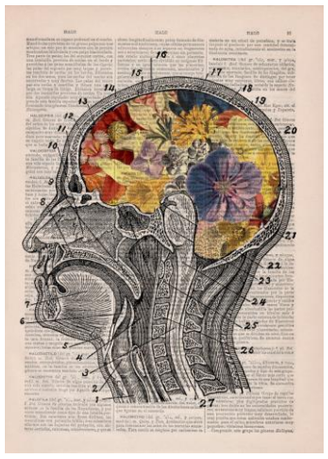
Cerebellar Imaging of Parkinson's disease

Rôle fonctionnel du cervelet dans la maladie de Parkinson par analyse en imagerie multimodale

Dr Audrey RIOU - EA 4712 - CHU Rennes



Journées Françaises de Médecine Nucléaire

Nantes - 18 Mai 2017

UNIVERSITÉ DE RENNES 1

CHU Rennes

NIST NeuroImaging & Surgical Technologies Lab

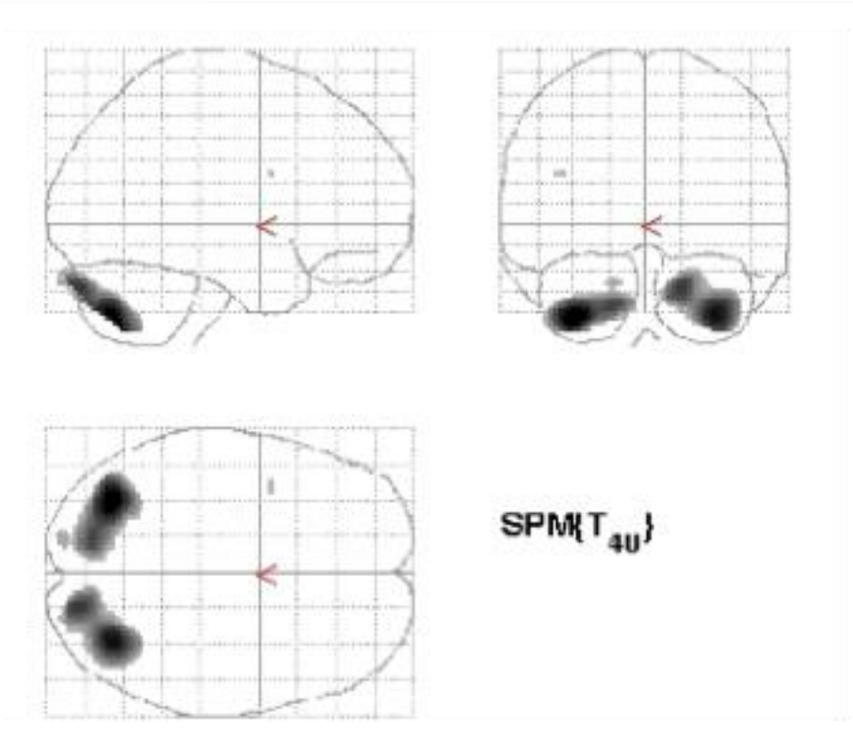
Comportement et Noyaux Gris Centraux

Où l'histoire a commencé…

Apathy in patients with Parkinson disease without dementia or depression

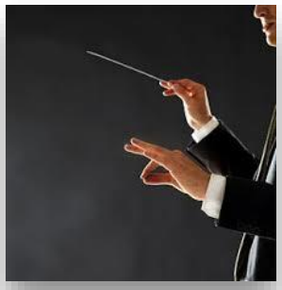
A PET study

Gabriel Robert, MD
Florence Le Jeune, MD, PhD
Clément Lozachmeur, MD
Sophie Drapier, MD
Thibault Dondaine, MSc
Julie Péron, PhD
David Travers, MD
Paul Sauleau, MD, PhD
Bruno Millet, MD, PhD
Marc Vérin, MD, PhD
Dominique Drapier, MD, PhD



