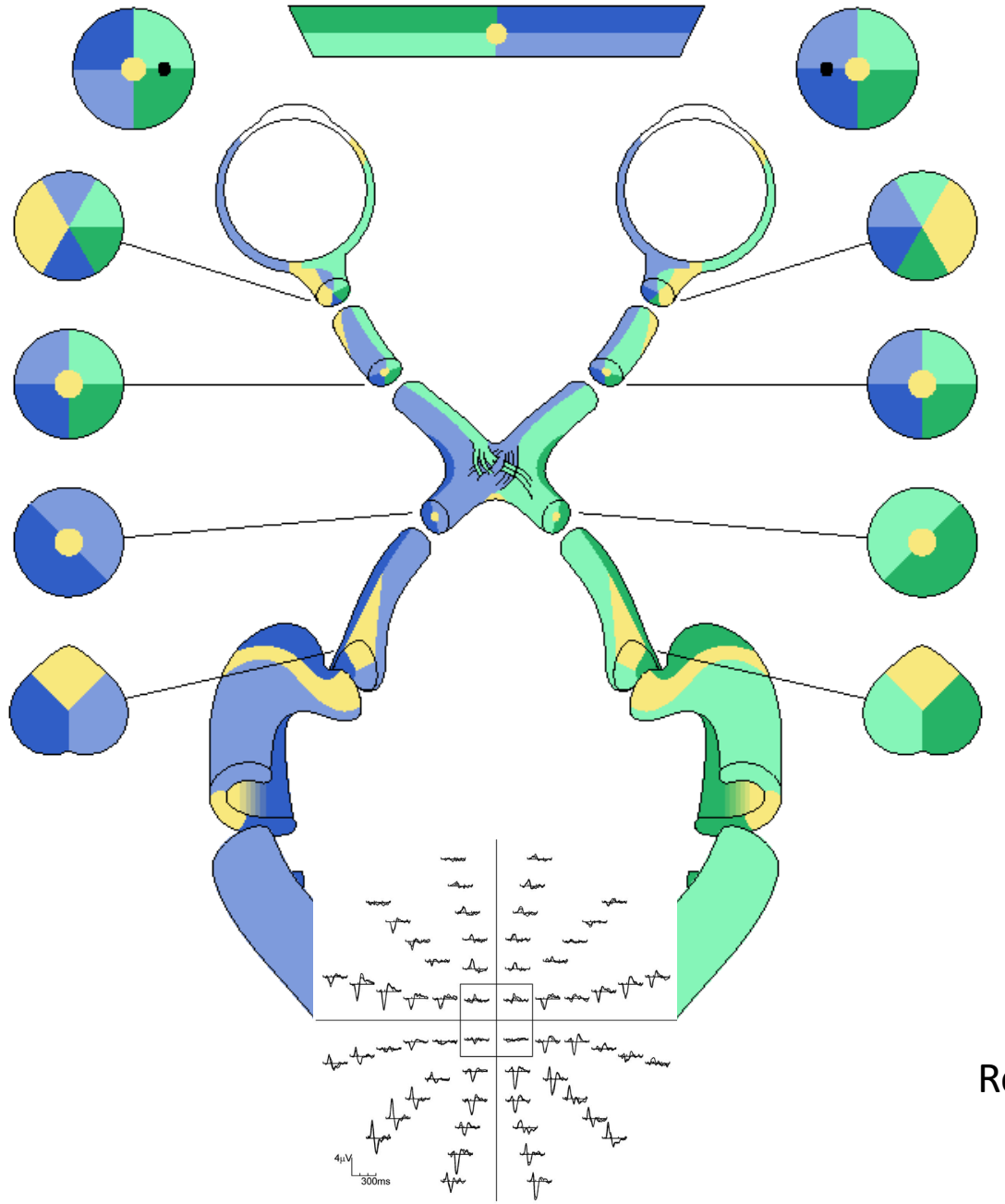
Multifocal Response

Average responses to flashes at each location

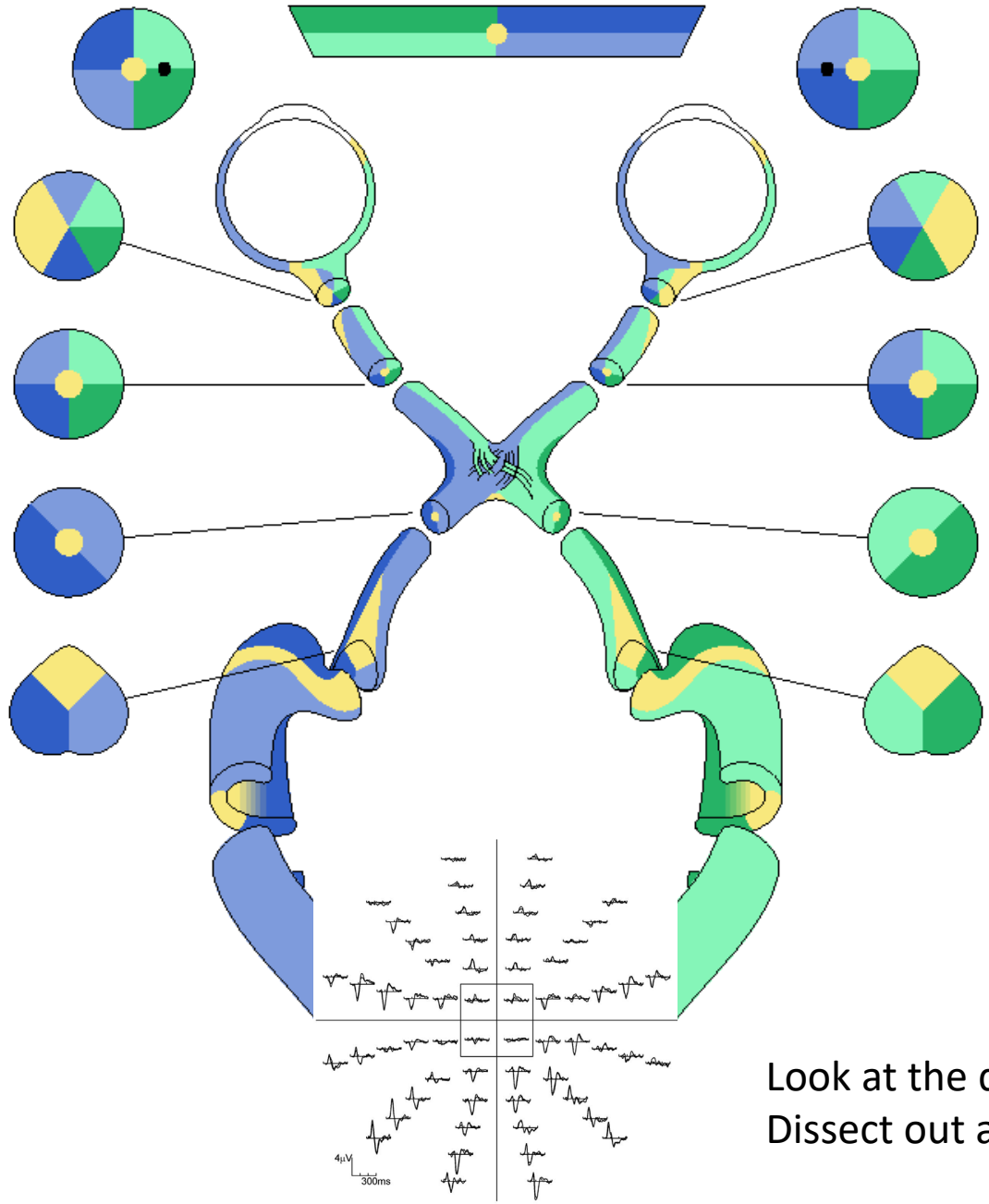
Multifocal Response

Tell you about visual function in small parts of the visual pathway


Mid-brain
Cortex



Records from the scalp

