

Évaluation fMRI de la rétinotopie de patients avec glaucome monoculaire ou fortement asymétrique

Étude en cours

Laurent G. Brosseau (R111 - radiologie diagnostique)

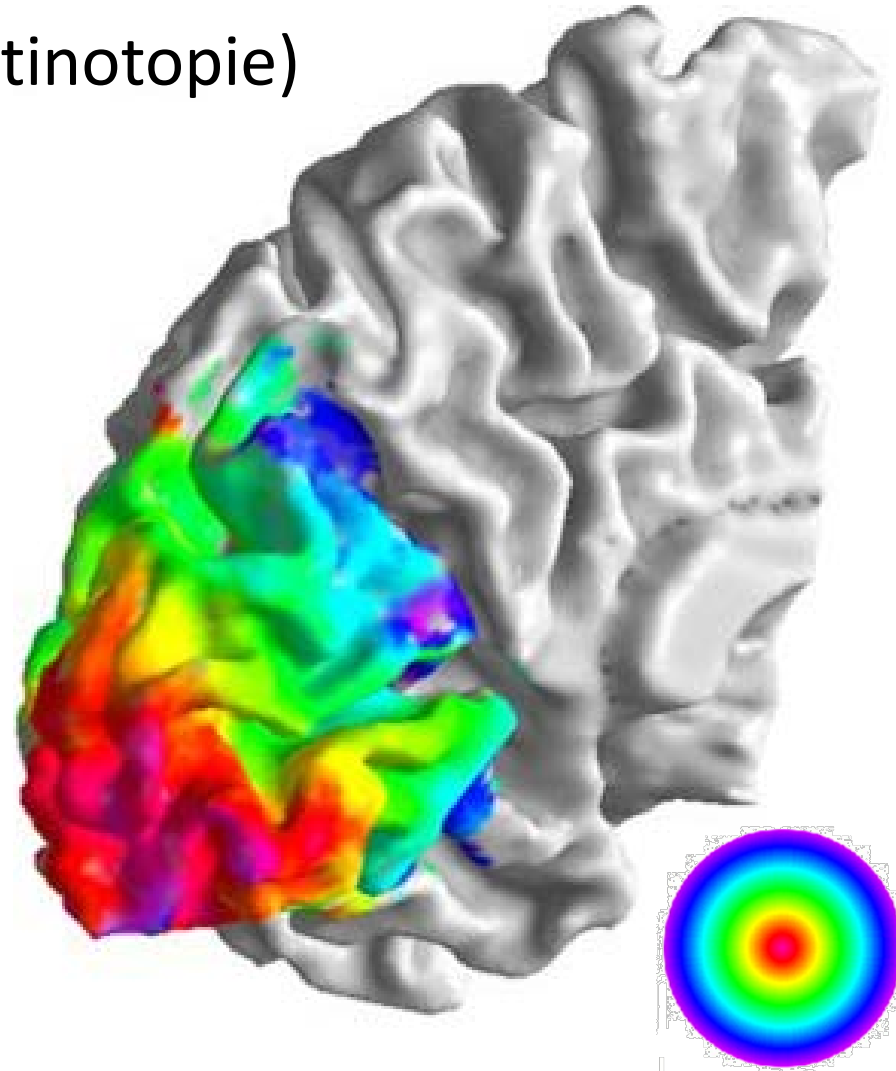
Lyes Bachatene (PhD)

Kevin Whittingstall (PhD)

Marjorie Carbonneau (MD - ophtalmologie)

Ordre du jour

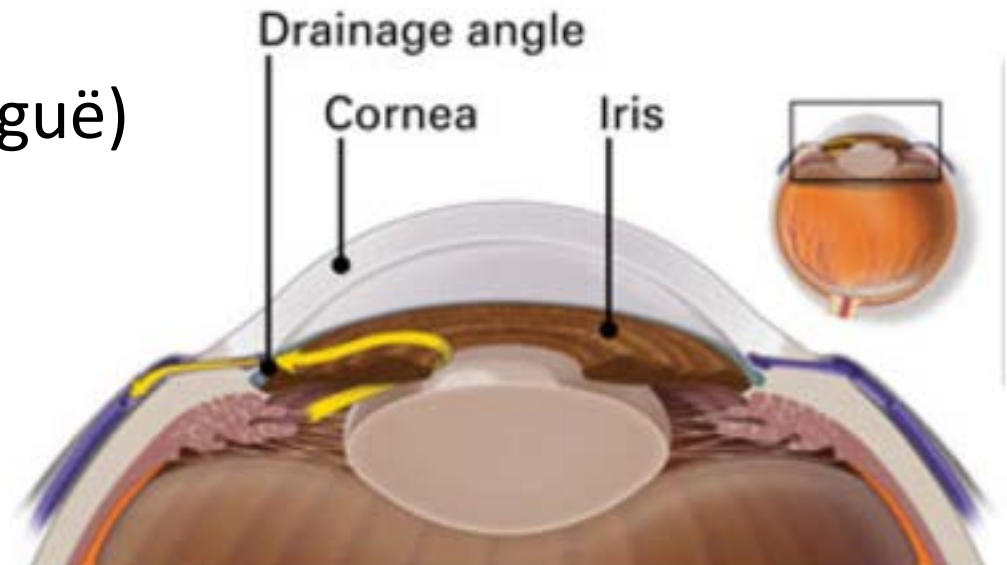
- État des connaissances actuelles (glaucome, rétinopathie)
- Notre étude:
 - Objectifs
 - Hypothèses
 - Méthodologie
- Résultats actuels
- À venir, avenues futures



Glaucome

- Définition vulgarisée (*American Academy of Ophthalmology*):
*Glaucoma is a disease that damages your eye's **optic nerve**. It usually happens when **fluid builds up in the front part of your eye**. That extra fluid increases the pressure in your eye, damaging the optic nerve.*

- Angle ouvert ou fermé (présentation aiguë)



Nouvelles données émergentes...

Distal axonopathy with structural persistence in glaucomatous neurodegeneration

Samuel D. Crish^a, Rebecca M. Sappington^a, Denise M. Inman^b, Phillip J. Horner^b, and David J. Calkins^{a,1}

Progression axonale typique maladies neurodégénératives

^aDepartment of Neurobiology, University of Washington, Seattle, WA 98104

^bDepartment of Neurosurgery, University of Washington, Seattle, WA 98104

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Atteinte axonale distale antégrade

An early hallmark of neuronal degeneration is distal transport loss and axon pathology. Glaucoma affects retinal ganglion cell (RGC) neurons and their axons in the optic nerve. Here we show that, like other neurodegenerations, distal axon injury appears early in mouse glaucoma. Where RGC axons terminate in the superior colliculus, reduction of active transport results in a pattern resembling glaucomatous vision loss. Like glaucoma, susceptibility to transport deficits increases with age and is not necessarily associated with elevated ocular pressure. Distal transport loss is distal-to-proximal, appearing in the colliculus first followed by more proximal secondary targets and then the optic tract. Transport persists through the optic nerve head before finally failing in the retina. Although axon degeneration also progresses distal-to-proximal, myelinated RGC axons and their presynaptic terminals persist in the colliculus well after transport fails. Thus, distal transport loss is predegenerative and may represent a therapeutic target.

Rétine affectée tardivement

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Modèle animal

Peu de sujets à l'étude

Distal Loss of Transport Is Retinotopic and Age-Dependent. RGC axons course through layer III of the SC to contact layer II neurons retinotopically (20). These can be visualized by intraocular injection of cholera toxin β -subunit (CTB), which labels the entire retinotopic projection via active uptake and transport (21, 22). For a 5-mo C57 and a 5-mo DBA/2, CTB labeled the entire retinotopic projection in the SC except for the retinal optic disk, which does not contain RGCs (Fig. 1A and B). In contrast, the SC of an 8-mo DBA/2 demonstrated a focal deficit extending caudally from the optic disk gap (Fig. 1C), whereas a 10-mo DBA/2 SC contained a massive deficit that left the entire medial-caudal quadrant devoid of label (Fig. 1D).

The SC maps in Fig. 1C and D resemble sectorial vision loss in glaucoma, which extends to the RGC-rich central retina (23). Some degenerative markers in the aged DBA/2 optic nerve and retina also have this pattern (8, 14, 24, 25). The area around the optic disk in the rodent contains the highest RGC density, like the human central retina (26). Whereas C57 mice showed no change

axon transport | optic neuropathy | retinal ganglion cell | glaucoma | optic nerve

Nouvelles données émergentes...

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SCIENTIFIC REPORTS

OPEN Retinal Structures and Visual Cortex Activity are Impaired Prior to Clinical Vision Loss in Glaucoma

Signes atteinte rétine & nerf optique,
↓ activation cérébrale corticale
précèdent perte vision

areas in glaucoma. Within the visual cortex, choline metabolism was perturbed along with increasing disease severity in the eye, optic radiation and visual field. In summary, this study showed evidence that glaucoma deterioration is already present in the eye and the brain before substantial vision loss can be detected clinically using current testing methods. In addition, cortical cholinergic abnormalities are involved during trans-neuronal degeneration and can be detected non-invasively in glaucoma. The current results can be of impact for identifying early glaucoma mechanisms, detecting and monitoring pathophysiological events and eye-brain-behavior relationships, and guiding vision preservation strategies in the visual system, which may help reduce the burden of this irreversible but preventable neurodegenerative disease.

