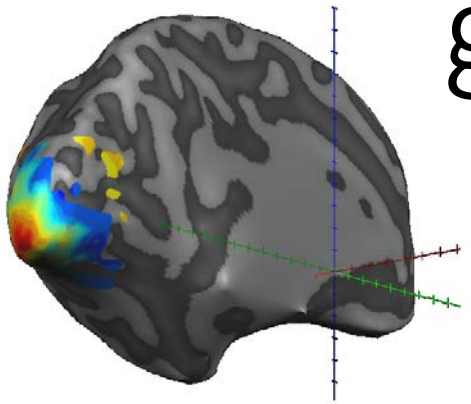
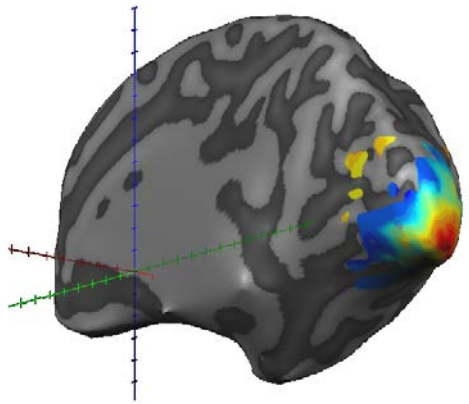
Évaluation IRMf de la rétinotopie de patients avec glaucome monoculaire ou fortement asymétrique





Journée scientifique d'imagerie 2018

Lyes Bachatene (PhD)

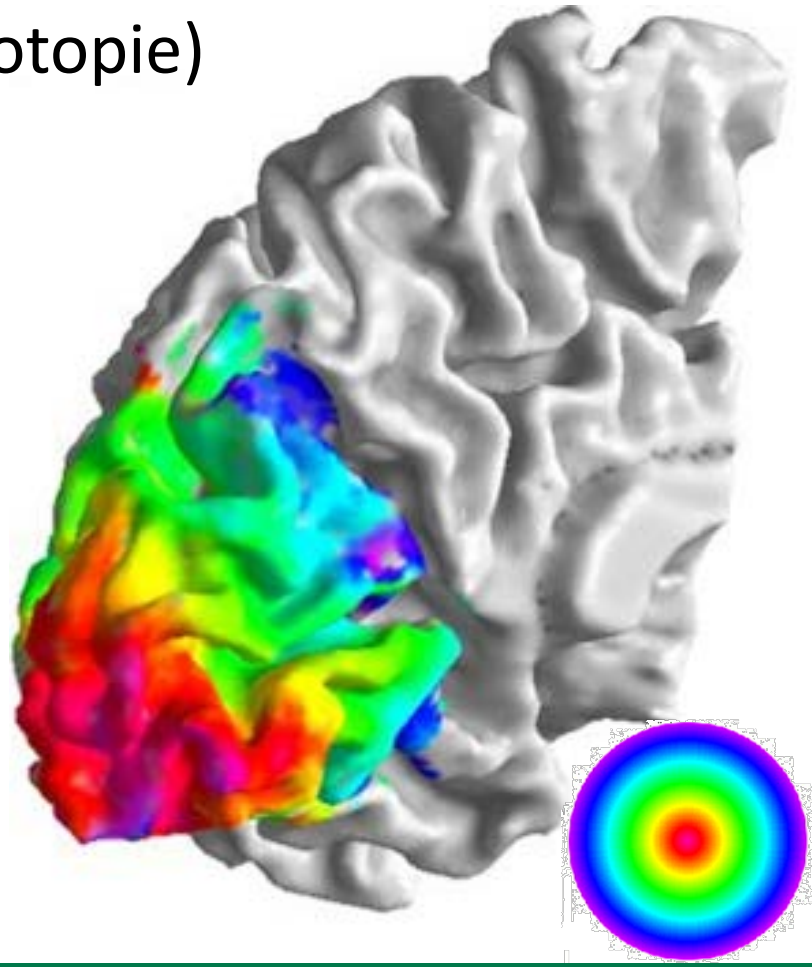
Laurent G. Brosseau (R4 - radiologie)

Kevin Whittingstall (PhD)

Marjorie Carbonneau (MD - opthalmologie)

Ordre du jour

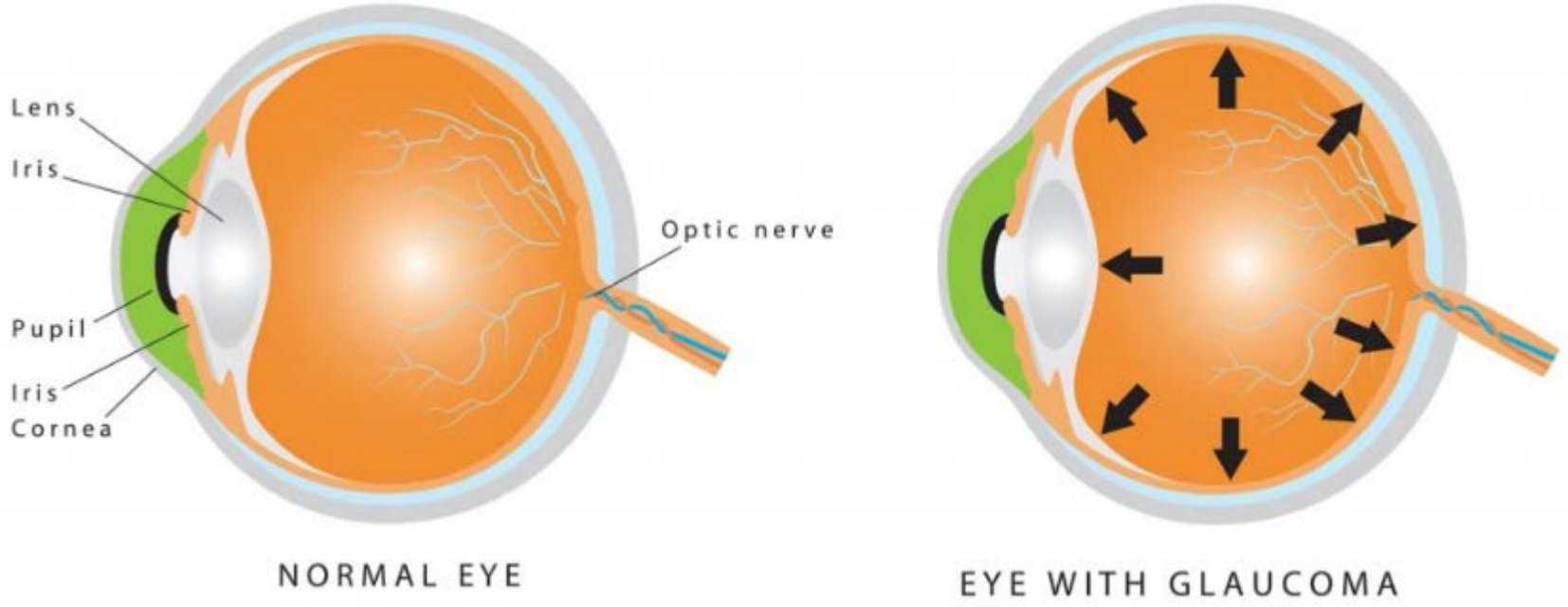
- État des connaissances actuelles (glaucome, rétinotopie)
- Notre étude:
  - Objectifs
  - Hypothèses
  - Méthodologie
- Résultats et discussion



Glaucome

- Définition vulgarisée (*American Academy of Ophtalmology*):