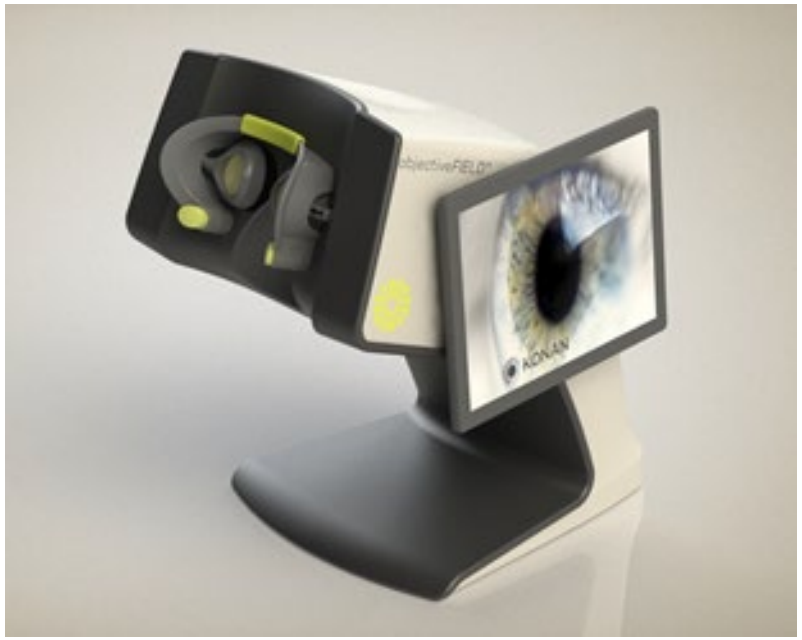


Look at the delays due to demyelination
Dissect out affected bits of the pathways

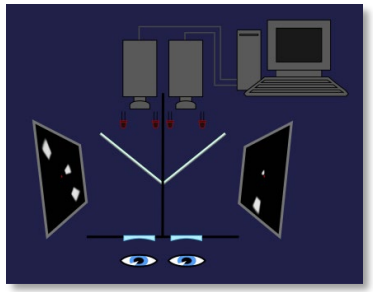
EEG caps no fun, peoples' brains are different

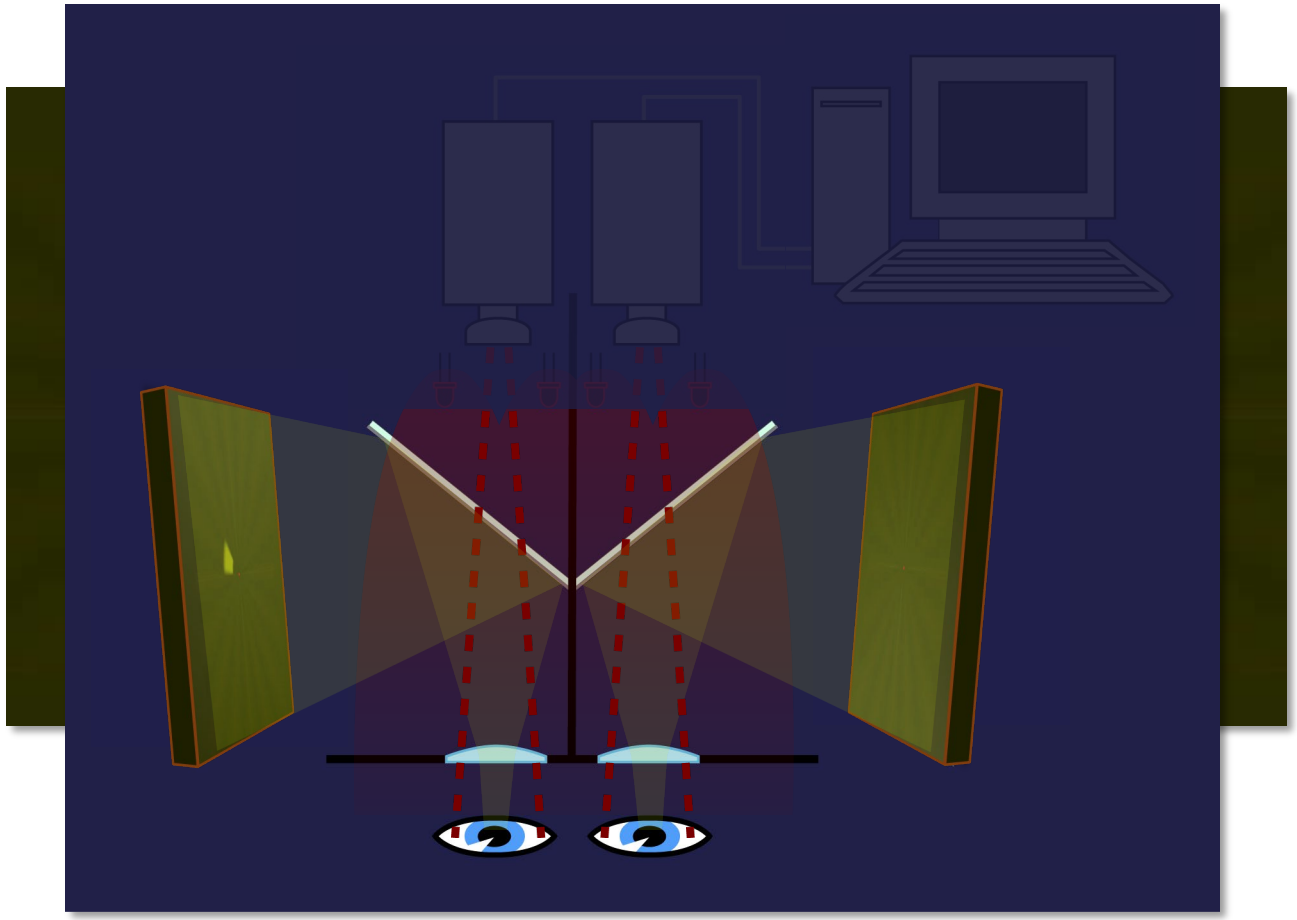
ObjectiveFIELD Analyser (OFA)