Nouvelles données émergentes...

tvst

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Article

Refined Data Analysis Provides Clinical Evidence for Central Nervous System Control of Chronic Glaucomatous Neurodegeneration

William E. Sponsel^{1,2,3,4}✉, Sylvia L. Groth⁵✉, Nancy Satsangi⁶✉, Ted Maddess⁴✉, and Matthew A. Reilly¹✉

¹ Department of Biomedical Engineering, University of Texas at San Antonio, San Antonio, TX, USA

² Rosenberg School of Optometry, University of the Incarnate Word, San Antonio, TX, USA

³ Baptist Medical Center, El Paso, TX, USA

⁴ Australian Research Council Centre of Excellence in Vision Science, Canberra, Australia

⁵ University of Minnesota Medical Center, Minneapolis, MN, USA

⁶ University of Sydney, Sydney, Australia

Optimisation vision binoculaire
Contrôle via SNC semble explication plus probable

Correspondence: William Eric Sponsel, Suite 306 Madison Square Building, 311 Camden St., San Antonio, TX 78215, USA. e-mail: sponsel@earthlink.net

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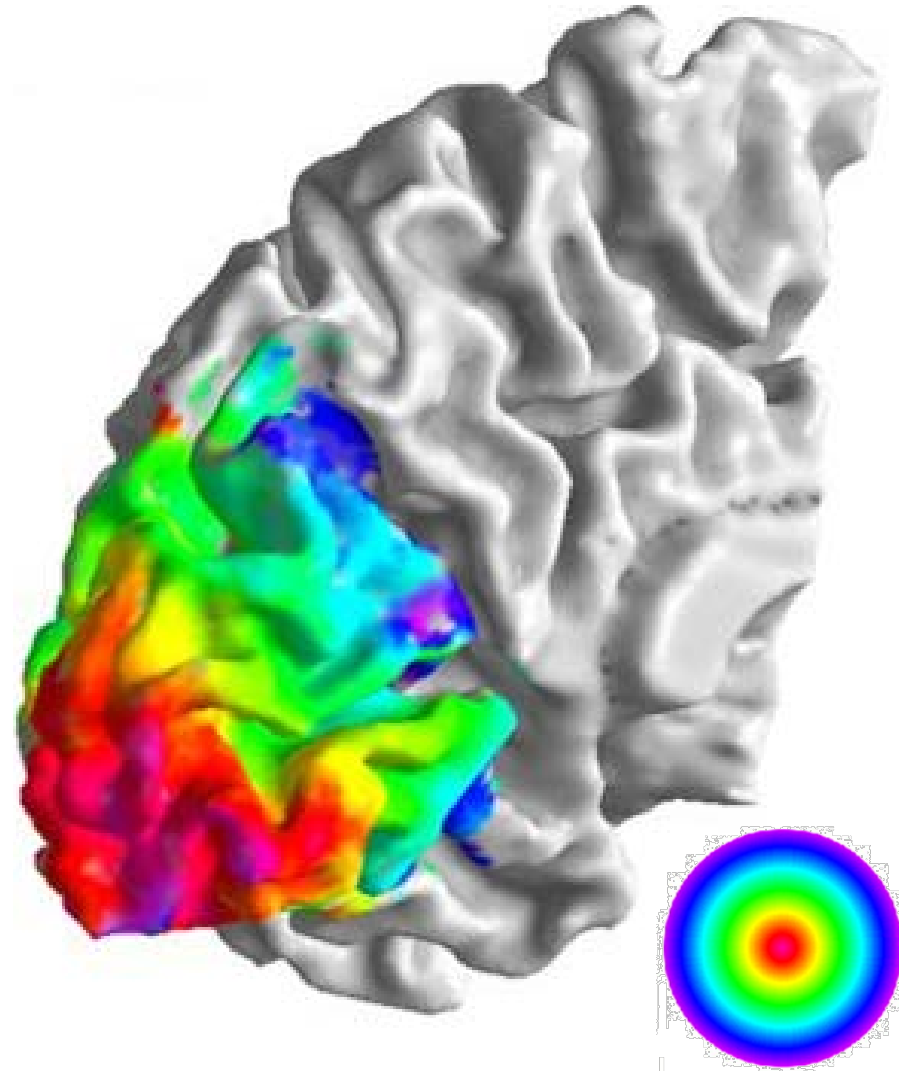
Accepted: 15 March 2014

Purpose: Refined data analysis was performed to assess binocular visual field conservation in patients with bilateral glaucomatous damage to determine whether unilateral visual field loss is random, anatomically symmetric, or nonrandom in relation to the fellow eye.

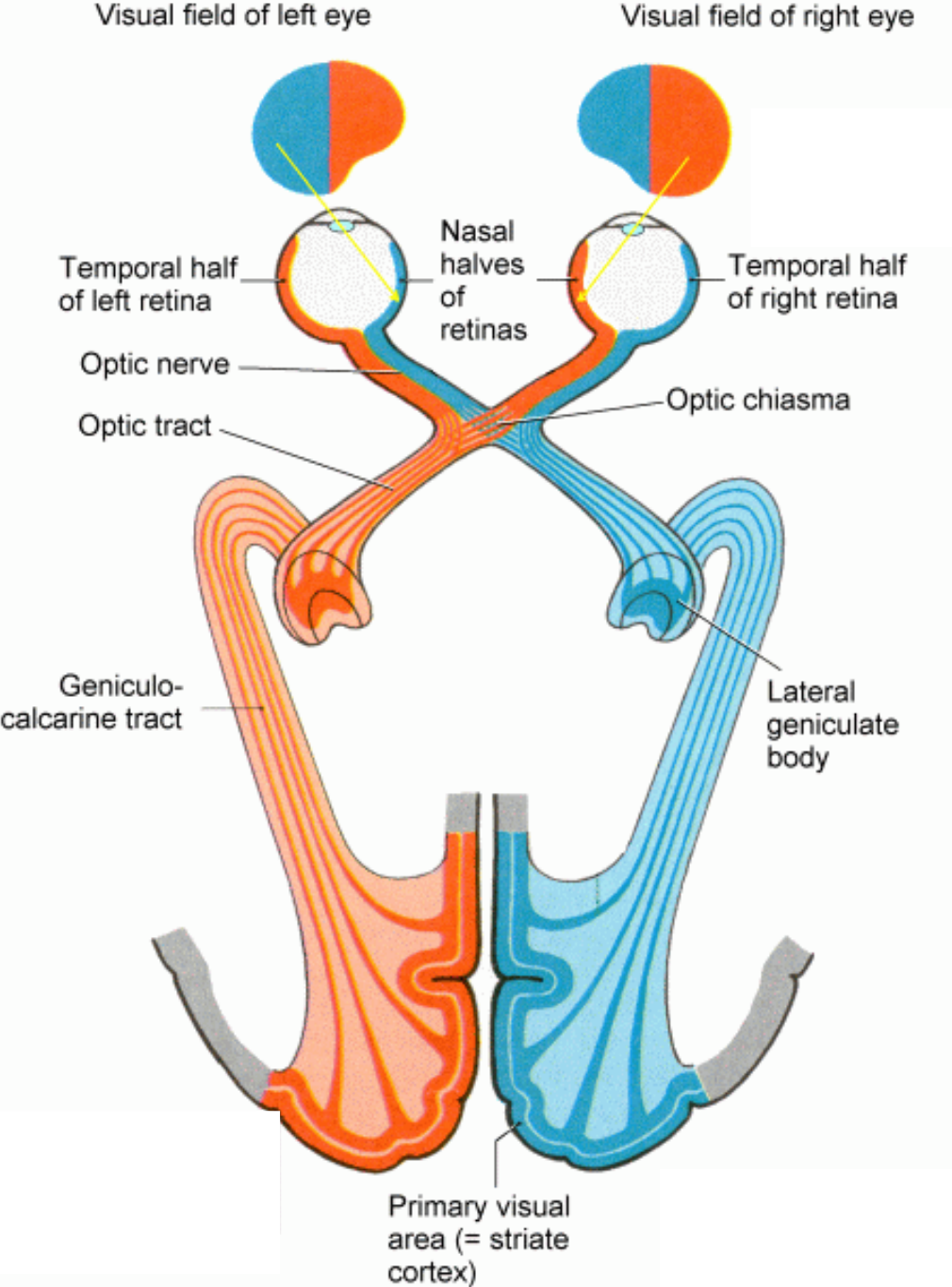
Methods: This was a case-control study of 47 consecutive patients with bilaterally severe glaucoma; each right eye visual field locus was paired with randomly selected coisopteretic left eye loci, with 760,000 (10,000 complete sets of 76 loci) such iterations

Rétinotopie

- Représentation corticale du champ visuel
- Cartes rétinotopiques normales connues
- Méthodes bien établies pour évaluation IRMf