*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.*



http://glaucomaassociates.com/glaucoma/types-of-glaucoma/

Contexte

Distal axonopathy with structural persistence in glaucomatous neurodegeneration

Progression axonale typique maladies neurodégénératives

Atteinte axonale distale antégrade

Rétine affectée tardivement

Modèle animal

Peu de sujets à l'étude

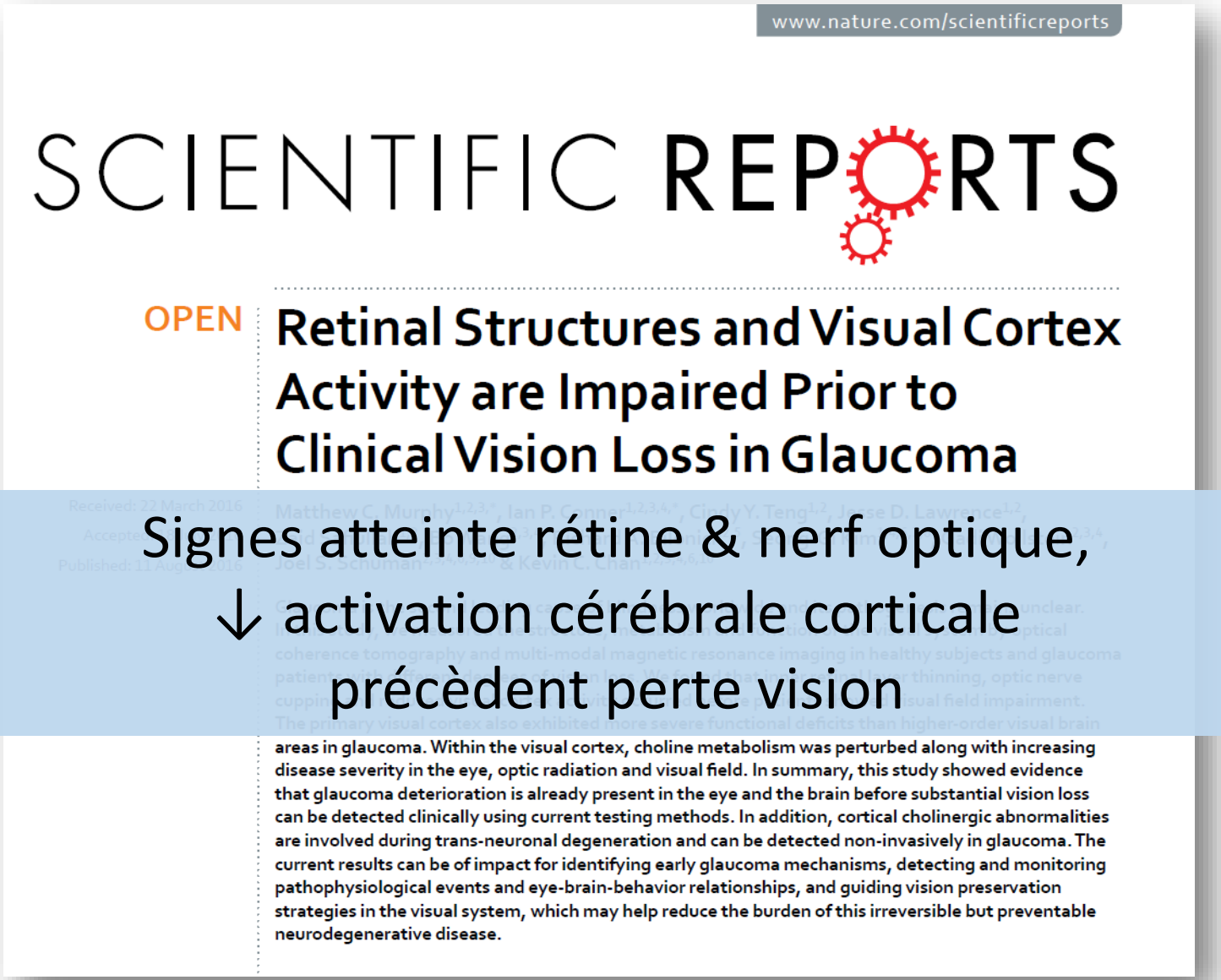
ganglion cell (RGC) neurons and their axons in the optic nerve. Here we show that, like other neurodegenerations, distal axon injury appears early in mouse glaucoma. Where RGC axons terminate in the superior colliculus, reduction of active transport [illegible] pattern resembling glaucomatous vision loss. Like glaucoma, susceptibility to transport deficits increases with age and is not necessarily associated with elevated ocular pressure. [illegible] 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.**

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

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 projection via active uptake and transport (21, 22). For a 5-mo C57 and a 5-mo DBA/2, CTB labeled the entire retinotopic [illegible] the SC except for the retinal optic disk, which does not contain RGCs (Fig. 1*A* and *B*). In contrast, the SC of an 8-mo DBA/2 demonstrated a focal deficit extending caudally from the optic disk gap (Fig. 1*C*), whereas a 10-mo DBA/2 SC contained a massive deficit that left the entire medial-caudal quadrant devoid of label (Fig. 1*D*).

The SC maps in Fig. 1 *C* 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

Contexte



www.nature.com/scientificreports

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.

Contexte

tvst

DOI: 10.1167/tvst.3.3.1

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. Groth[5], Nancy Satsangi[6], Ted Maddess[4], and Matthew A. Reilly[1]

[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
[4] Australian Research Council Centre of Excellence in Vision Science, Canberra, Australia
[5] University of Minnesota Medical School, Minneapolis, MN, USA

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

Received: 15 December 2013
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 coisopteric left eye loci, with 760,000 (10,000 complete sets of 76 loci) such iterations

Contexte

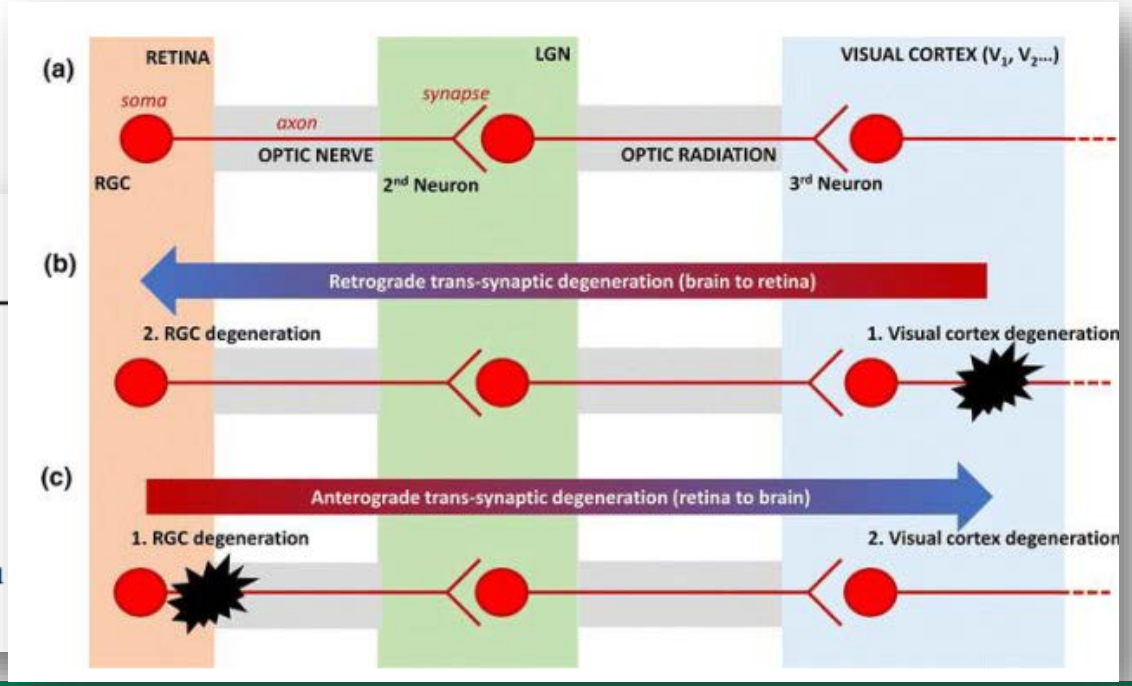
- Pathophysiologie demeure très incomprise
- Mécanisme post-rétinien? Dégénérescence neuronale antégrade vs rétrograde? Données contradictoires.
- Perte 50-60% des cellules ganglionnaires de la rétine lorsque déficits visuels se manifestent