Neurology® 2012;79:1155-1160

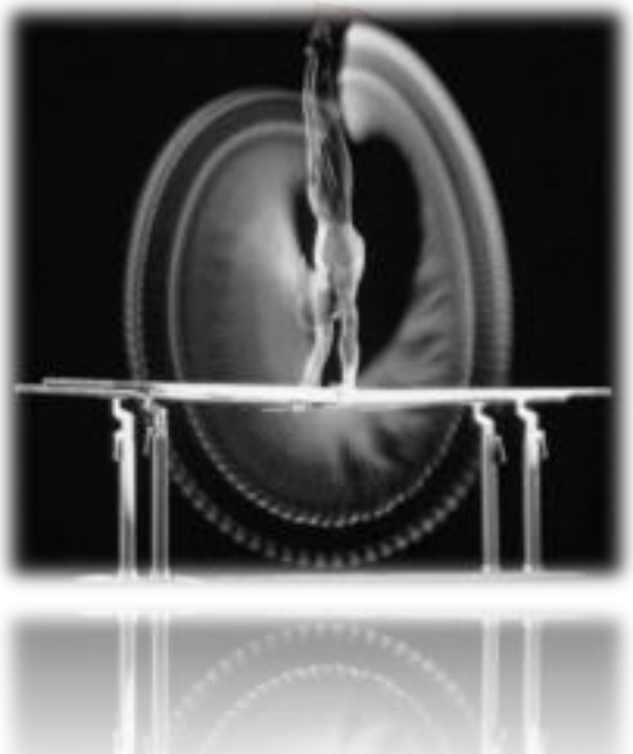
Contexte



« Modulateur du mouvement »

Physiologique:

—> **SYNERGIE**

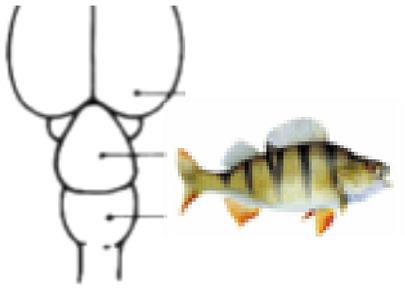


Dysfonction:

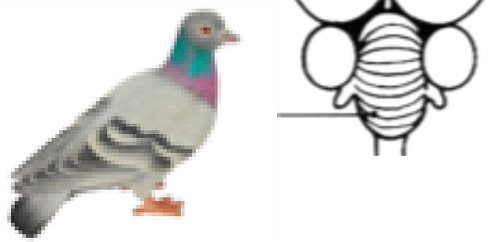
—> **DYSMETRIE**

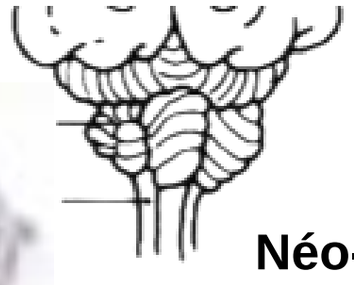
Phylogenèse

Archéo-cervelet



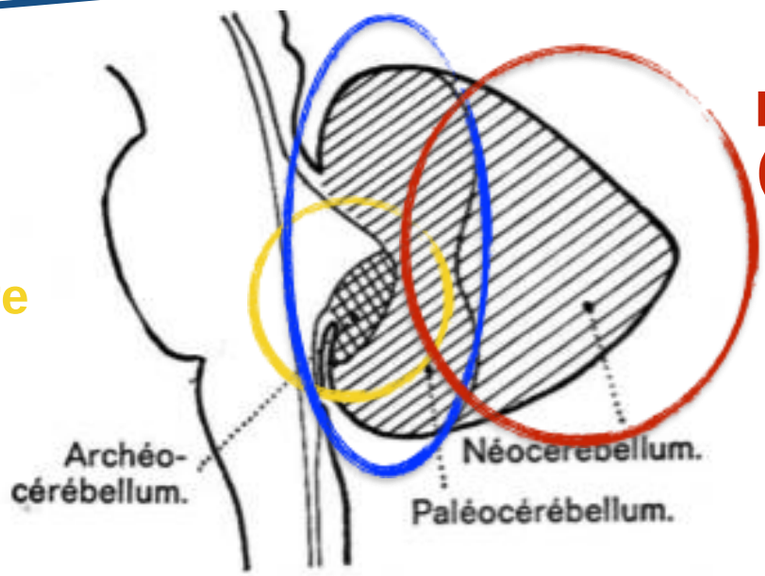
Paléo-cervelet





Néo-cervelet

Equilibre + **Tonus statique** + **Tonus dynamique**



Lobe floculo-nodulaire

Lobe postérieur (Lobules VI à X)

Lobe antérieur (Lobules I à V) et vermis

Néo-cervelet = Gain de fonction

CCAS nouveau concept

Brain (1998), **121,** 561–579

The cerebellar cognitive affective syndrome

Jeremy D. Schmahmann and Janet C. Sherman

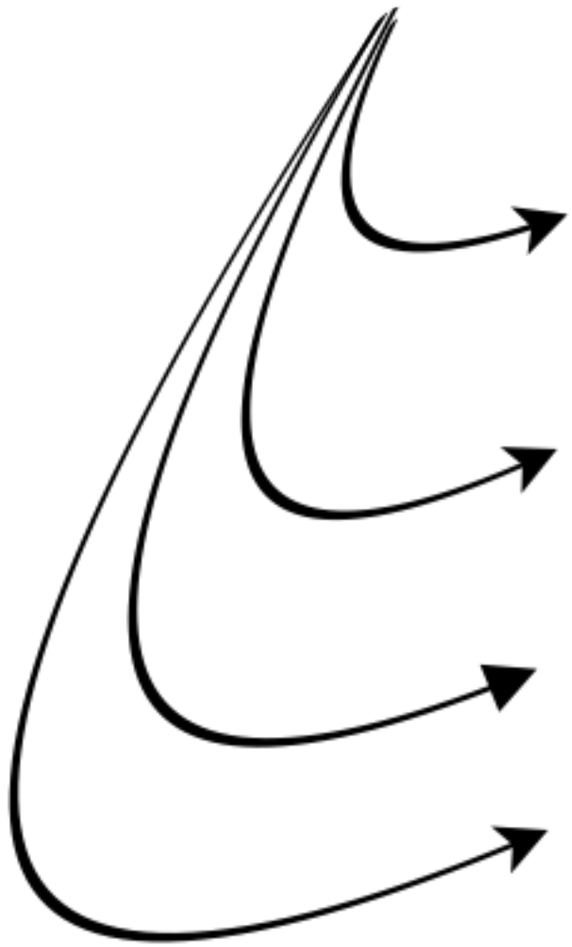


Table 1 Deficits that characterize the cerebellar cognitive affective syndrome

1. Executive function

Deficient planning, motor or ideational set-shifting, abstract reasoning, working memory. Decreased verbal fluency, sometimes to the point of telegraphic speech or mutism. Perseverative ideation in thought and/or action.

2. Spatial cognition

Visuospatial disintegration with impaired attempts to draw or copy a diagram. Disorganized conceptualization of figures. Impaired visual–spatial memory. Simultanagnosia in some.