Konan Medical USA

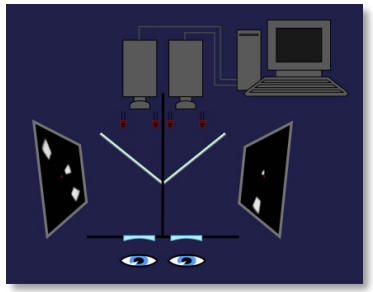


ObjectiveFIELD Analyser

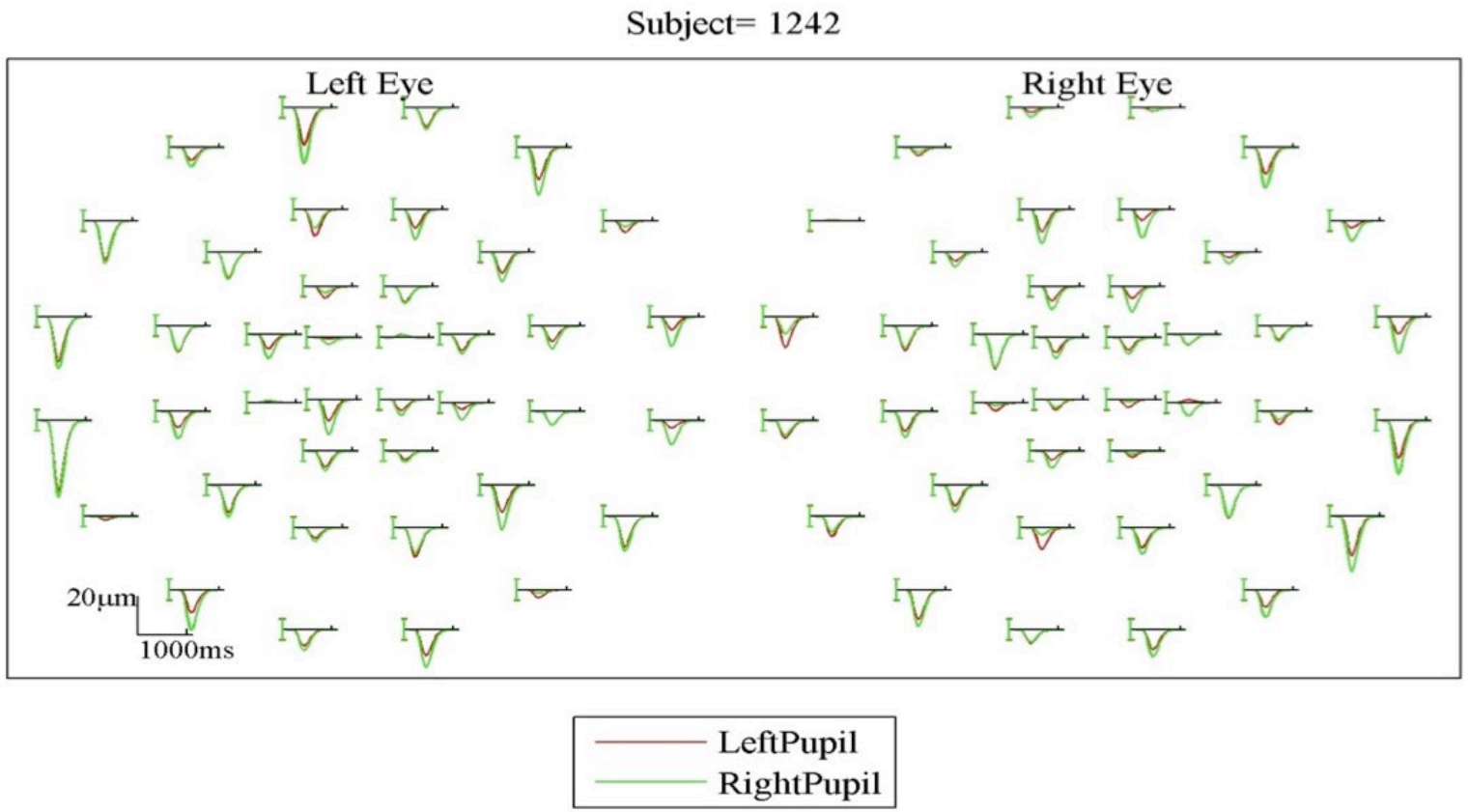




ObjectiveFIELD Analyser



ObjectiveFIELD example results



10-year follow-up study

eNeurologicalSci 29 (2022) 100430

Contents lists available at ScienceDirect

eNeurologicalSci

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

Objective perimetry and progression of multiple sclerosis

Ted Maddess [a,*], Corinne F. Carle [a], Emilie M.F. Rohan [a], Jonathan Baird-Gunning [b], Josh P. van Kleef [a], Christian J. Lueck [c,d]

[a] Eccles Institute of Neuroscience, John Curtin School of Medical Research, Australian National University, Acton, ACT, Australia
[b] Royal North Shore Hospital, Saint Leonards, New South Wales, Australia
[c] Department of Neurology, the Canberra Hospital, Canberra, ACT, Australia
[d] Australian National University Medical School, Acton, ACT, Australia

10-year follow-up study

- 44 persons who were tested with an older, *3rd Generation*, method were brought back *10 years later* to re-evaluate their EDSS scores
- Question: could the results of the old OFA test predict which persons living with MS progress?
- Answer: yes
- The mean of the 3 most delayed visual field regions in 2009 was correlated with progression of MS by 2019 ($p = 0.023$)
- Significant association between delay and odds of progression ($p = 0.045$)
  - e.g. an individual with 3 regions at least 1 SD (40 ms) slower than the mean in 2009 had 2.05× the odds (±SE: 1.43× to 2.95×)