Acta Neuropathol (2016) 132:807–826
DOI 10.1007/s00401-016-1609-2

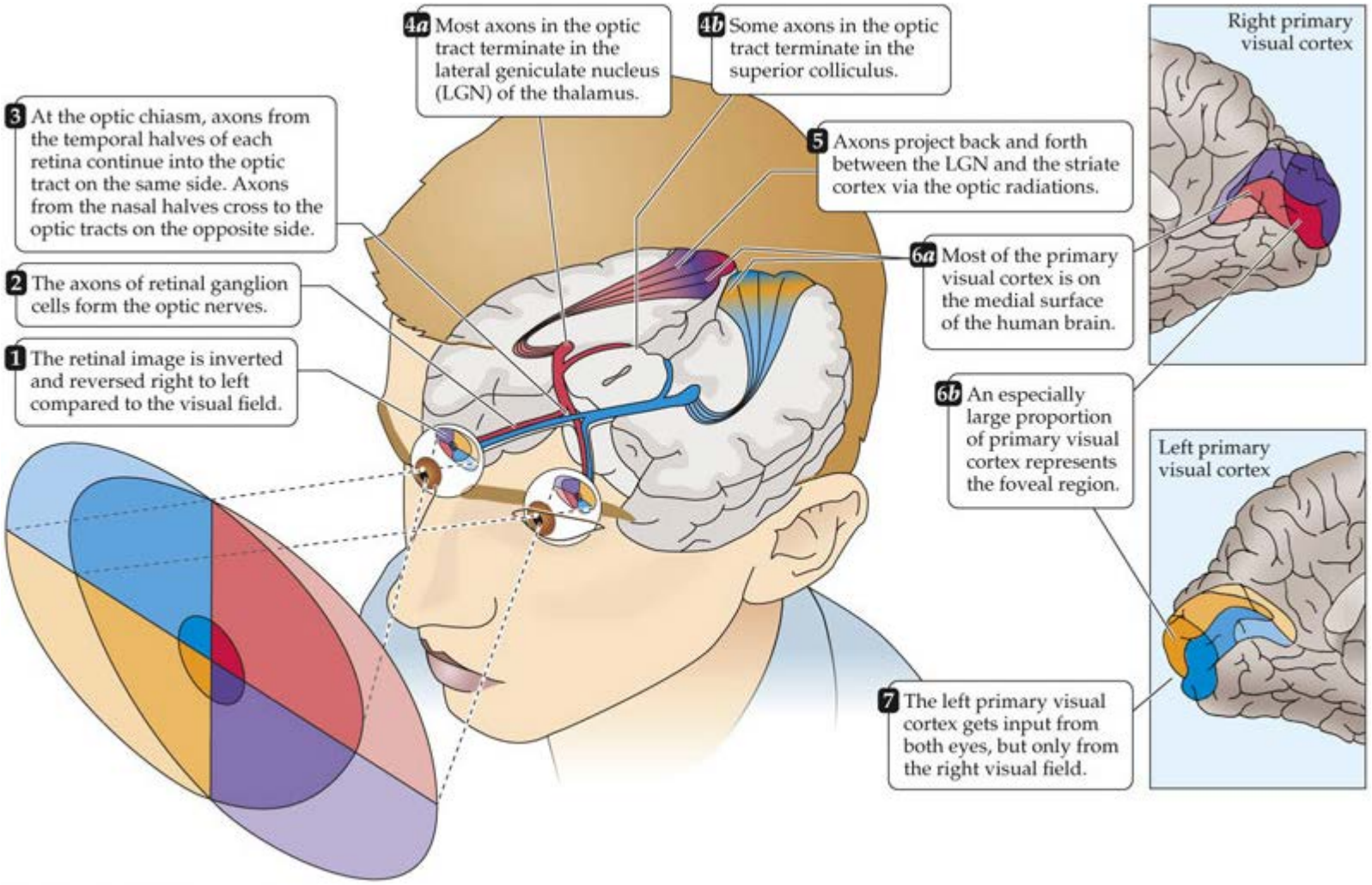
REVIEW

Glaucoma: the retina and beyond

Benjamin Michael Davis[1] · Laura Crawley[2] · Milena Pahlitzsch[1] · Fatimah Javaid[1]
Maria Francesca Cordeiro[1,2]



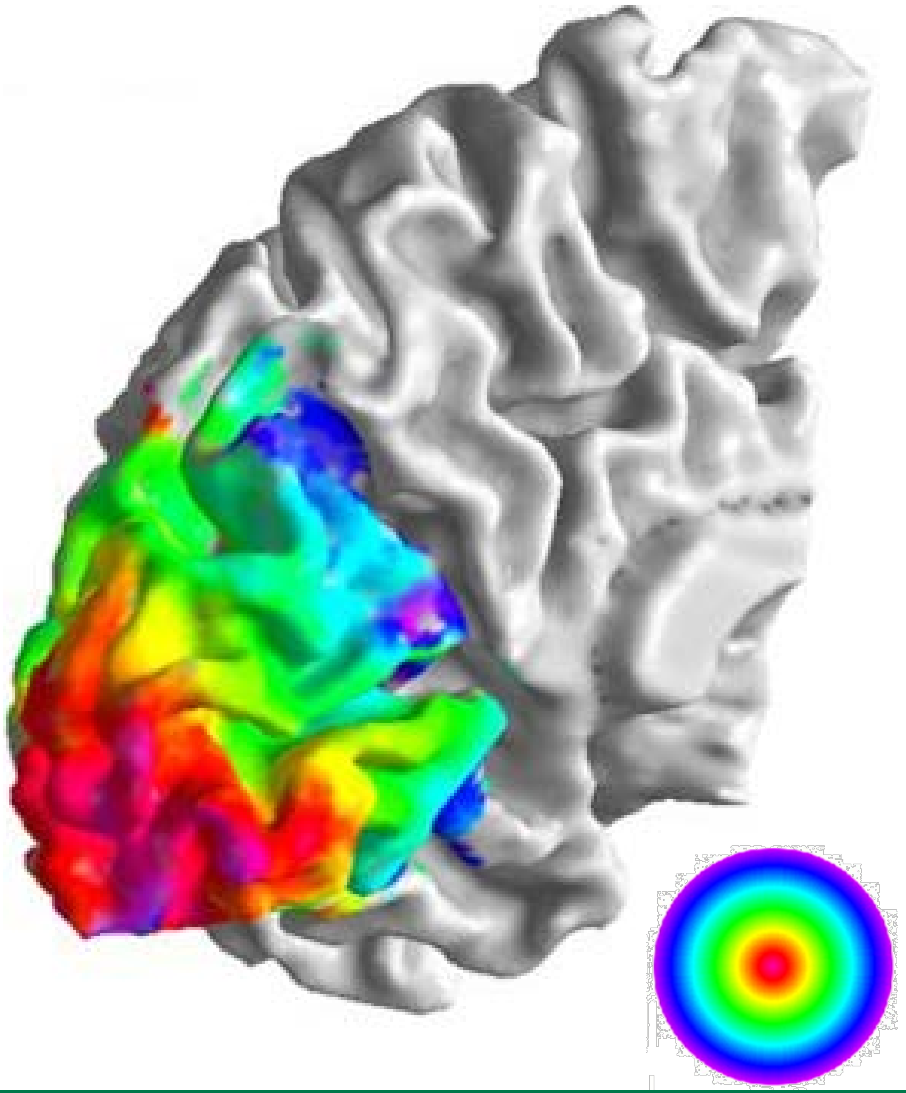
Voies optiques



***THE MIND'S MACHINE 2e*, Figure 7.10**

Rétinotopie

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



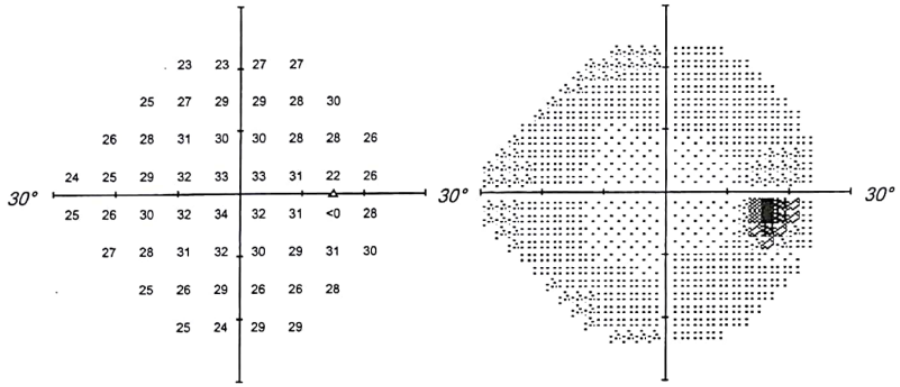
Évaluation IRMf de la rétinotopie de patients avec glaucome monoculaire ou fortement asymétrique

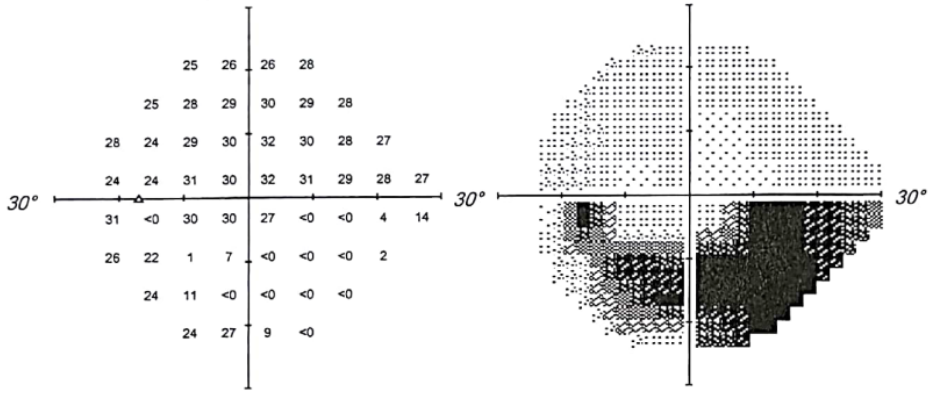
- n = 5 patients, stimulation monoculaire bilatérale et binoculaire

- **Hypothèses:**
  - Corrélation entre scotomes et activation cérébrale
  - Signes de neuroplasticité dans une minorité des patient

- **Objectifs:**
  - Démontrer neuroplasticité
  - Meilleure compréhension pathophysiologie glaucome
  - (Nouvelles avenues diagnostiques, thérapeutiques)

Comparaison avec champs visuels *Humphrey Field Analyzer* (HFA)