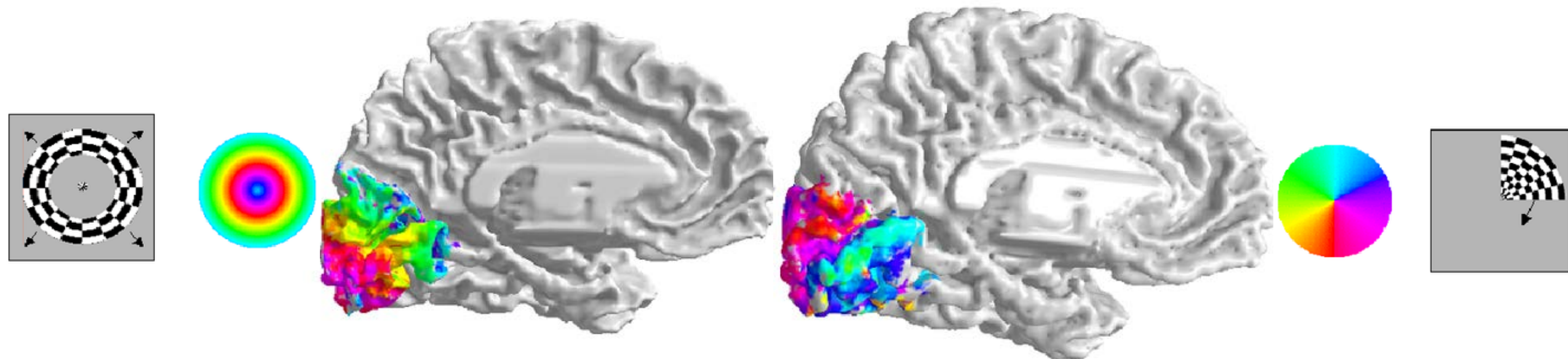


Rappel anatomique: voies optiques



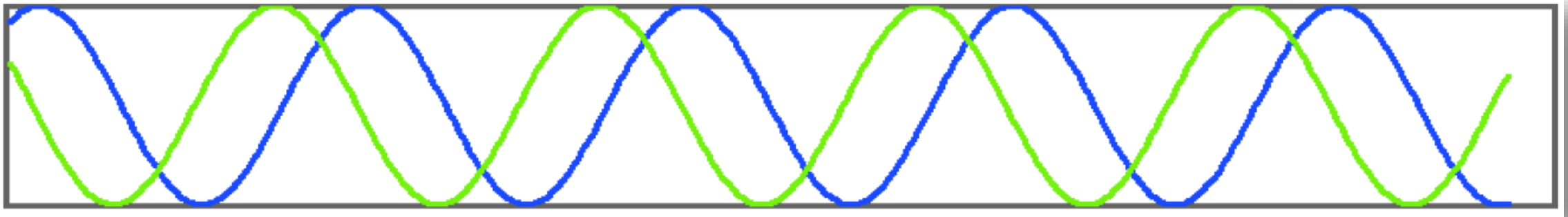
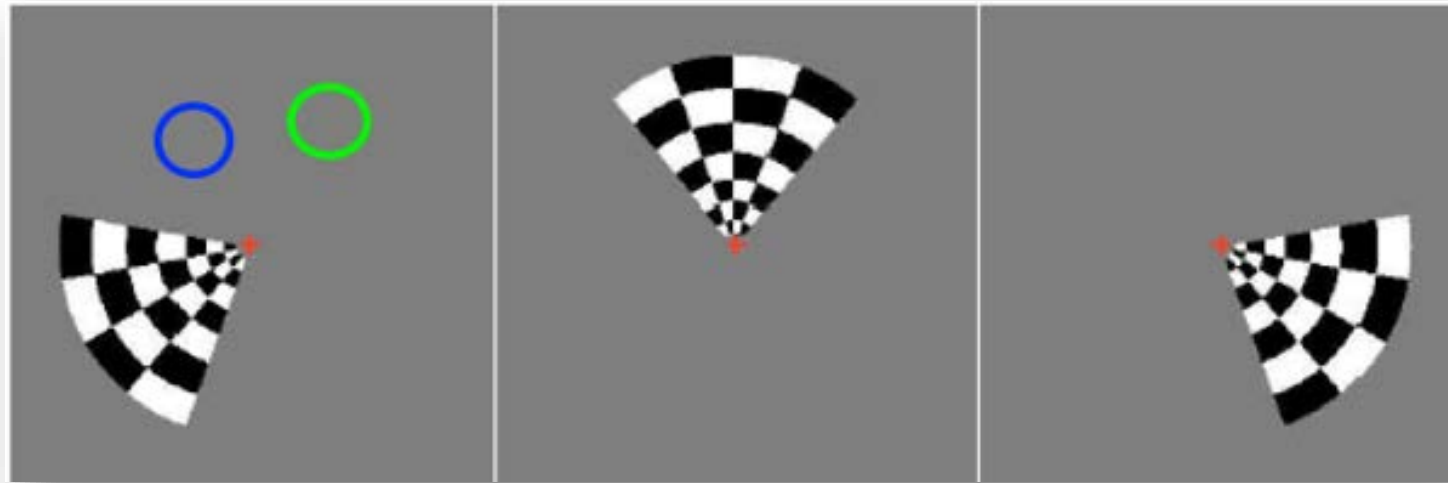
IRMf

- Mesure du signal BOLD (*blood oxygen level dependent*) lors stimulation visuelle
- Stimulation excentrique et polaire



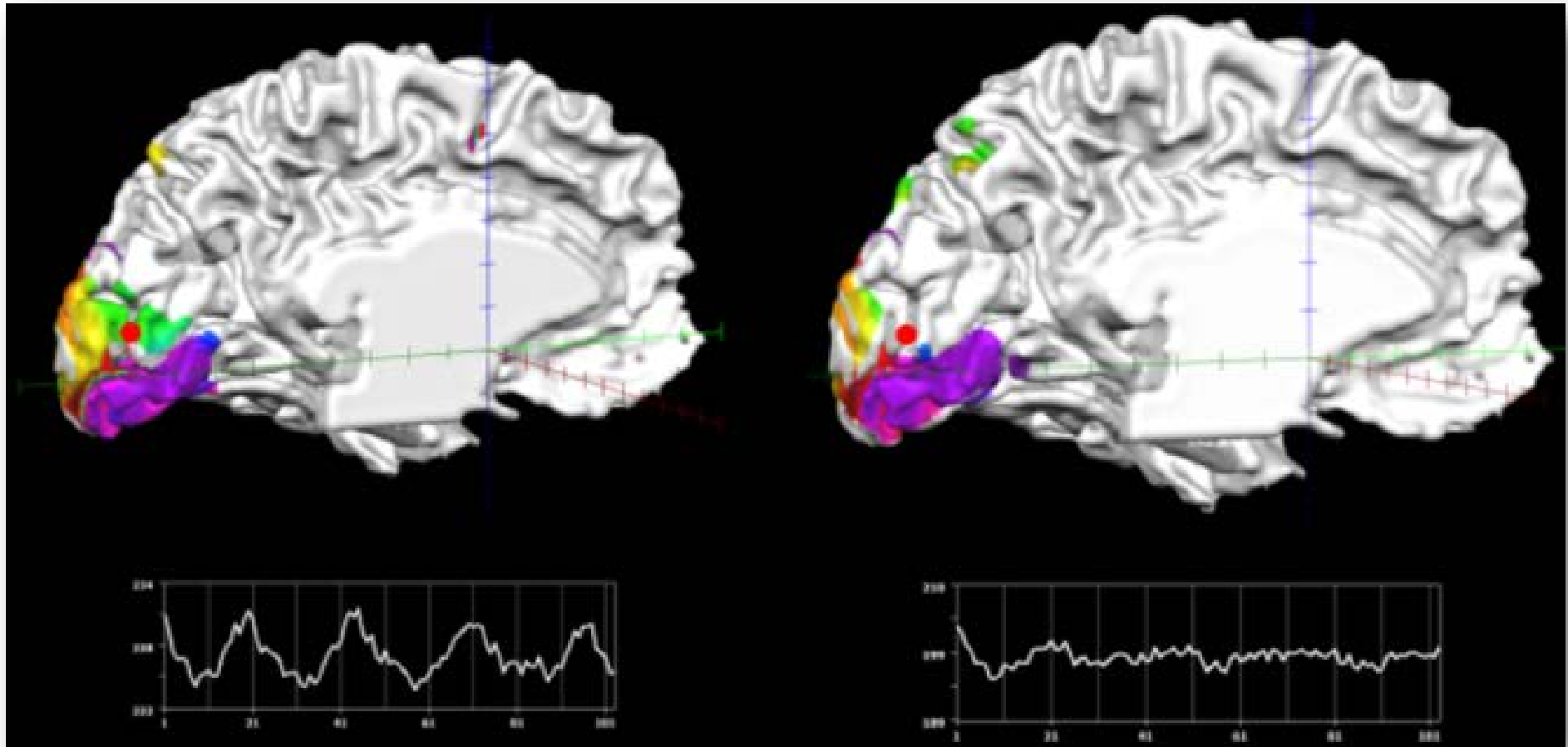
IRMf

- Résultats obtenus: signal BOLD cyclique



IRMf

- Résultats obtenus: signal BOLD cyclique



Notre étude:

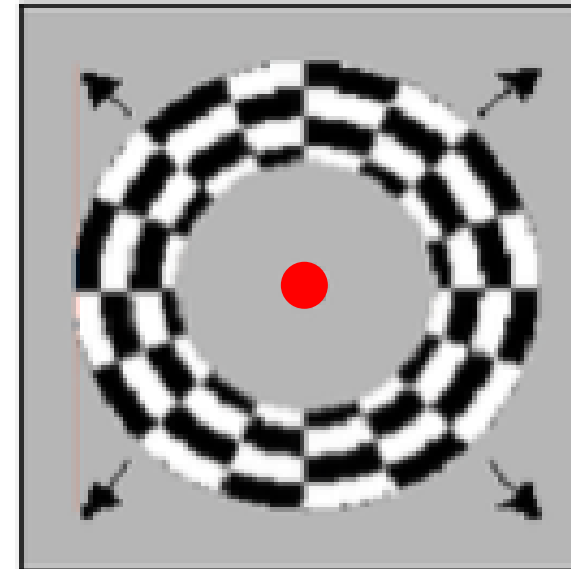
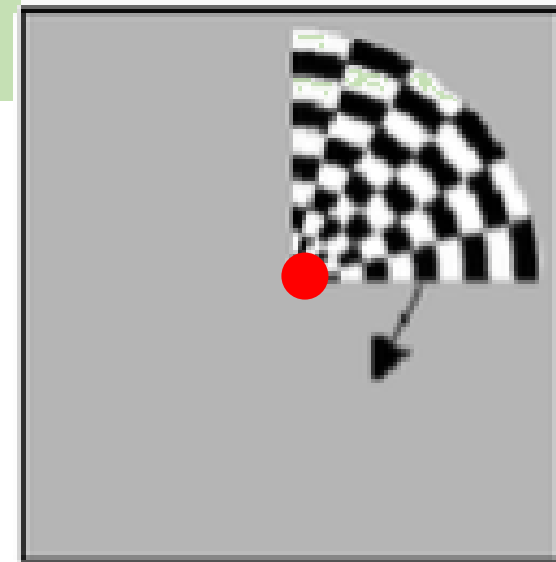
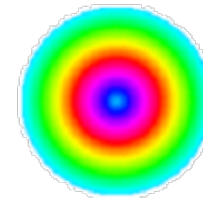
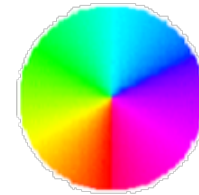
Évaluation IRMf de la rétinotopie de patients avec glaucome monoculaire ou fortement asymétrique

- **Hypothèses:**
 - Corrélation entre scotomes et activation cérébrale
 - Signes de neuroplasticité dans une minorité des patient
- **Objectifs:**
 - Démontrer neuroplasticité
 - Meilleure compréhension pathophysiologie glaucome
 - (Nouvelles avenues thérapeutiques)