New 5th Generation stimuli

Neurological Sciences
https://doi.org/10.1007/s10072-022-06387-z

ORIGINAL ARTICLE

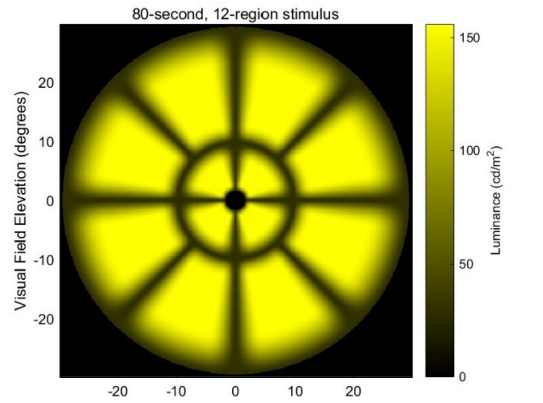
Check for updates

Rapid, non-contact multifocal visual assessment in multiple sclerosis

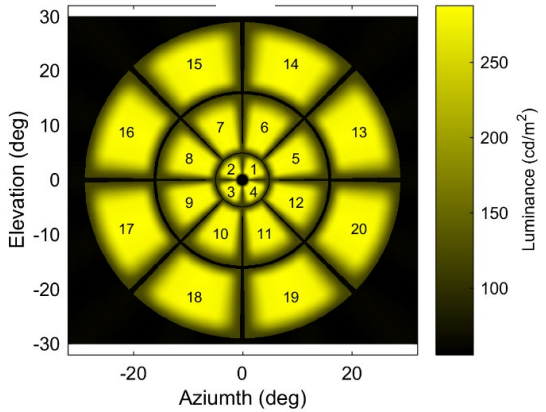
Ted Maddess[1] · Joshua P. van Kleef[1] · Emilie M. F. Rohan[1] · Corinne F. Carle[1] · Jonathan Baird-Gunning[2] · Bhim B. Rai[1] · Anne Bruestle[3] · Jo Lane[4] · Christian J. Lueck[5,6]

New 5th Generation stimuli

- **Test both eyes in 82 seconds**
- **W12** (wide-field, 12 regions) **±30°**
- **W20** designed to augment W12 **±30°**



W12

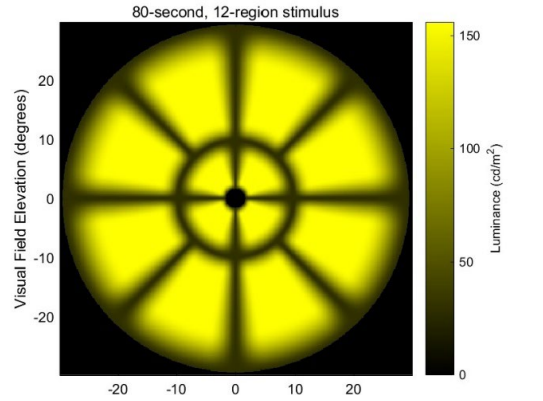


W20

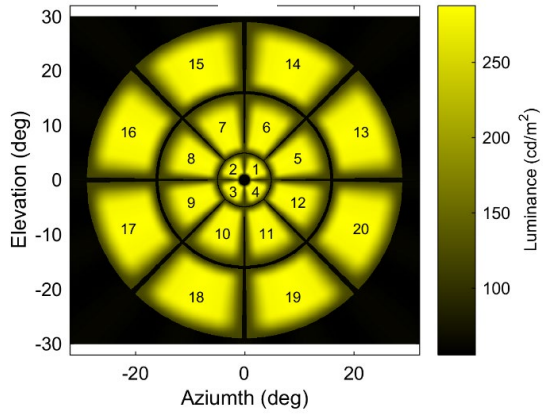
New 5th Generation stimuli

- **Test both eyes in 82 seconds**
- **W12** (wide-field, 12 regions) **±30°**
- **W20** designed to augment W12 **±30°**

- **Since both eyes are tested concurrently can examine the left-right *asymmetries* of regional delays**



W12



W20

New 5th Generation stimuli

Table 2 Area under receiver operator characteristic (AUROC) curves and Hedges' g values for the 4- and 12-worst per-region delay asymmetries of individuals' visual fields as a function of increasing EDSS severity, comparing P129, W12 and W20 mfPOP algorithms

	EDSS	AUROC (% ± SE)		Hedges' g	
		$N=4$	$N=12$	$N=4$	$N=12$
P129	≤2.5	73.9 ± 7.00	77.7 ± 5.80	1.12	1.25
	2.5 to 4.5	80.5 ± 6.62	82.9 ± 6.48	1.73	2.06
	≥4.5	90.3 ± 6.19	91.1 ± 6.13	2.74	2.93
W12	≤2.5	75.0 ± 8.33	76.4 ± 7.53	1.12	1.12
	2.5 to 4.5	89.8 ± 4.74	88.4 ± 4.58	1.70	1.62
	≥4.5	95.4 ± 2.62	93.3 ± 3.77	1.91	1.88
W20	≤2.5	81.1 ± 6.69	81.5 ± 6.00	1.32	1.26
	2.5 to 4.5	86.5 ± 6.26	84.6 ± 6.03	1.85	1.70
	≥4.5	94.1 ± 3.12	94.4 ± 3.16	2.37	2.35

New 5th Generation stimuli

- 4th Generation
- 5th Generation
- 5th Generation

Table 2 Area under receiver operator characteristic (AUROC) curves and Hedges' g values for the 4- and 12-worst per-region delay asymmetries of individuals' visual fields as a function of increasing EDSS severity, comparing P129, W12 and W20 mfPOP algorithms

	EDSS	AUROC (% ± SE)		Hedges' g	
		$N=4$	$N=12$	$N=4$	$N=12$
P129	≤2.5	73.9 ± 7.00	77.7 ± 5.80	1.12	1.25
	2.5 to 4.5	80.5 ± 6.62	82.9 ± 6.48	1.73	2.06
	≥4.5	90.3 ± 6.19	91.1 ± 6.13	2.74	2.93
W12	≤2.5	75.0 ± 8.33	76.4 ± 7.53	1.12	1.12
	2.5 to 4.5	89.8 ± 4.74	88.4 ± 4.58	1.70	1.62
	≥4.5	95.4 ± 2.62	93.3 ± 3.77	1.91	1.88
W20	≤2.5	81.1 ± 6.69	81.5 ± 6.00	1.32	1.26
	2.5 to 4.5	86.5 ± 6.26	84.6 ± 6.03	1.85	1.70
	≥4.5	94.1 ± 3.12	94.4 ± 3.16	2.37	2.35

New 5th Generation stimuli

Table 2 Area under receiver operator characteristic (AUROC) curves and Hedges' g values for the 4- and 12-worst per-region delay asymmetries of individuals' visual fields as a function of increasing EDSS severity, comparing P129, W12 and W20 mfPOP algorithms

	EDSS	AUROC (% ± SE)		Hedges' g	
		$N=4$	$N=12$	$N=4$	$N=12$
P129	≤2.5	73.9 ± 7.00	77.7 ± 5.80	1.12	1.25
	2.5 to 4.5	80.5 ± 6.62	82.9 ± 6.48	1.73	2.06
	≥4.5	90.3 ± 6.19	91.1 ± 6.13	2.74	2.93
W12	≤2.5	75.0 ± 8.33	76.4 ± 7.53	1.12	1.12
	2.5 to 4.5	89.8 ± 4.74	88.4 ± 4.58	1.70	1.62
	≥4.5	95.4 ± 2.62	93.3 ± 3.77	1.91	1.88
W20	≤2.5	81.1 ± 6.69	81.5 ± 6.00	1.32	1.26
	2.5 to 4.5	86.5 ± 6.26	84.6 ± 6.03	1.85	1.70
	≥4.5	94.1 ± 3.12	94.4 ± 3.16	2.37	2.35