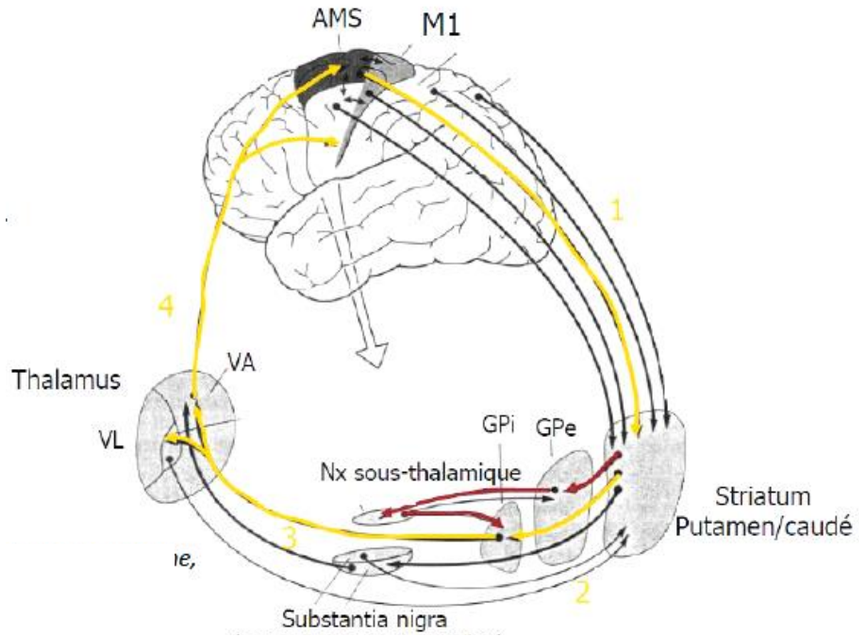
3. Linguistic difficulties

Anomia, agrammatic speech, and abnormal syntactic structure, with abnormal prosody.