Méthodologie

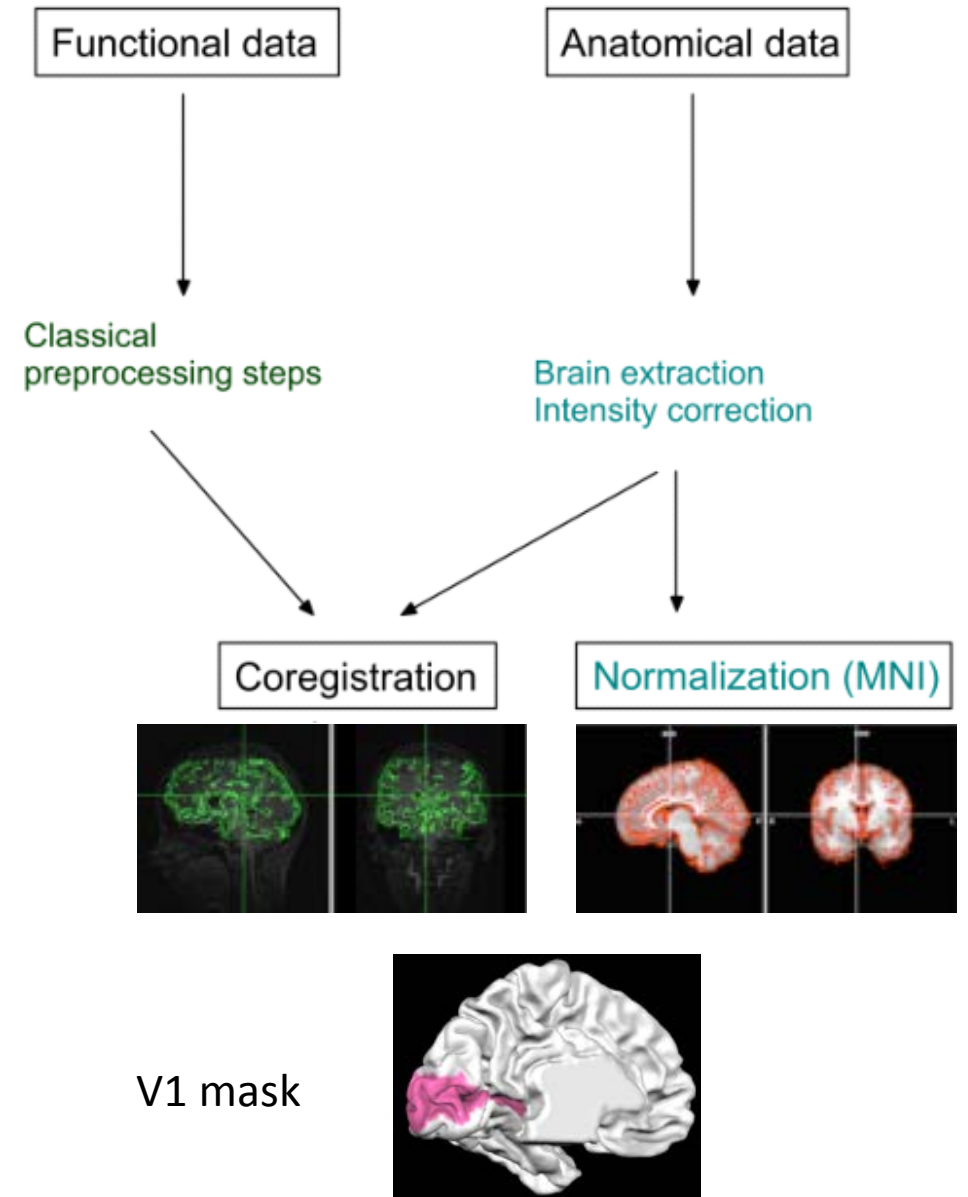
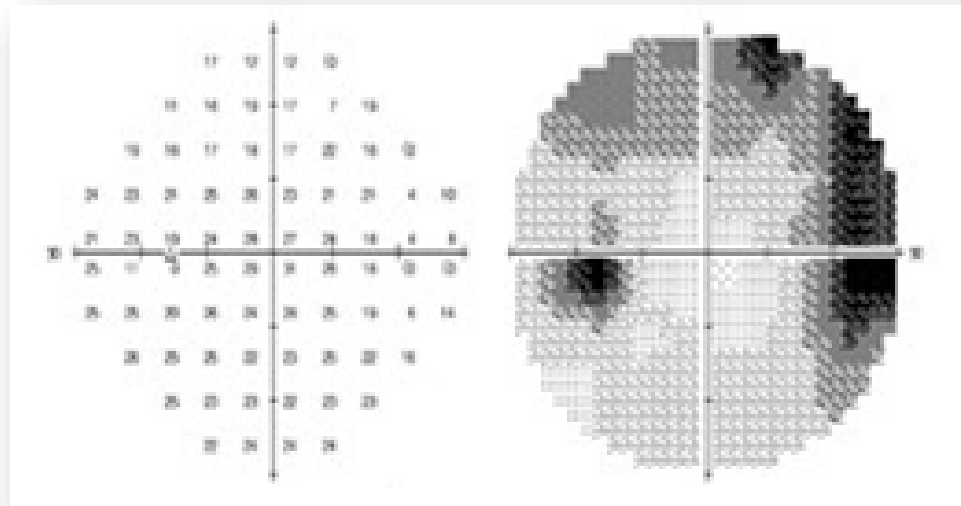
- Étude analytique transversale sans intervention
- Évaluation IRMf, stimulation monoculaire et binoculaire
- Cartes de rétinotopie V1, leur comparaison
- Comparaison avec cartes *Humphrey Field Analyzer* (HFA)
- Autres: DTI, TOF, *optical coherence tomography* (OCT)...



Traitement des données IRMf

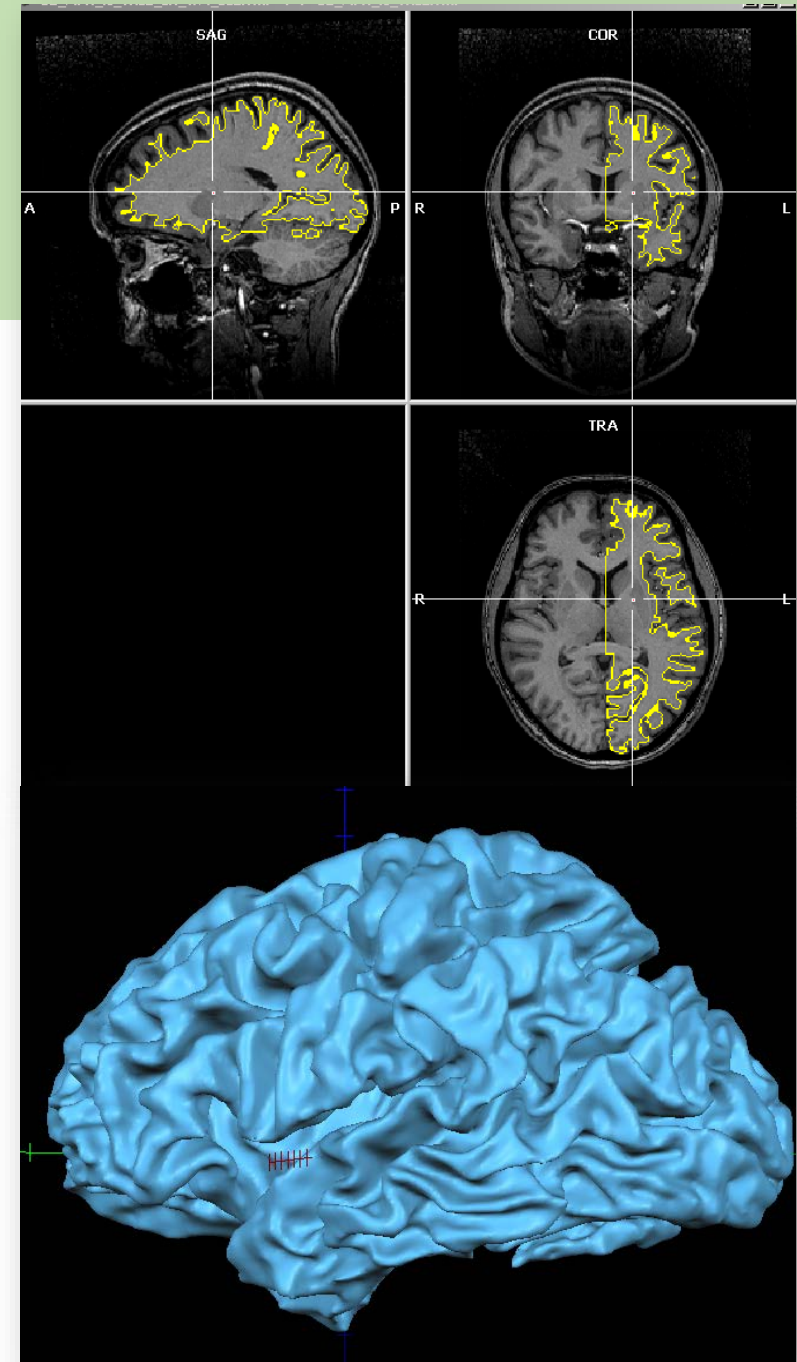
- Effectué principalement dans BrainVoyager© et AFNI©