New 5th Generation stimuli

- W12 and W20 better than P129?
- Certainly as good
- P129 takes 7 minutes

Table 2 Area under receiver operator characteristic (AUROC) curves and Hedges' *g* values for the 4- and 12-worst per-region delay asymmetries of individuals' visual fields as a function of increasing EDSS severity, comparing P129, W12 and W20 mfPOP algorithms

	EDSS	AUROC (% ± SE)		Hedges' *g*	
		N = 4	*N* = 12	*N* = 4	*N* = 12
P129	≤ 2.5	73.9 ± 7.00	77.7 ± 5.80	1.12	1.25
	2.5 to 4.5	80.5 ± 6.62	82.9 ± 6.48	1.73	2.06
	≥ 4.5	90.3 ± 6.19	91.1 ± 6.13	2.74	2.93
W12	≤ 2.5	75.0 ± 8.33	76.4 ± 7.53	1.12	1.12
	2.5 to 4.5	89.8 ± 4.74	88.4 ± 4.58	1.70	1.62
	≥ 4.5	95.4 ± 2.62	93.3 ± 3.77	1.91	1.88
W20	≤ 2.5	81.1 ± 6.69	81.5 ± 6.00	1.32	1.26
	2.5 to 4.5	86.5 ± 6.26	84.6 ± 6.03	1.85	1.70
	≥ 4.5	94.1 ± 3.12	94.4 ± 3.16	2.37	2.35

- Linear models: **P-values** ?

Table 3 Summary of linear models for W12 (upper) and W20 (lower) rapid stimulus methods. The models fitted the mean of the 4 biggest delay asymmetries (Asymm) to factors for normal controls and the 3 grades of EDDS severity from Table 3. Thus, the estimates for the 3 EDDS groups are differences compared to control subjects, and the significance of those differences is indicated by the *t*- and *p* values. Age and sex are also fitted but are non-significant

Parameter	Estimate (ms)	SE (ms)	*t*-stat	*p* value
W12				
Controls	−18.5	2.25	−8.21	-
EDSS ≤ 2.5	−7.7	3.32	−2.32	0.022
EDSS 2.5 to 4.5	−16.8	3.25	−5.17	6.64E−07
EDSS ≥ 4.5	−30.8	3.27	−9.42	3.76E−17
Sex	1.9	2.49	0.78	0.438
Age	−1.7	1.02	−1.68	0.095
W20				
Controls	−35.4	2.88	−12.30	-
EDSS ≤ 2.5	−15.4	4.23	−3.64	0.0004
EDSS 2.5 to 4.5	−32.7	4.15	−7.88	4.00E−13
EDSS ≥ 4.5	−39.8	4.18	−9.53	1.91E−17
Sex	4.2	3.18	1.33	0.186
Age	−0.8	1.30	−0.60	0.551

- T-statistics?
- P-values ?

Table 3 Summary of linear models for W12 (upper) and W20 (lower) rapid stimulus methods. The models fitted the mean of the 4 biggest delay asymmetries (Asymm) to factors for normal controls and the 3 grades of EDDS severity from Table 3. Thus, the estimates for the 3 EDDS groups are differences compared to control subjects, and the significance of those differences is indicated by the *t*- and *p* values. Age and sex are also fitted but are non-significant

Parameter	Estimate (ms)	SE (ms)	*t*-stat	*p* value
W12				
Controls	−18.5	2.25	−8.21	-
EDSS ≤ 2.5	−7.7	3.32	−2.32	0.022
EDSS 2.5 to 4.5	−16.8	3.25	−5.17	6.64E−07
EDSS ≥ 4.5	−30.8	3.27	−9.42	3.76E−17
Sex	1.9	2.49	0.78	0.438
Age	−1.7	1.02	−1.68	0.095
W20				
Controls	−35.4	2.88	−12.30	-
EDSS ≤ 2.5	−15.4	4.23	−3.64	0.0004
EDSS 2.5 to 4.5	−32.7	4.15	−7.88	4.00E−13
EDSS ≥ 4.5	−39.8	4.18	−9.53	1.91E−17
Sex	4.2	3.18	1.33	0.186
Age	−0.8	1.30	−0.60	0.551

New 5th Generation stimuli

- W12 and W20 better than P129?
- Certainly as good
- P129 takes 7 minutes

Table 2 Area under receiver operator characteristic (AUROC) curves and Hedges' *g* values for the 4- and 12-worst per-region delay asymmetries of individuals' visual fields as a function of increasing EDSS severity, comparing P129, W12 and W20 mfPOP algorithms

	EDSS	AUROC (% ± SE)		Hedges' *g*	
		N = 4	*N* = 12	*N* = 4	*N* = 12
P129	≤ 2.5	73.9 ± 7.00	77.7 ± 5.80	1.12	1.25
	2.5 to 4.5	80.5 ± 6.62	82.9 ± 6.48	1.73	2.06
	≥ 4.5	90.3 ± 6.19	91.1 ± 6.13	2.74	2.93
W12	≤ 2.5	75.0 ± 8.33	76.4 ± 7.53	1.12	1.12
	2.5 to 4.5	89.8 ± 4.74	88.4 ± 4.58	1.70	1.62
	≥ 4.5	95.4 ± 2.62	93.3 ± 3.77	1.91	1.88
W20	≤ 2.5	81.1 ± 6.69	81.5 ± 6.00	1.32	1.26
	2.5 to 4.5	86.5 ± 6.26	84.6 ± 6.03	1.85	1.70
	≥ 4.5	94.1 ± 3.12	94.4 ± 3.16	2.37	2.35