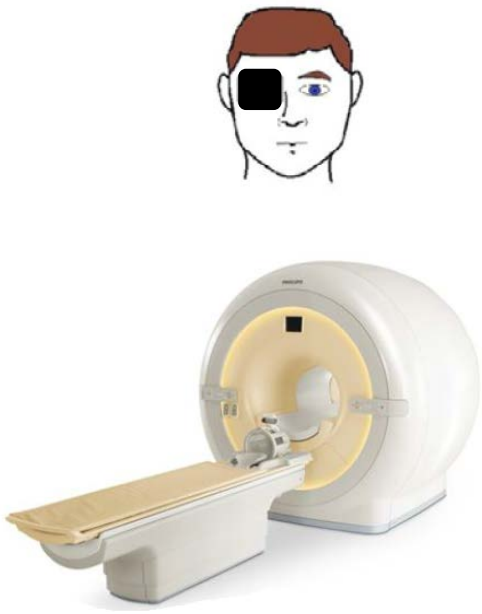




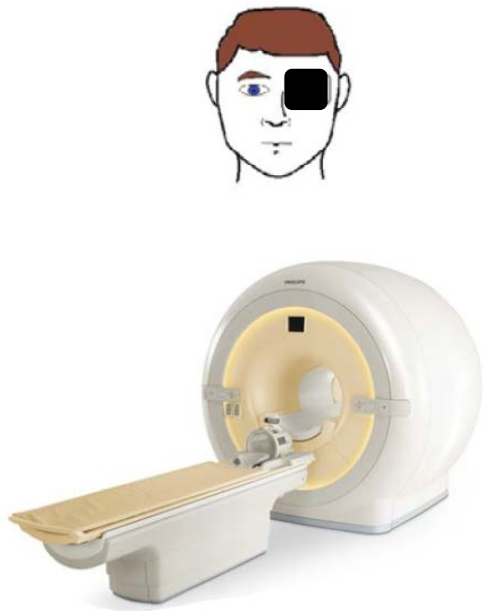
http://killinglyeyecare.com/technology/technology-glaucoma-management/humphrey-visual-field/

Méthode stimulation

Stimulation monoculaire

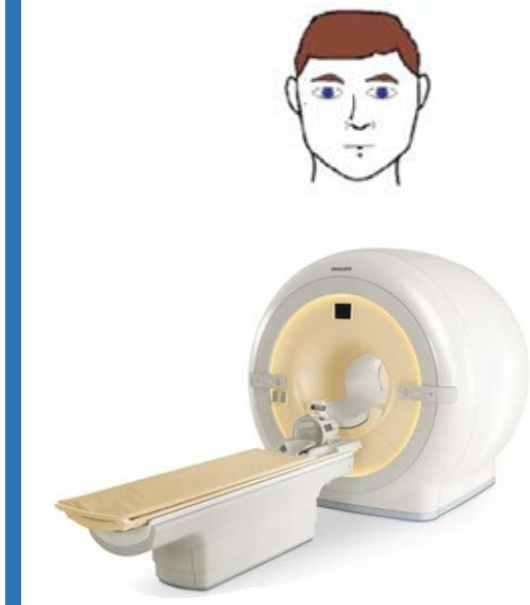


Œil avec glaucome

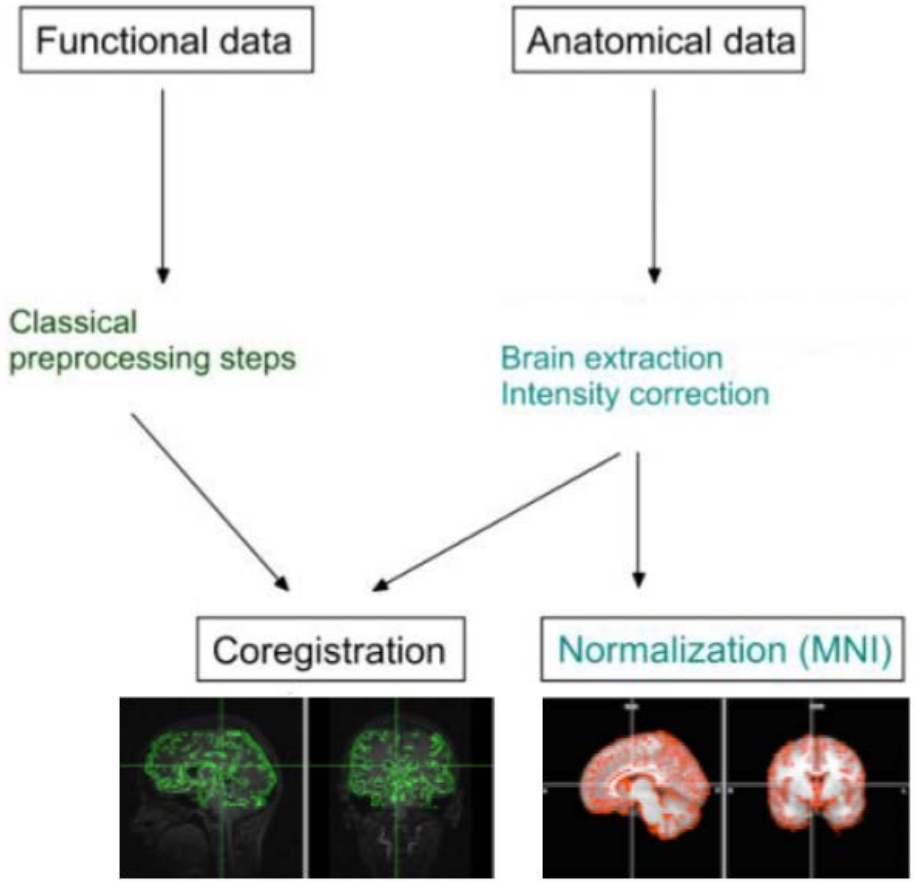


Œil sain

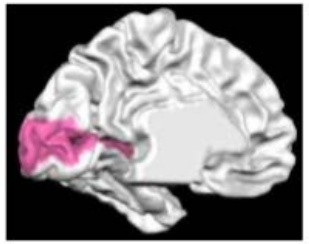
Stimulation binoculaire



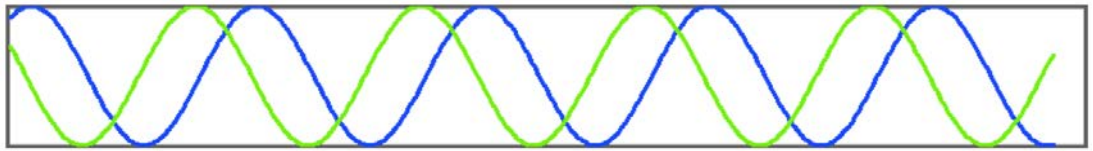
Méthodologie



V1 mask



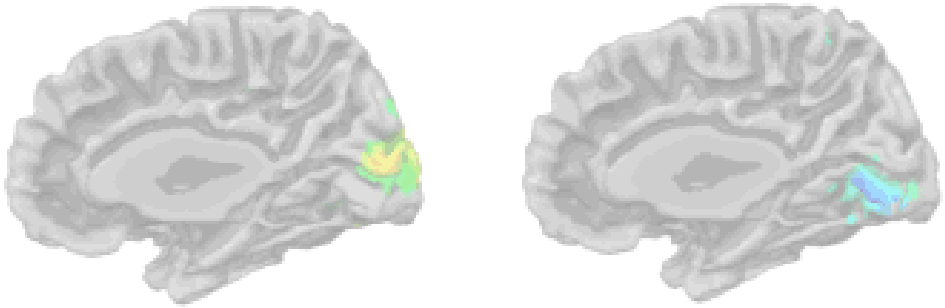
polar angle:

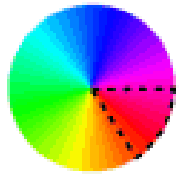


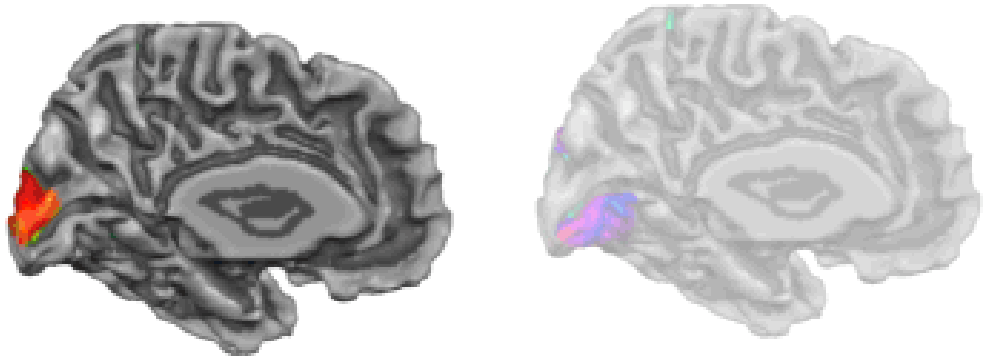
Signal cyclique

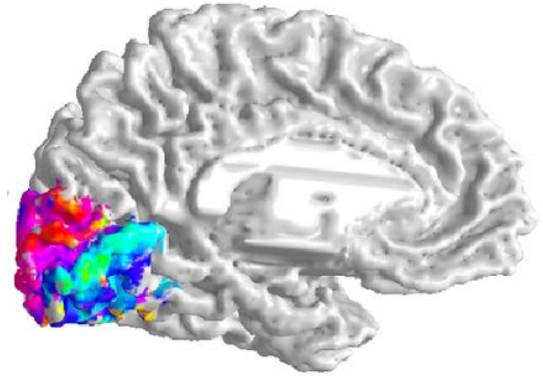
Rétinotopie

Stimulation polaire:
Chaque angle du champ visuel stimulé correspond à un site cortical précis