HFA

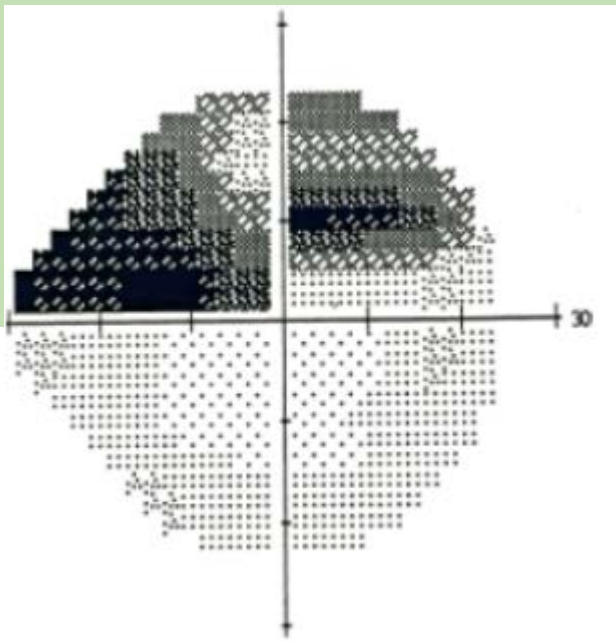


État de notre étude

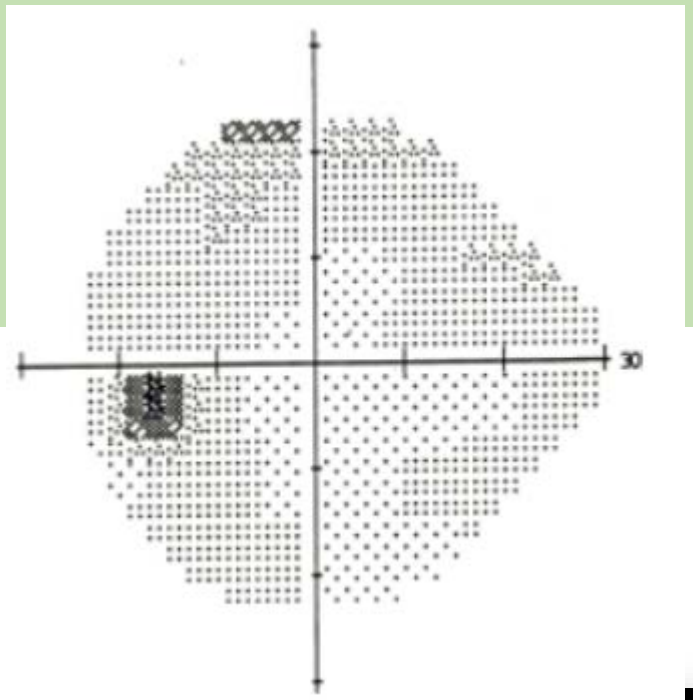
- 5 patients recrutés
 - 3 patients ayant complété l'étude
 - 1 patient avec données de qualité limitée, reprise □
 - 2 patients avec participation incomplète
- Analyse des données débutée
 - Quantification voxels
 - Corrélation cartes rétinotopie
 - Corrélation HFA
 - ...



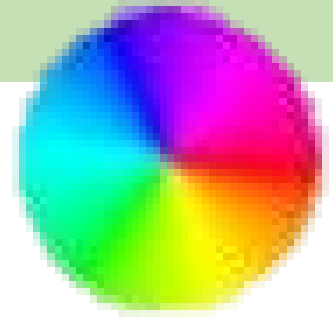
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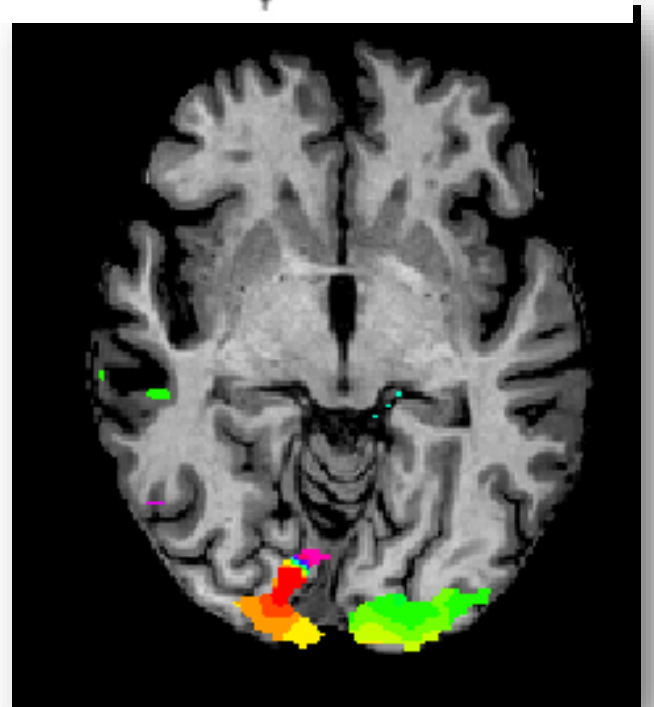
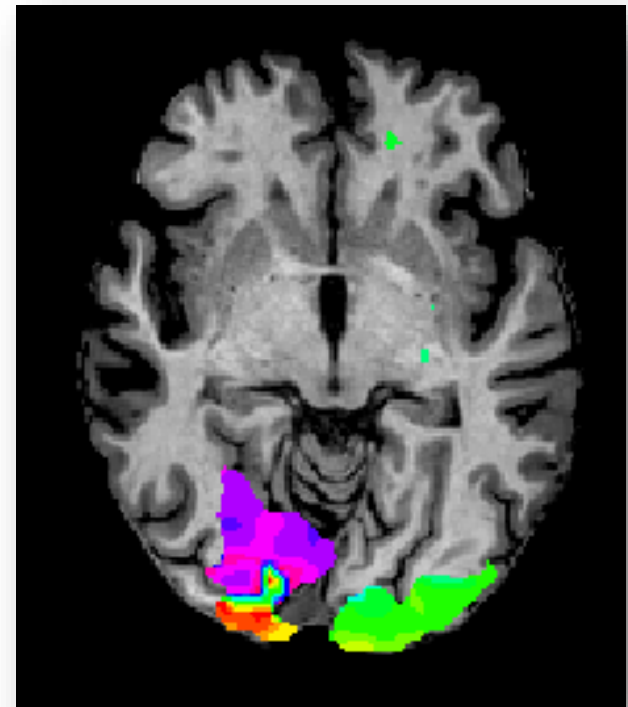
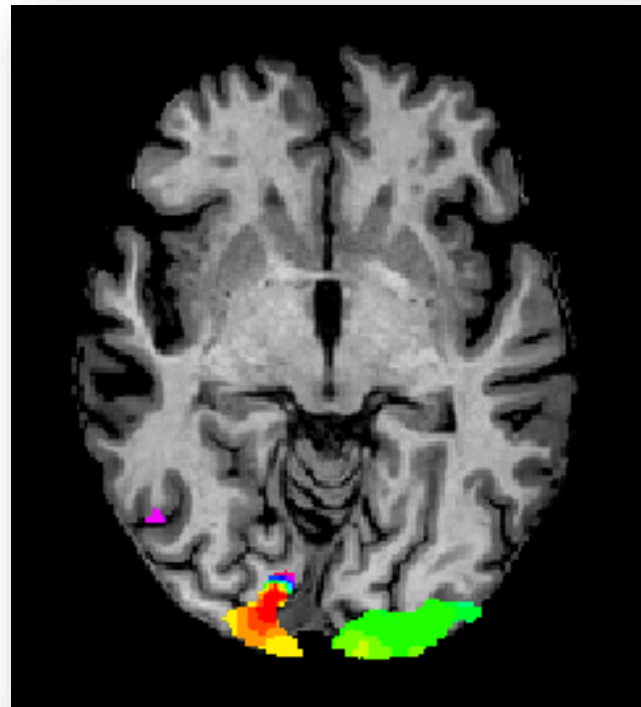
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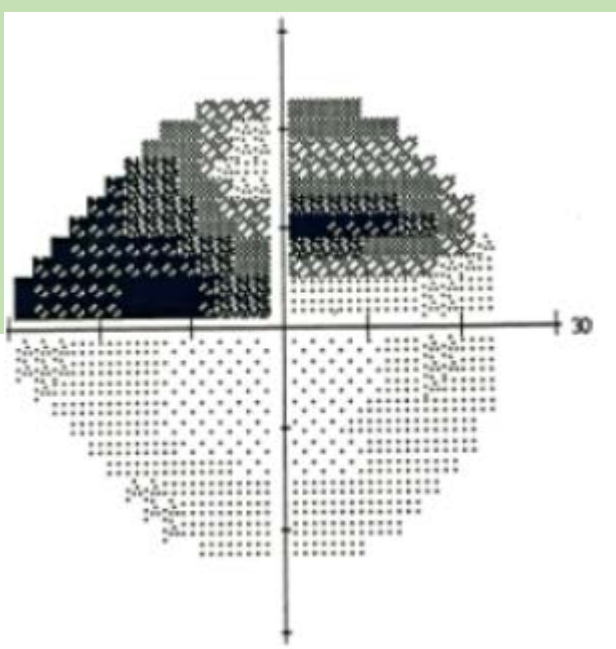
Patient 1