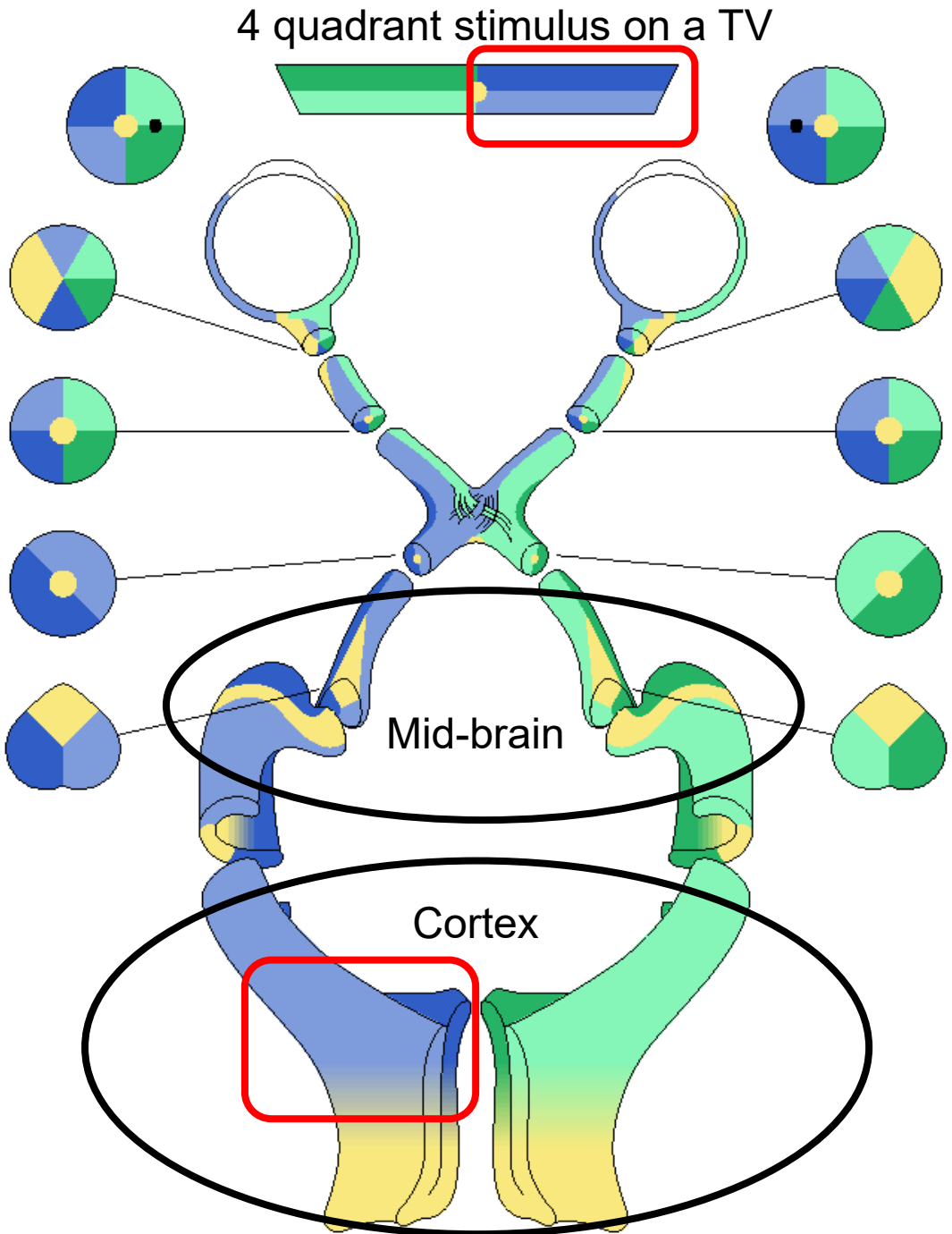
Conclusions

- OFA may provide a rapid, convenient method of monitoring and predicting MS progression
- May provide new clinical end-points for therapeutics
- Will be sold in early 2023
- More portable unit coming
  - Both the desktop and the portable can do telemedicine
- Thanks for listening!

Conclusions

- OFA may provide a rapid, convenient method of monitoring and predicting MS progression
- May provide new clinical end-points for therapeutics
- Will be sold in early 2023
- More portable unit coming
  - Both the desktop and the portable can do telemedicine
- Thanks for listening!

ted.maddess@anu.edu.au



Notice left and right parts of image wind up on the opposite side of the head

Follow the blue and green

Occipital pole stroke

- Damage to one side of early visual cortex
- Due to chiasm right half of visual fields from both eyes processed on left cortex (and visa versa)
- “Homonymous hemianopia”

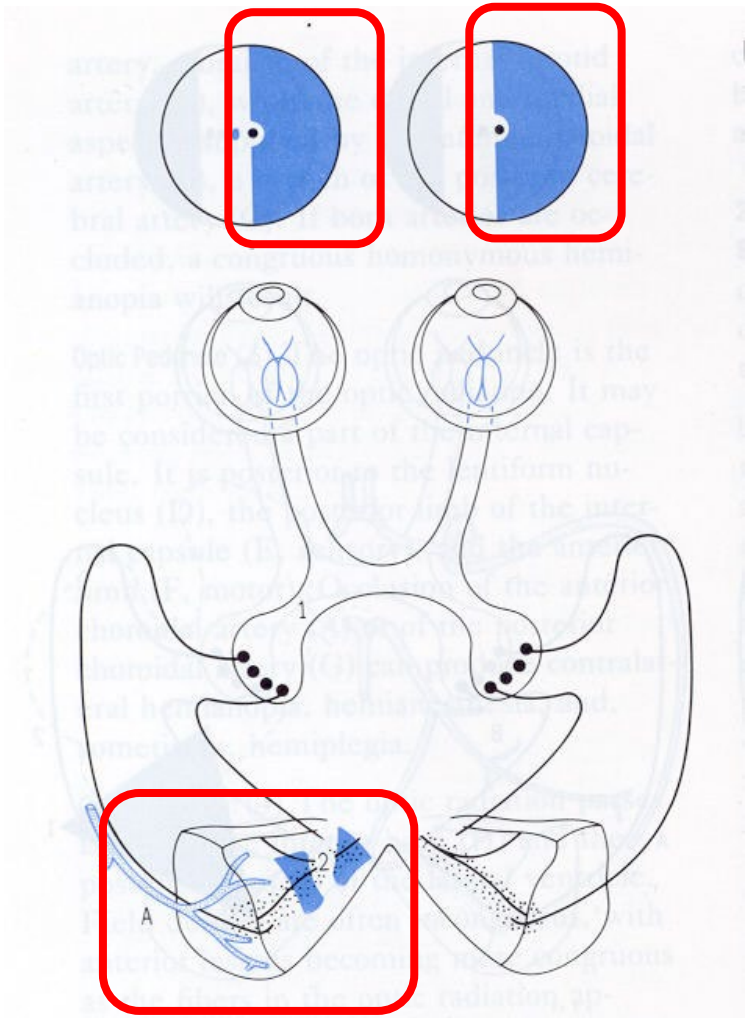


Figure 2-13 *A homonymous hemianopia with macular sparing.*

Chiasmic compression

- A tumour presses down on chiasm
- Often benign and treatable without surgery
- Bi-temporal hemianopia