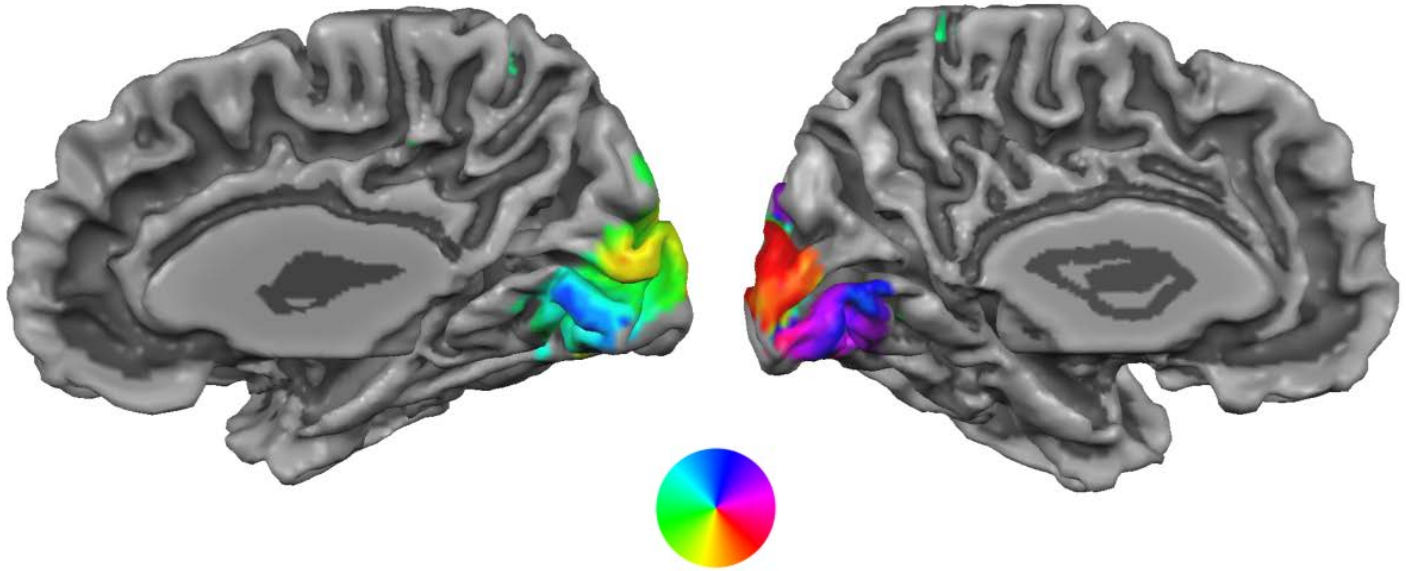






Rétinotopie

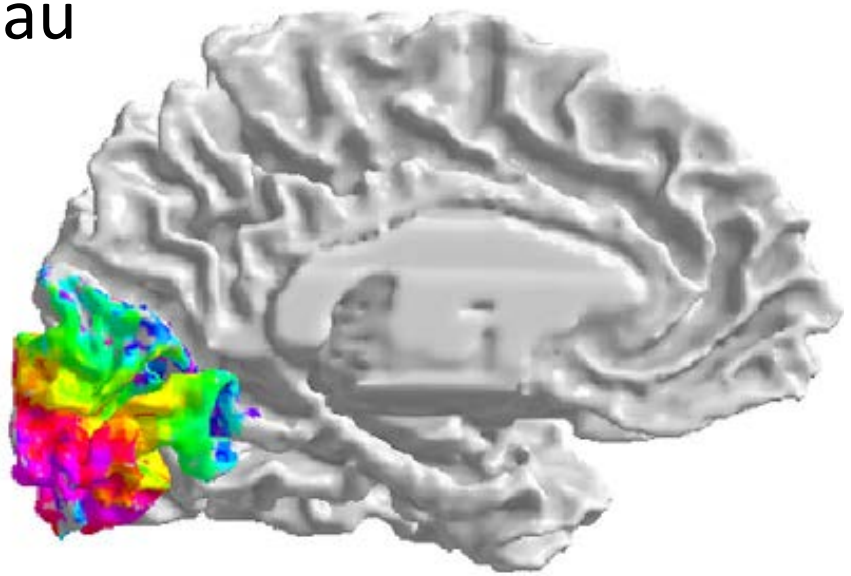
Scotome devrait entraîner défaut d'activation cortical au site correspondant de l'aire visuelle cérébrale

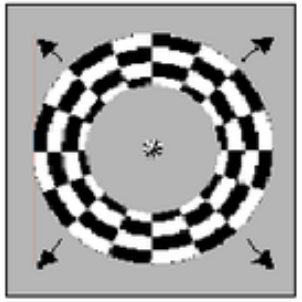


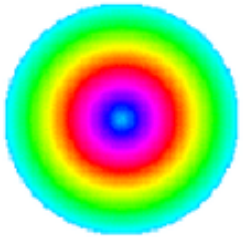
Rétinotopie

Stimulation excentrique:

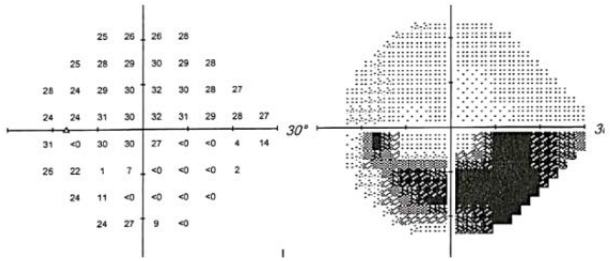
Chaque degré d’éloignement correspond à une augmentation de la distance par rapport au pôle occipital

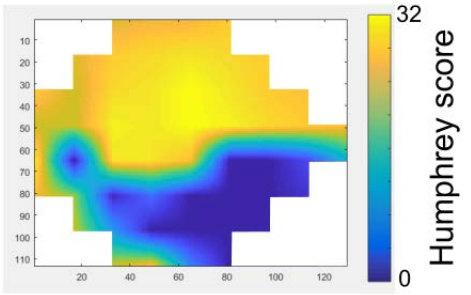


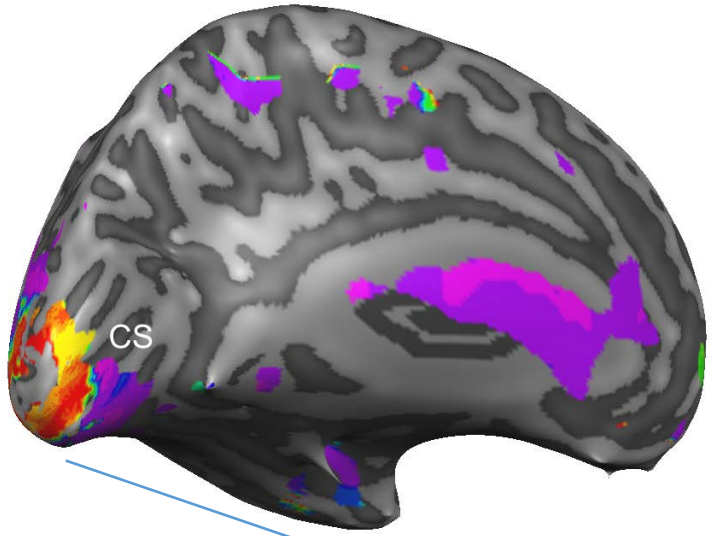


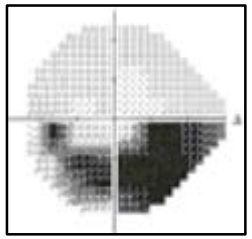


Résultats

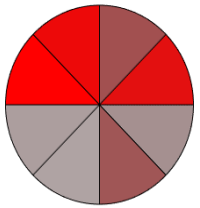


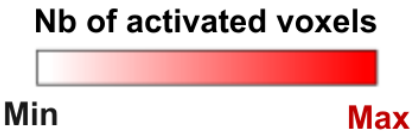






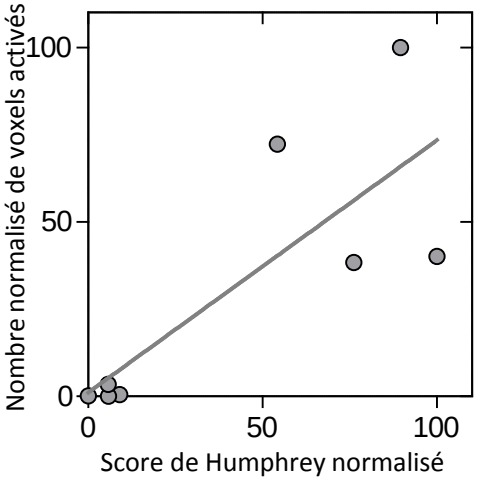
Reconstruction stimuli perçus
à partir données IRMf