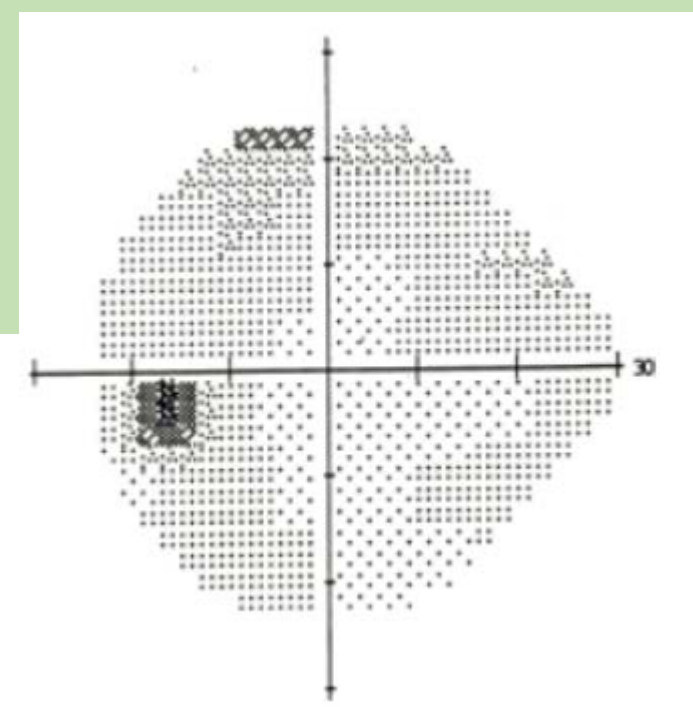
Binoculaire



OD

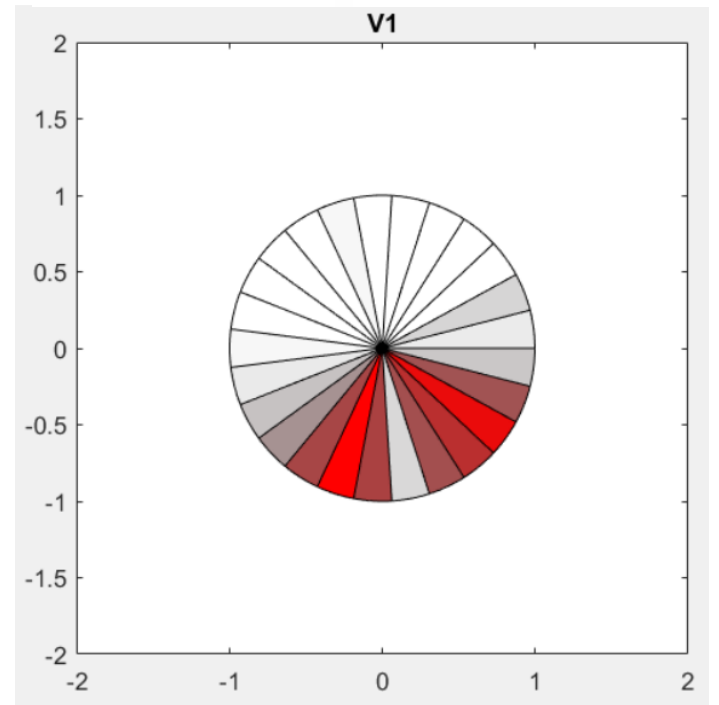
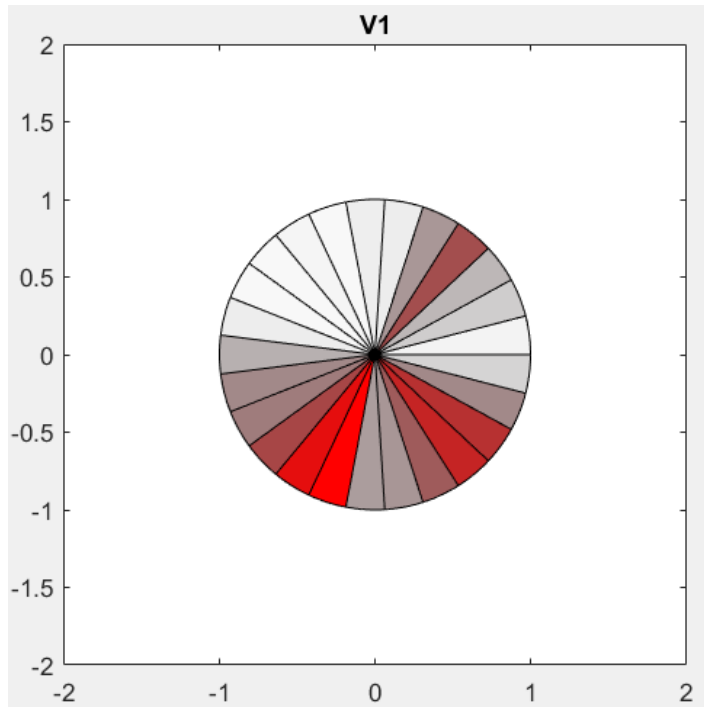
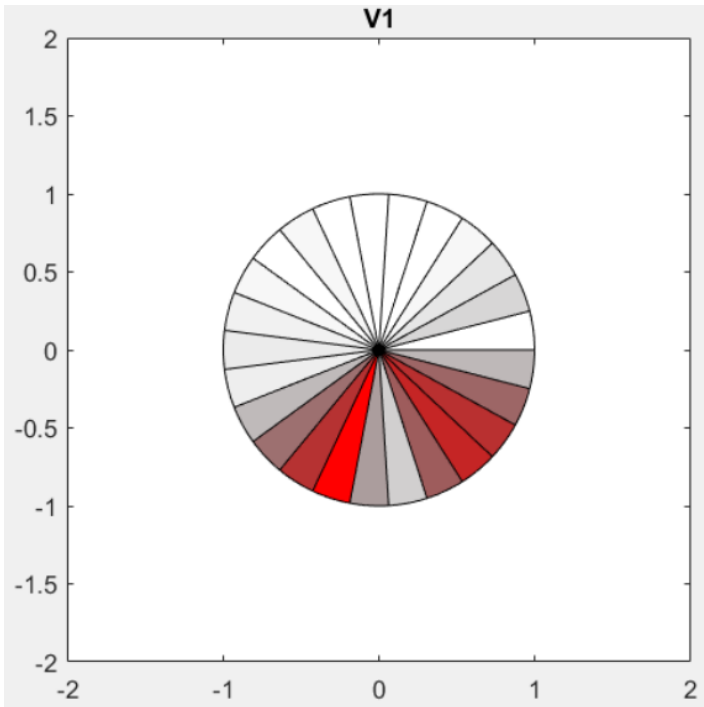


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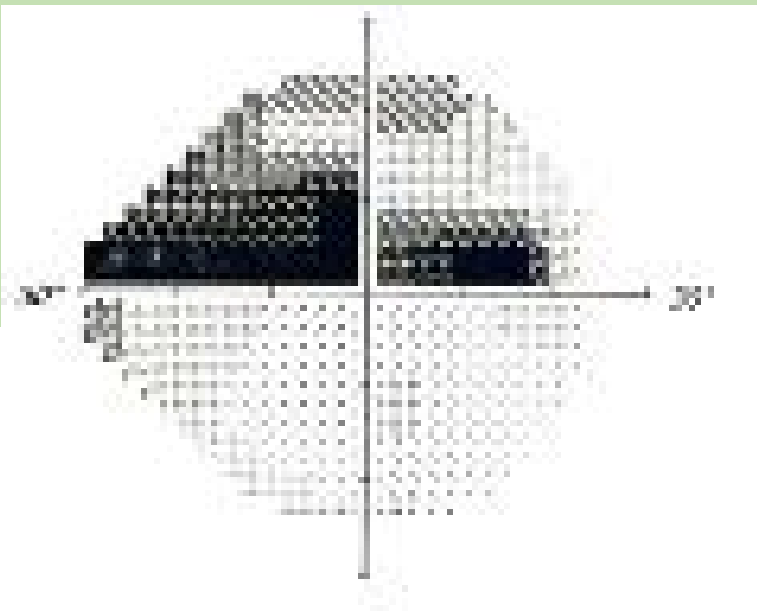