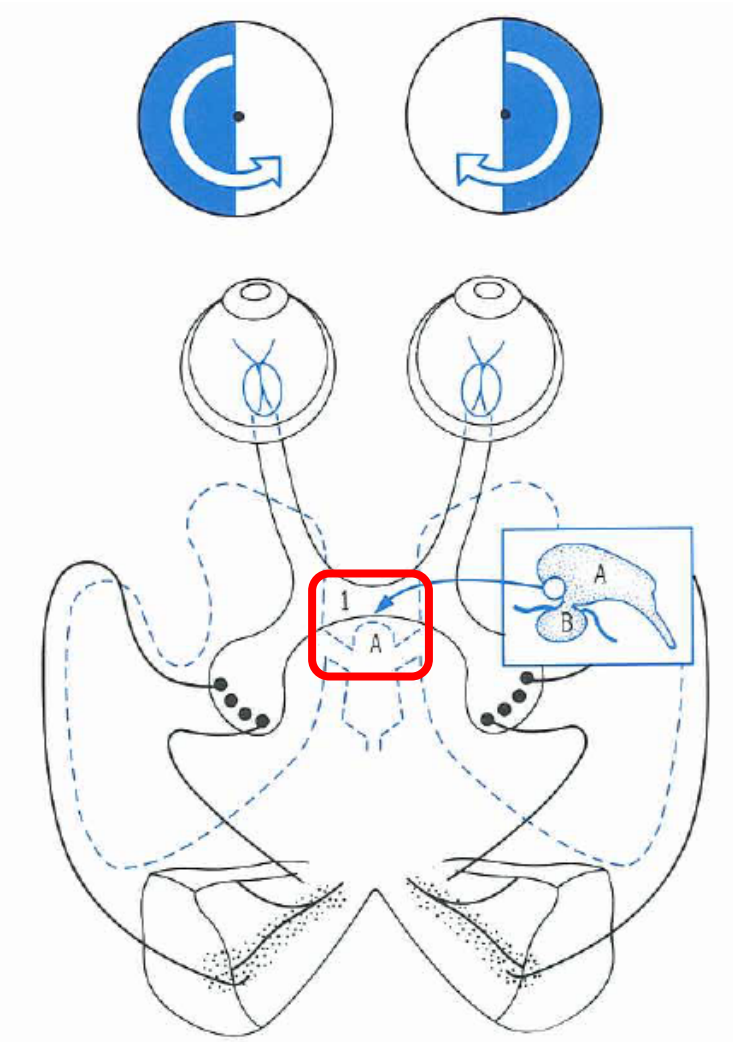
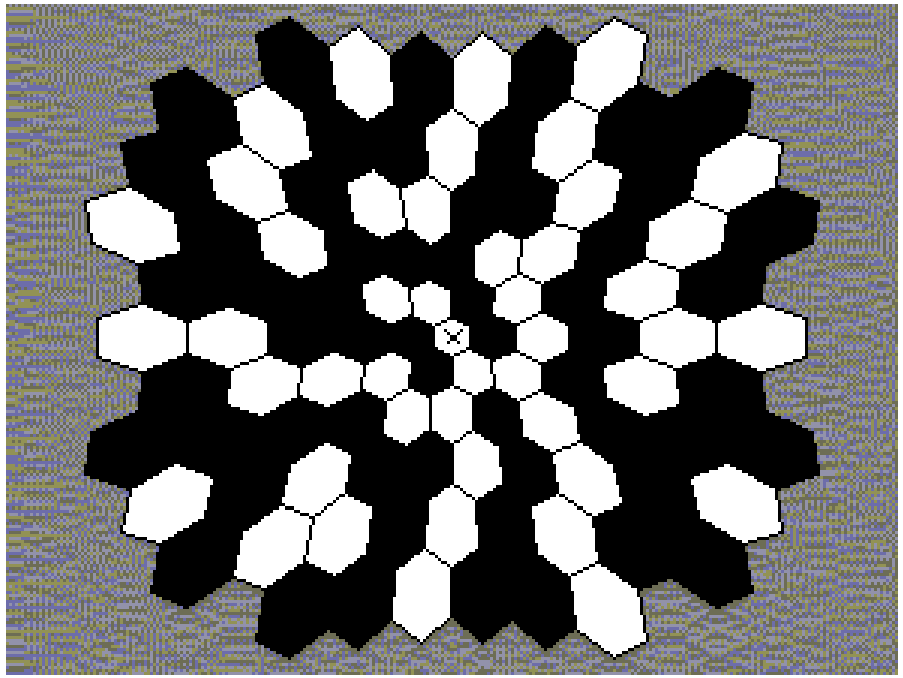
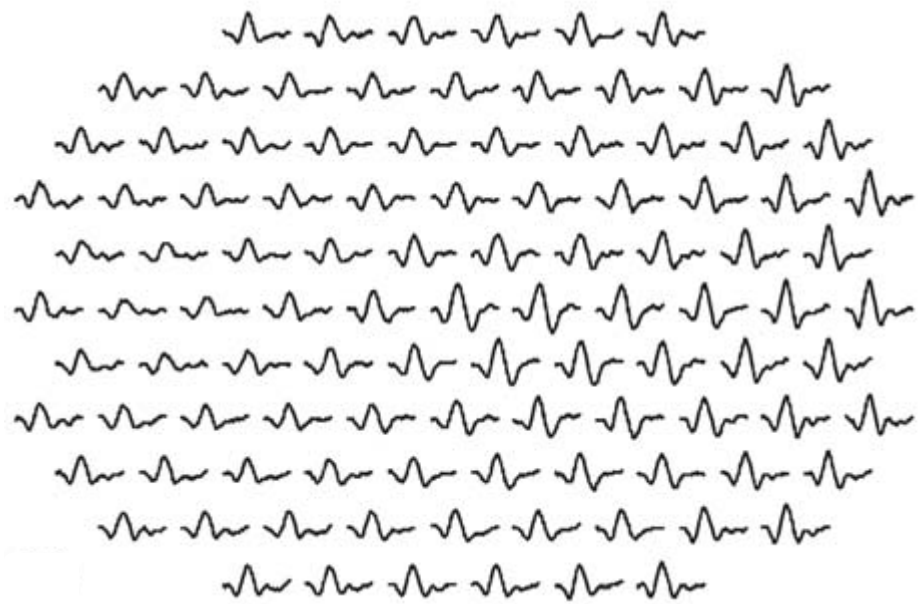