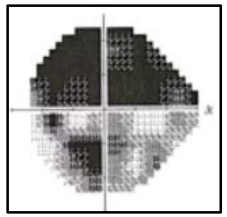


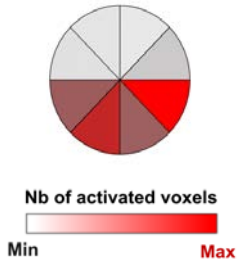


Résultats: stimulation œil atteint de glaucome

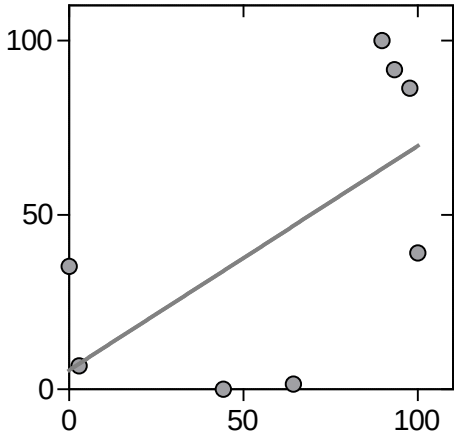
R-sq = 0.63
P = 0.01

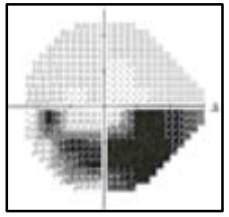


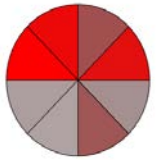




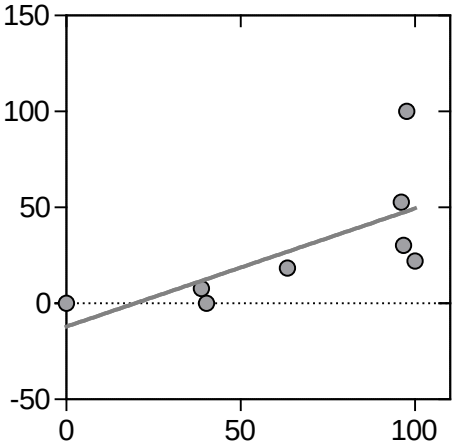
R-sq = 0.4
P = 0.09

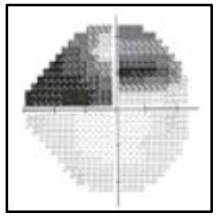


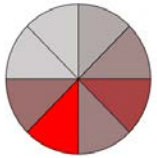




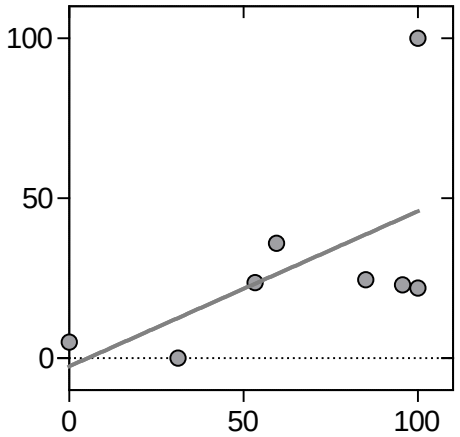
R-sq = 0.46
P = 0.06

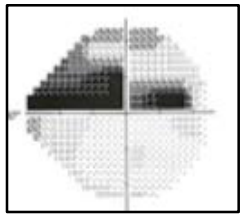


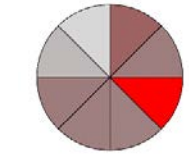




R-sq = 0.33
P = 0.13







R-sq = 0.45
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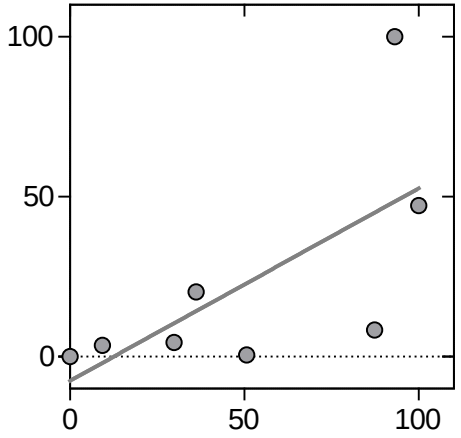
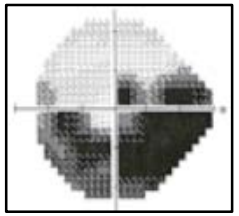
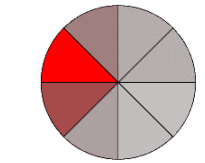
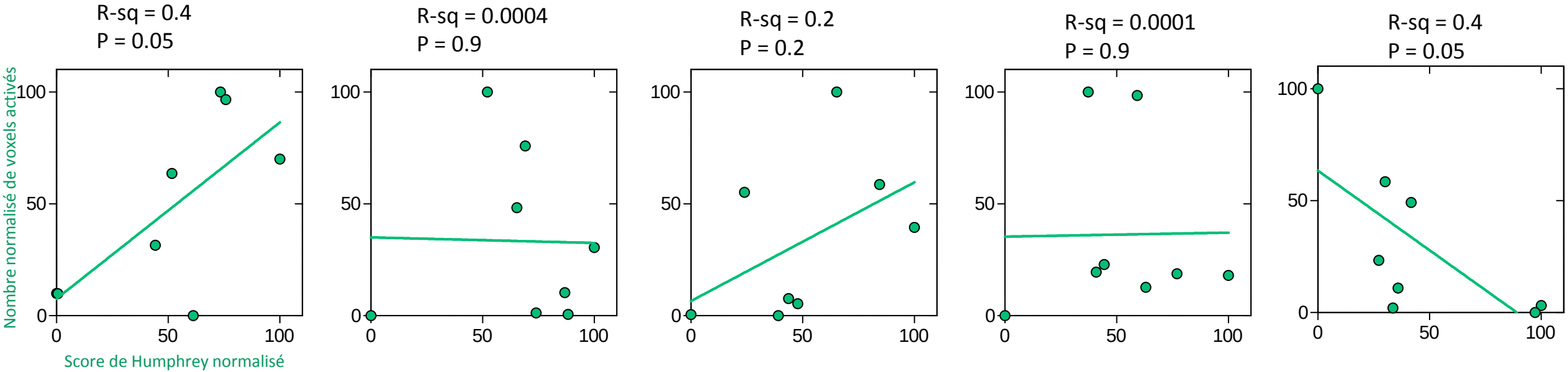
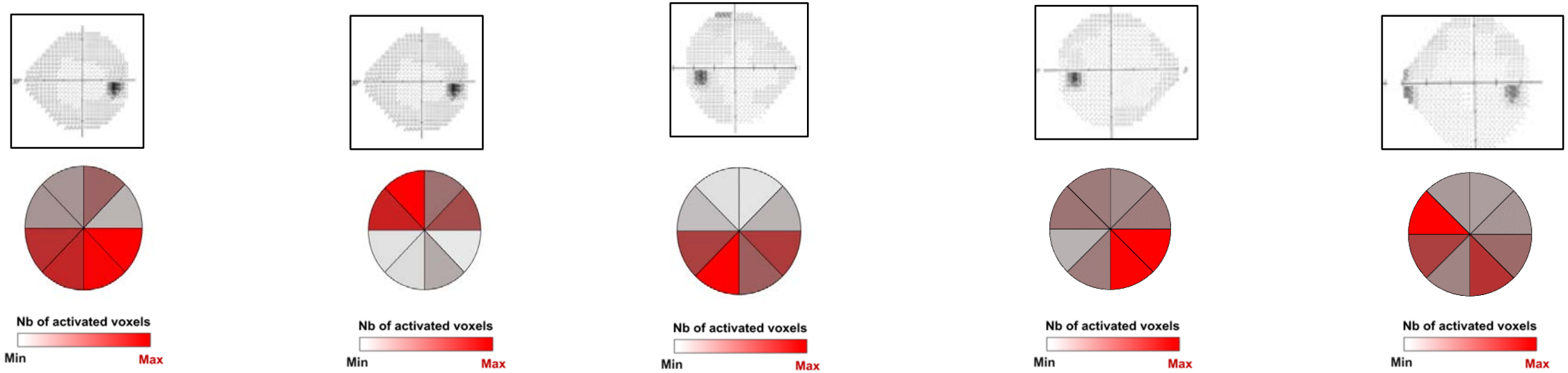