Patient 1

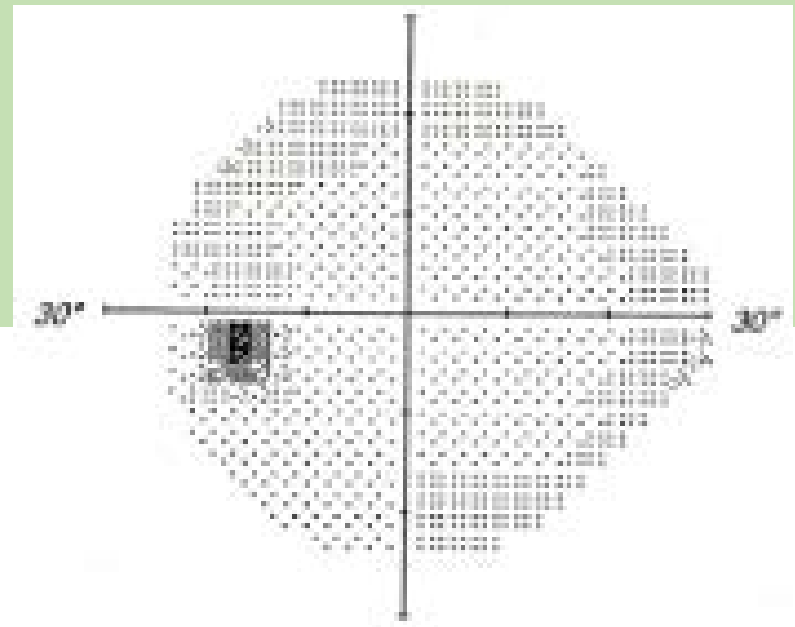
Binoculaire



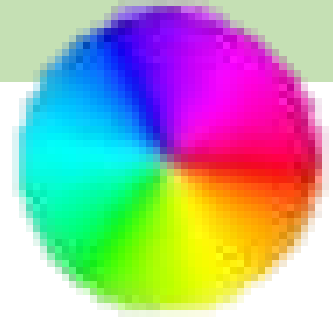
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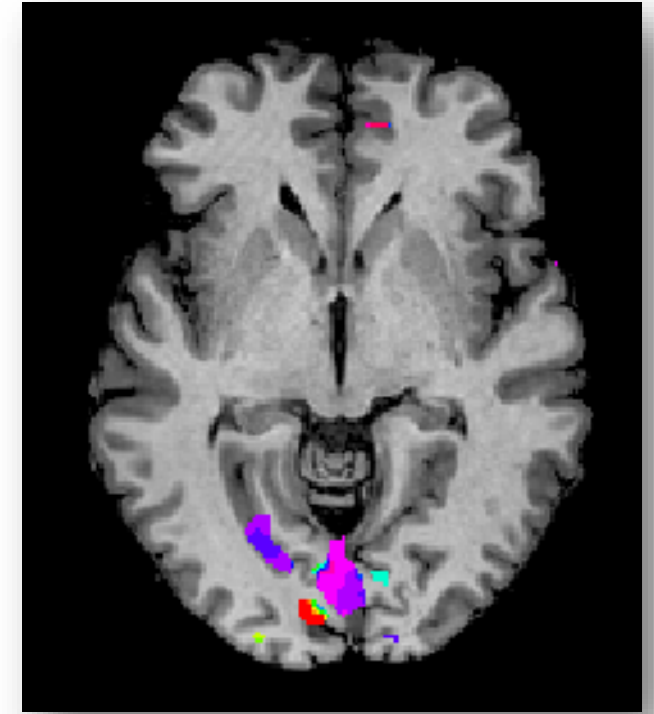
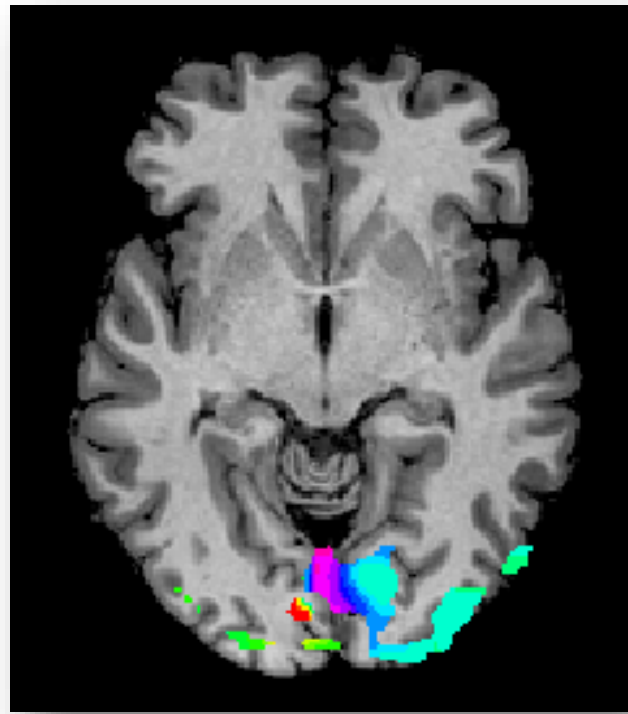
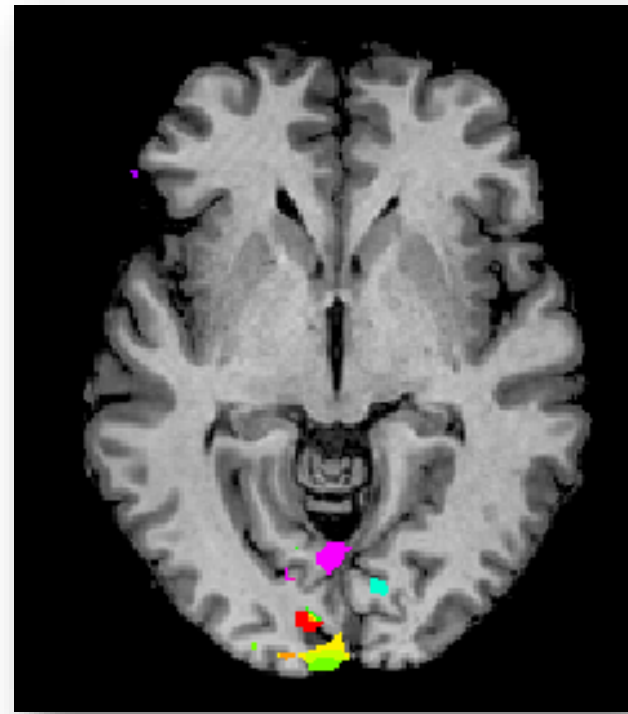
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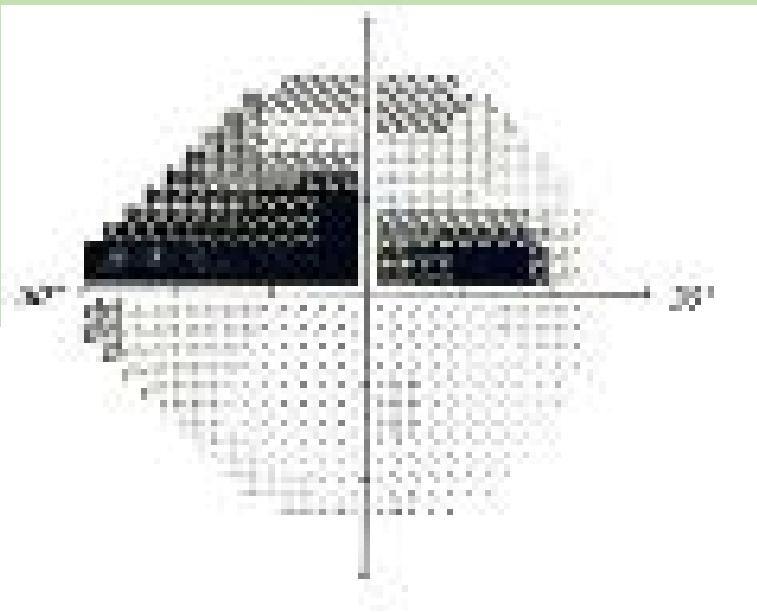
Patient 2



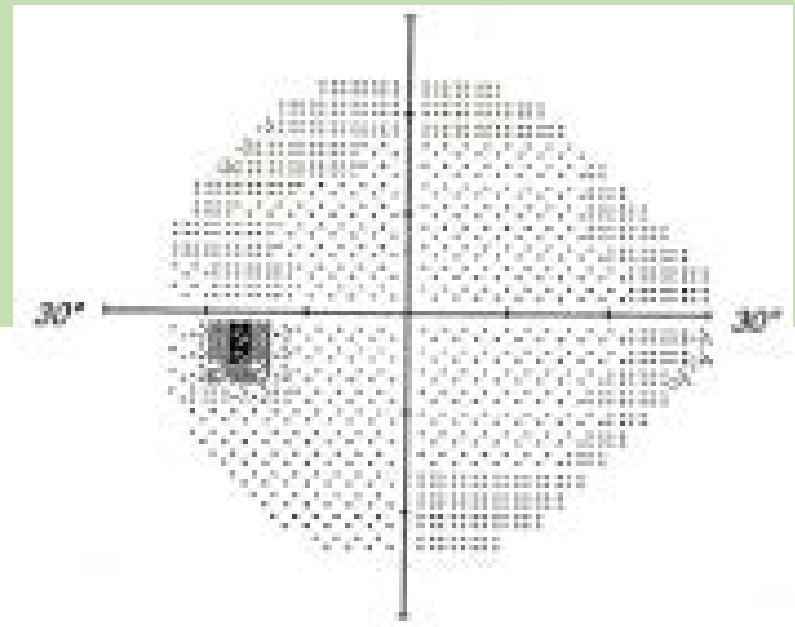
Binoculaire



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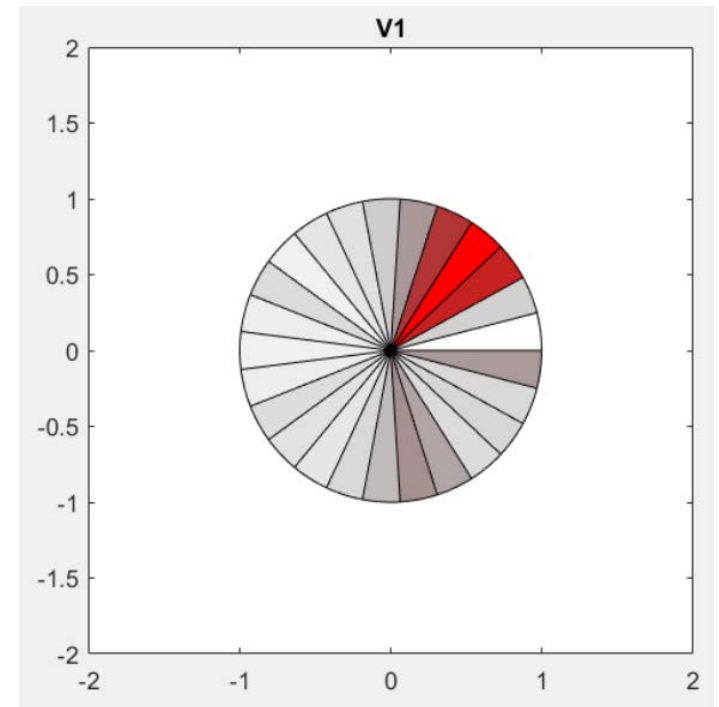
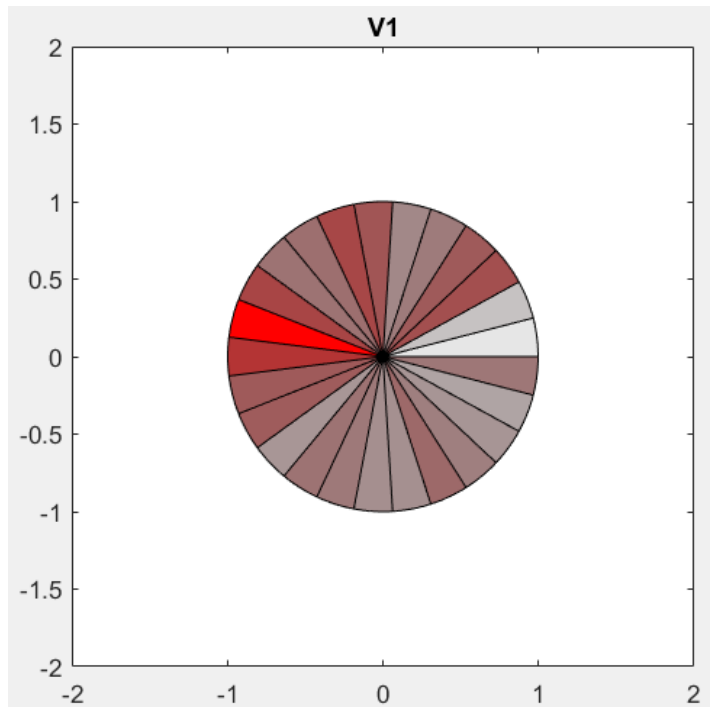
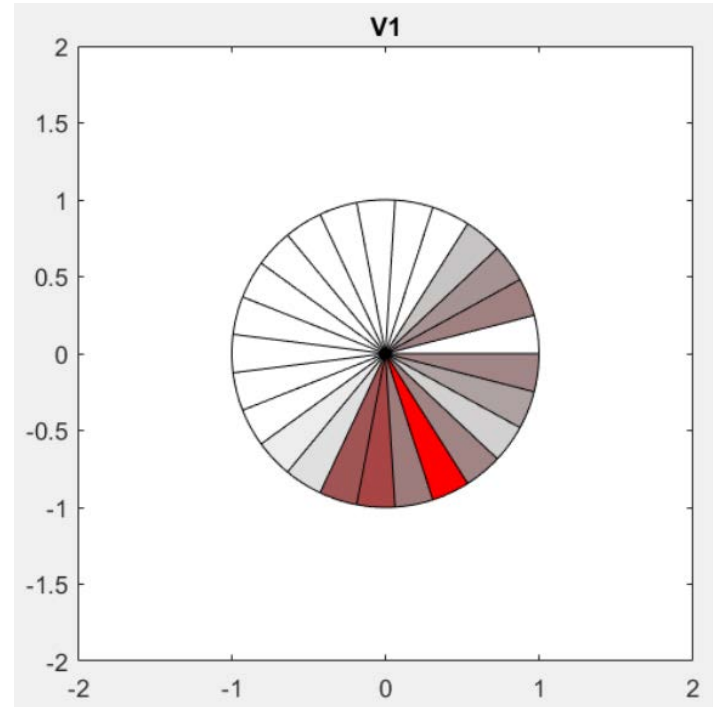