Figure 2-18 *A complete bitemporal hemianopia.*

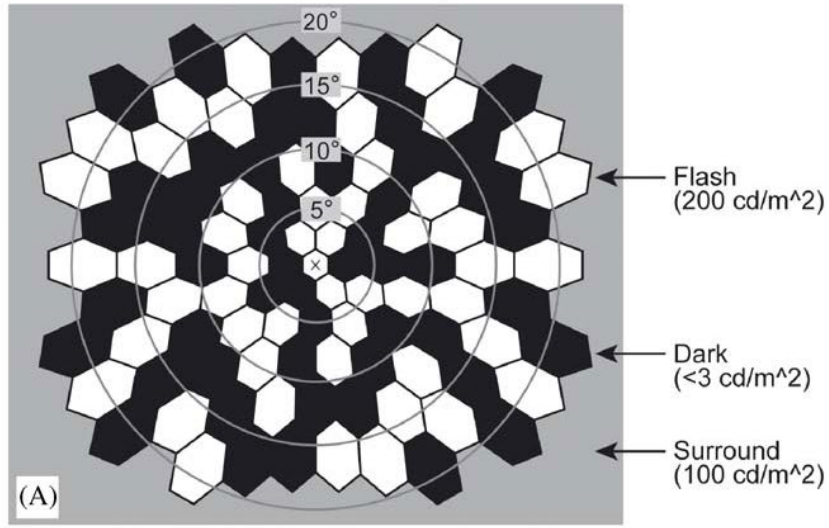
Dense Multifocal – two states, fast



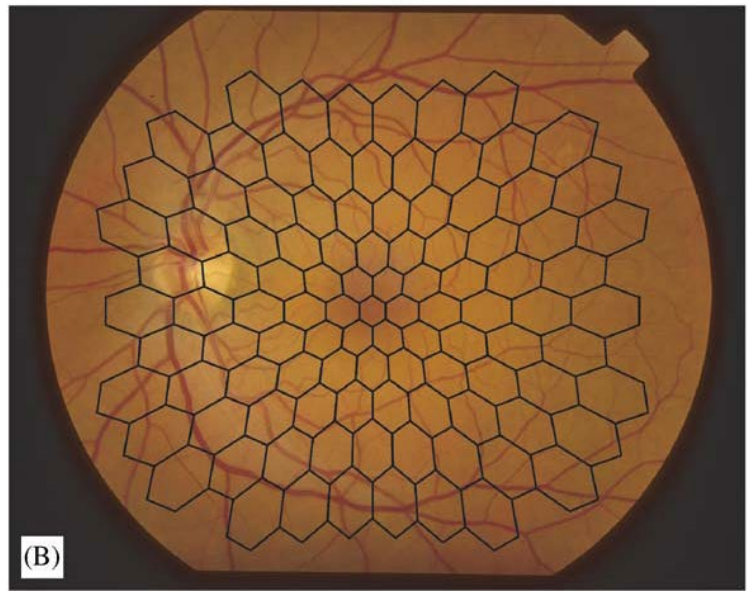


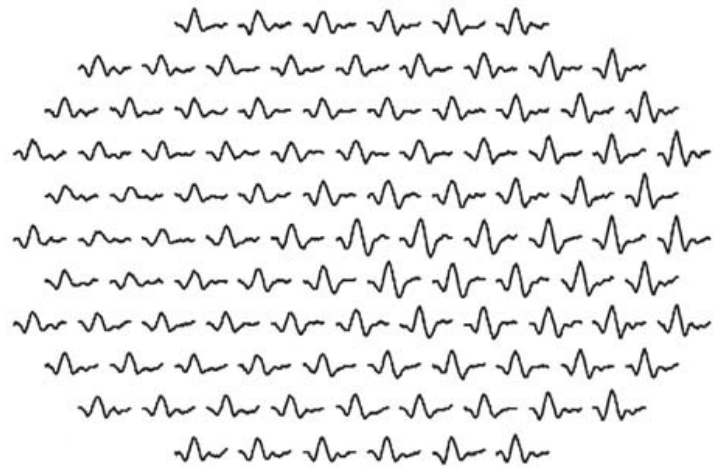
Average responses to flashes at each location

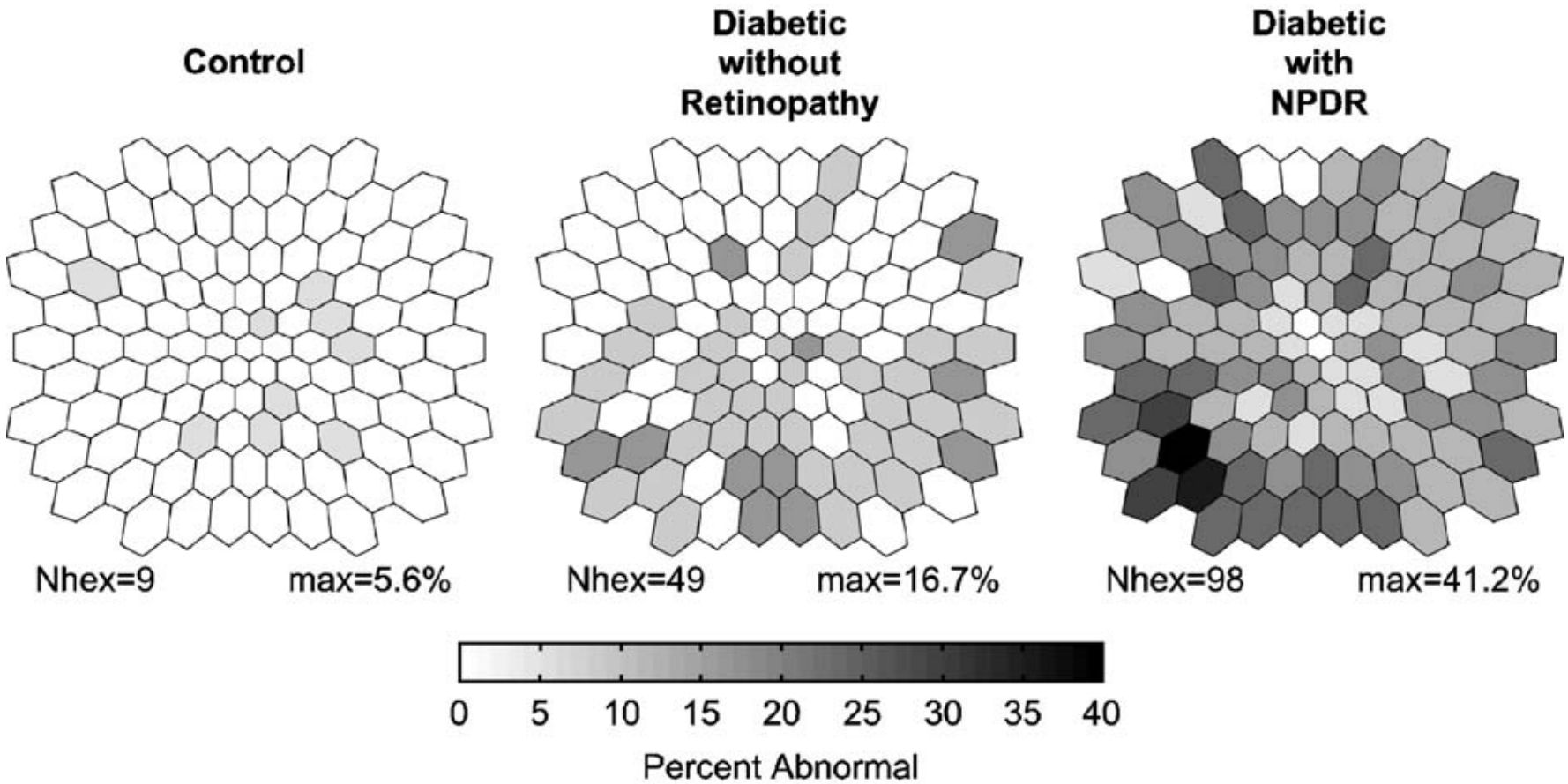
mfERG Stimulus Array



Fundus Correspondence







NPDR = nonproliferative diabetic retinopathy = relatively early stage