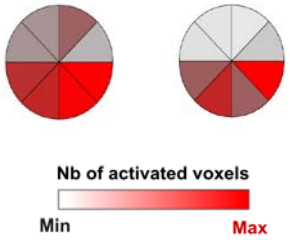
Résultats: stimulation œil sain

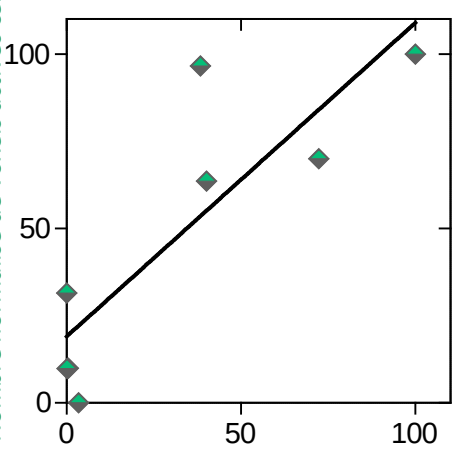




Résultats: corrélation entre les deux yeux

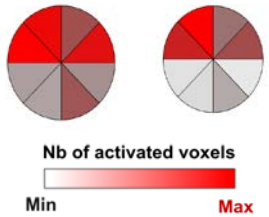
R-sq = 0.73
P = 0.006

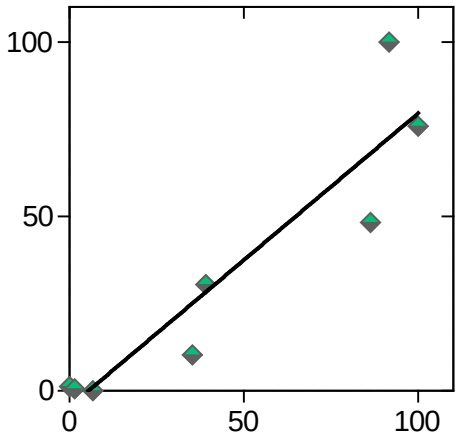




Pearson coef. = 0,85

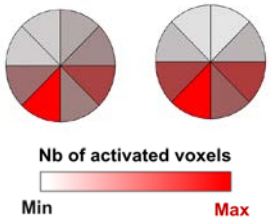
R-sq = 0.86
P = 0.0009

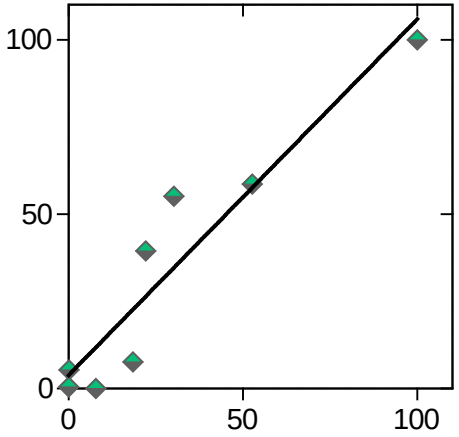




Pearson coef. = 0,92

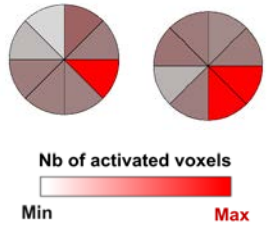
R-sq = 0.89
P = 0.0004

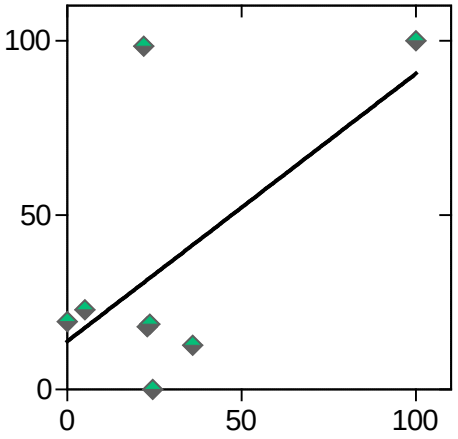




Pearson coef. = 0,94

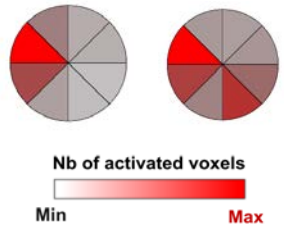
R-sq = 0.36
P = 0.11

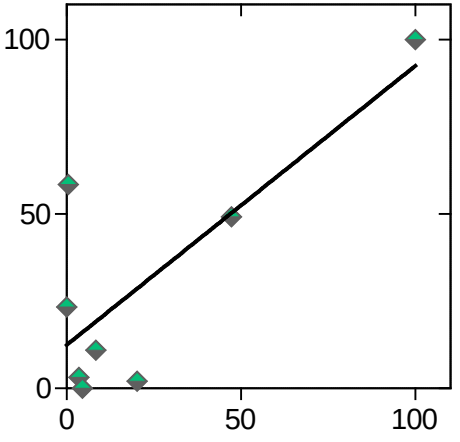




Pearson coef. = 0,59

R-sq = 0.61
P = 0.02



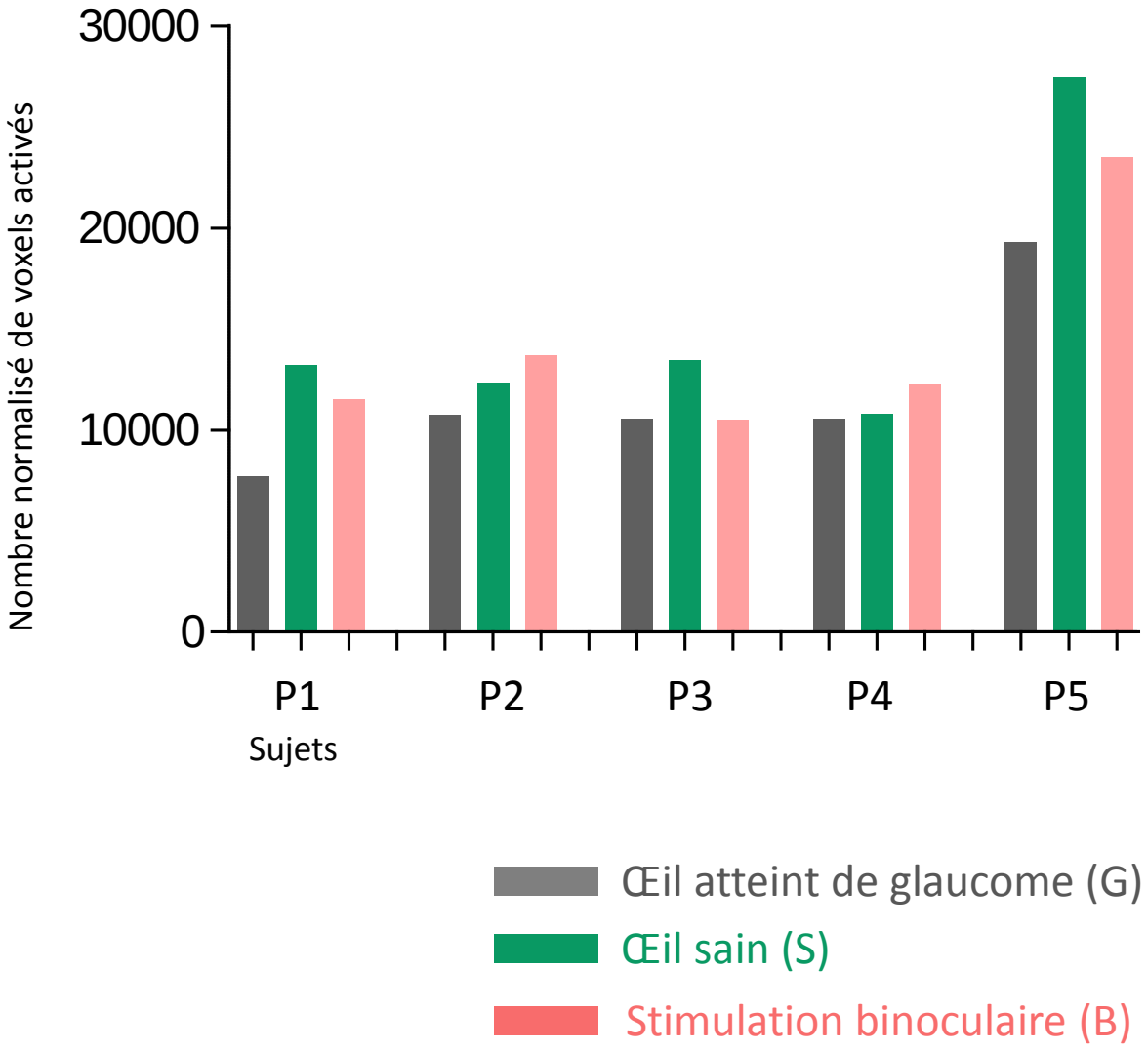


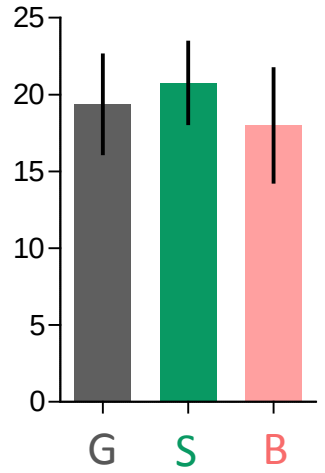
Pearson coef. = 0,78

Nombre normalisé de voxels activés œil sain

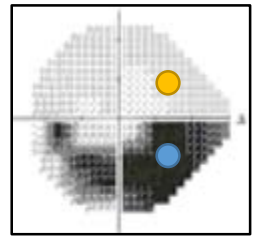
Nombre normalisé de voxels activés œil atteint de glaucome

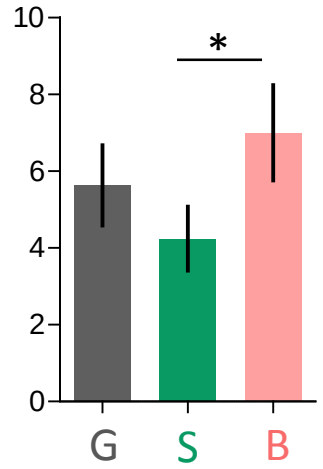
Résultats: réponses à stimulation monoculaire et binoculaire