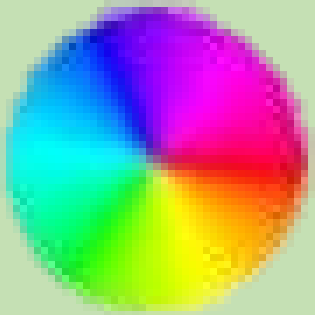
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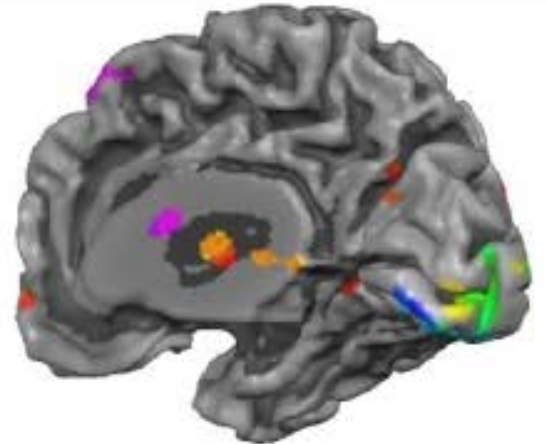
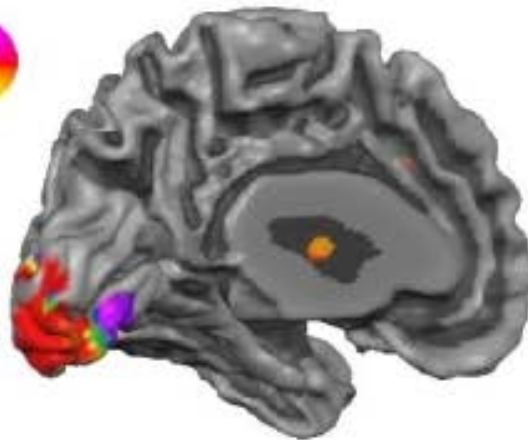
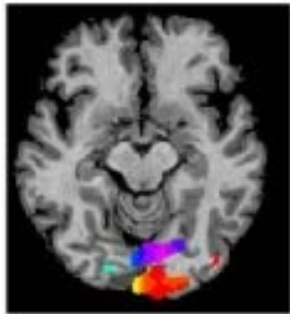
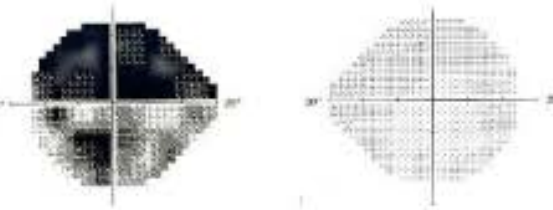
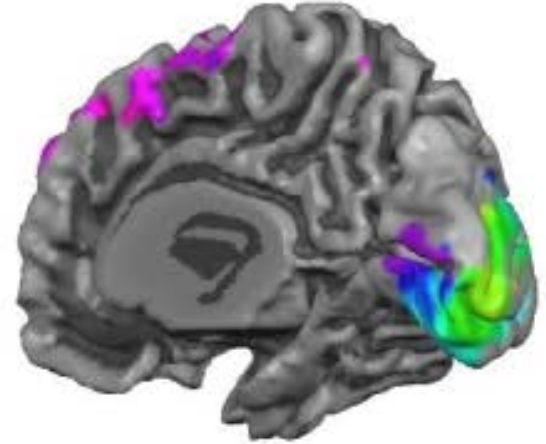
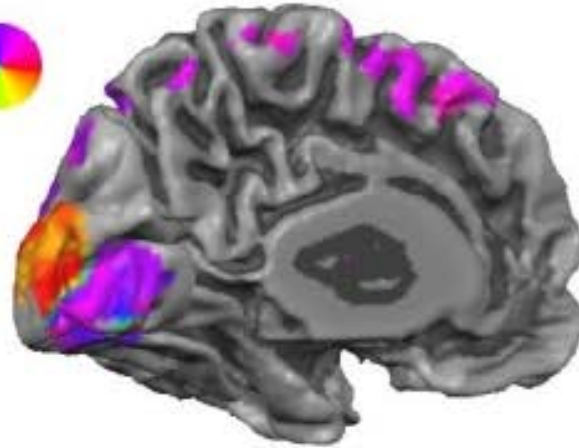
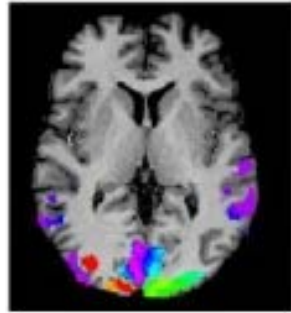
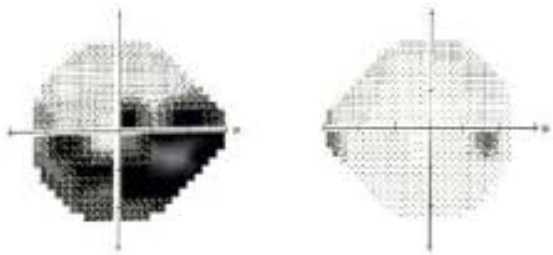
Patient 2

Binoculaire





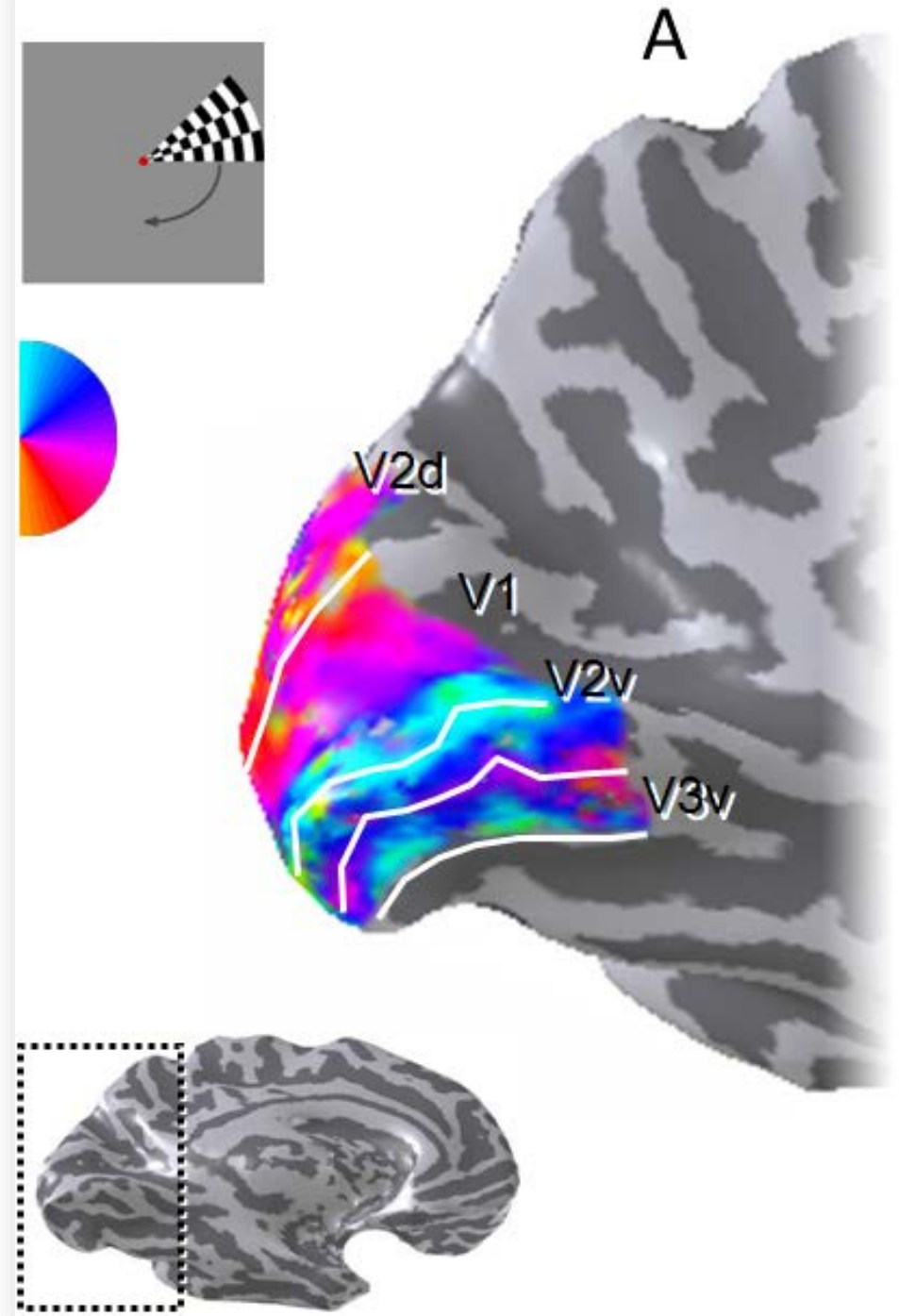
Patients 3 & 4 - Binoculaire



À venir

- Obtenir données 5 patients
- Compléter analyse données
- Hypothèses pour expliquer résultats
- Résultats finaux Journée scientifique 2018

- Arguments supplémentaires pour nouvelles méthodes investigation-évaluation, avenues thérapeutiques, etc.



Merci!