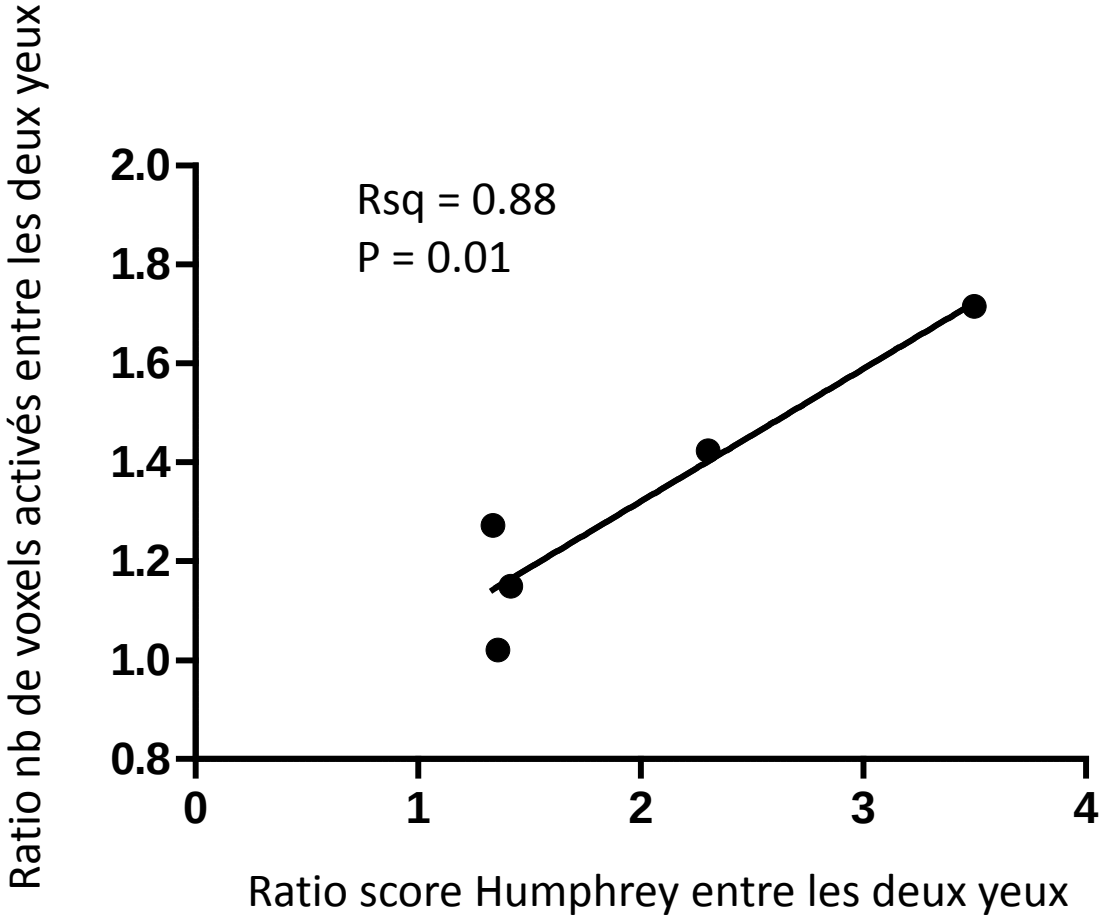
Zone saine





Site scotome (LPZ – *lesion projection zone*)

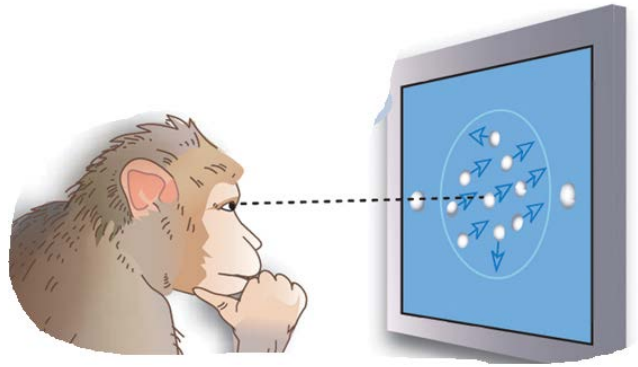
Réponses corticales vs réponses perçues au Humphrey



Hypothèse: diminution de l'inhibition pour contrebalancer la dégénérescence rétinienne?

Études animales:

- Modifications neurochimiques présentes a/n de l'œil sain et de l'œil atteint de glaucome, soit ↓ GABA
- Diminution du nombre et de la taille des cellules recevant signaux de l'œil sain (Yucel et al., 2003), traduisant un environnement toxique (Luthra et al., 2005)
- Pas de signe de diminution de l'inhibition (Borges et al., 2015)



Neuroplasticité démontrée (modèle animal)

Évaluation en cours

Expansion of visual receptive fields in experimental glaucoma

WAYNE MICHAEL KING [a1] [a2], VIMAL SARUP [a1], YVES SAUVÉ [a3], COLLEEN M. MORELAND [a1] ...

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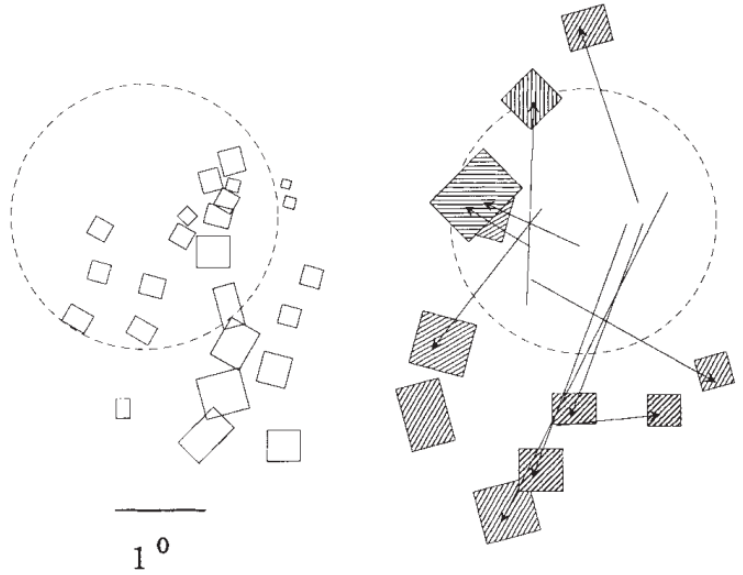
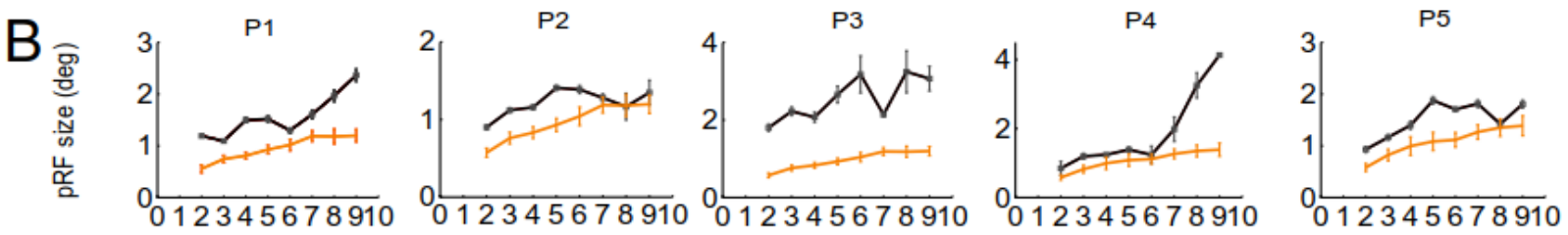
Abstract

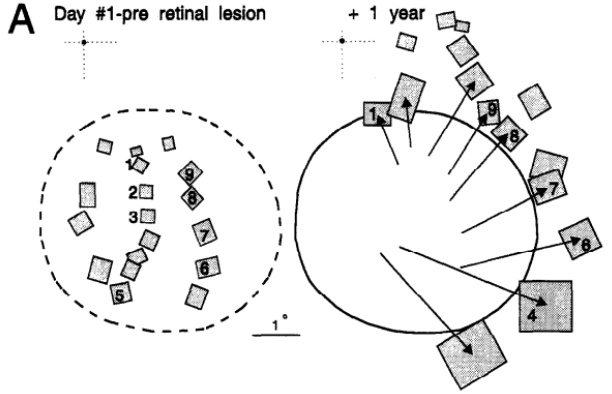
Glaucoma is a major cause of blindness and is characterized by death of retinal ganglion cells. In a rat model of glaucoma in which intraocular pressure is raised by cautery of episcleral veins, the somata and dendritic arbors of surviving retinal ganglion cells expand. To assess physiological consequences of this change, we have measured visual receptive-field size in a primary retinal target, the superior colliculus. Using multiunit recording, receptive-field sizes were measured for glaucomatous eyes and compared to both those measured for contralateral control eyes and to homolateral eyes of unoperated animals. Episcleral vein occlusion increased intraocular pressure. This was accompanied by a significant increase in receptive-field size across the superior colliculus. The expansion of receptive fields was proportional to both degree and duration of the increase of intraocular pressure. We suggest that this increase in the size of receptive fields of glaucomatous eyes may be related to the increase in the size of dendritic arbors of the surviving ganglion cells in retina.



Gilbert and Wiesel, 1992



Papanikolaou et al., 2014



Darian smith and Gilbert, 1995

MRCI