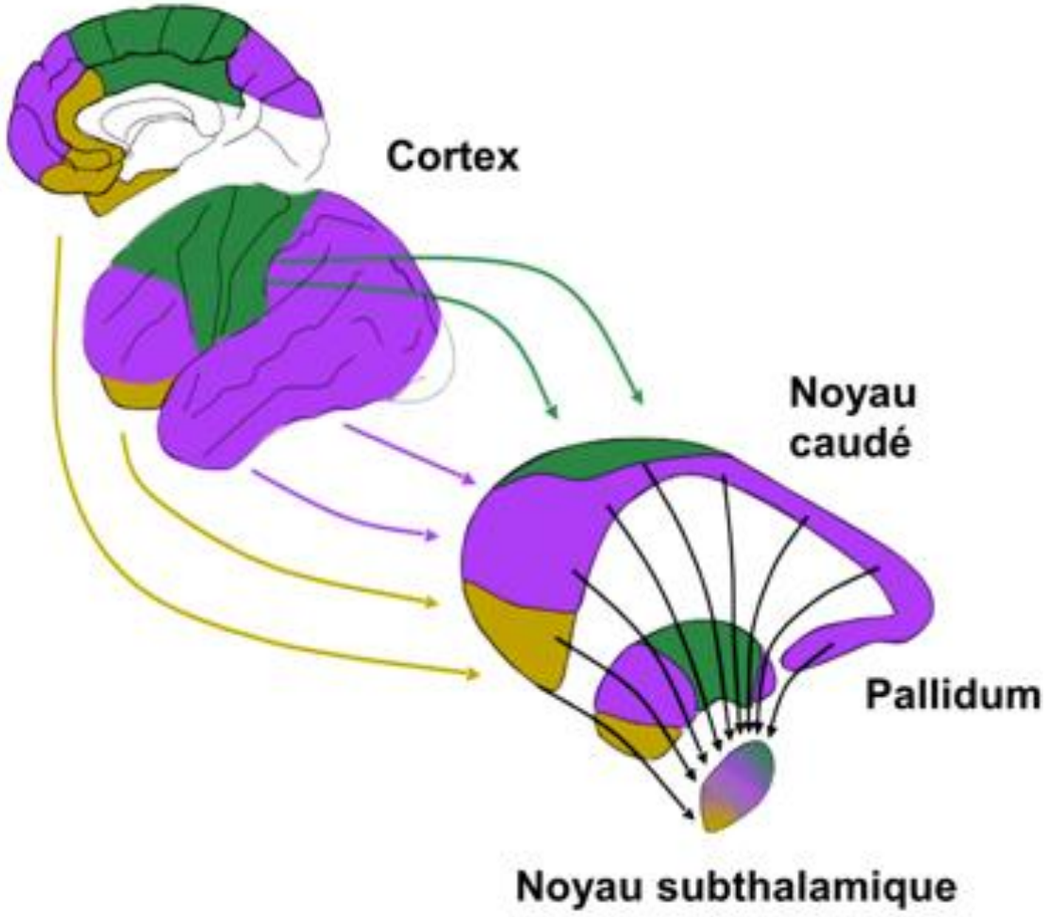
4. Personality change

Aberrant modulation of behavior and personality with posterior lobe lesions that involve midline structures. Manifests as flattening or blunting of affect alternating or coexistent with disinhibited behaviors such as over-familiarity, flamboyant and impulsive actions, and humorous but inappropriate and flippant comments. Regressive, childlike behaviors and obsessive-compulsive traits can be observed (see Table 2).

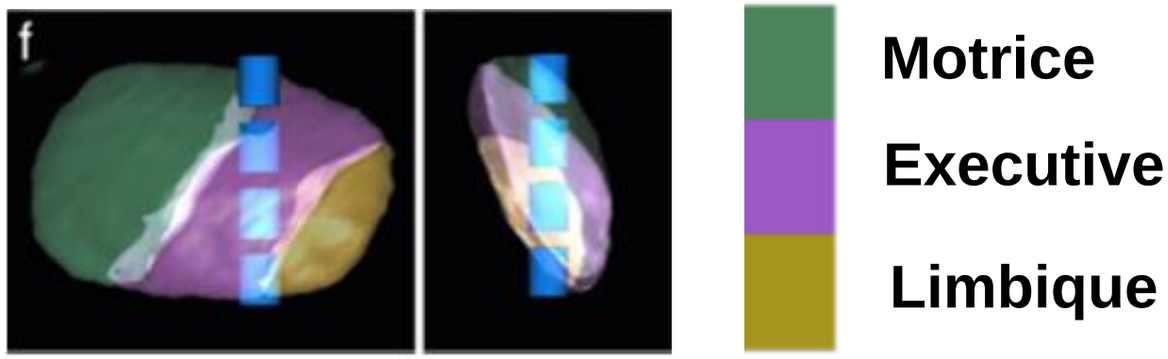
Pertinence de la Maladie de Parkinson



Défect de la boucle striato-thalamo-corticale

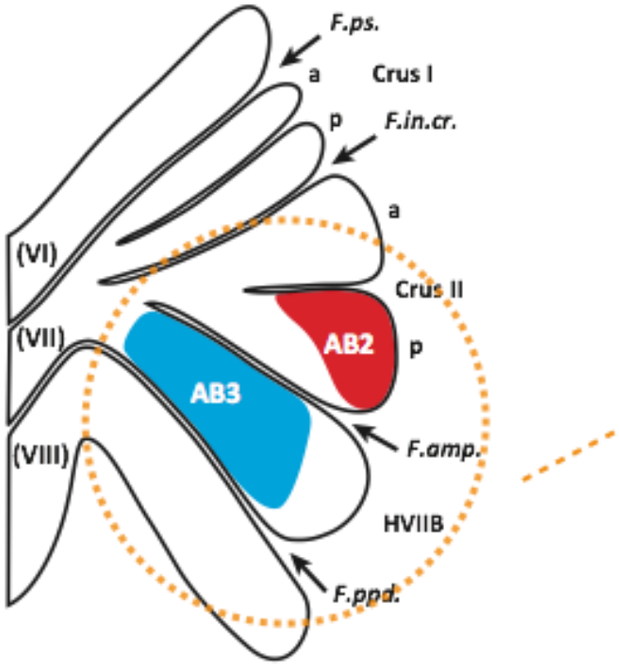


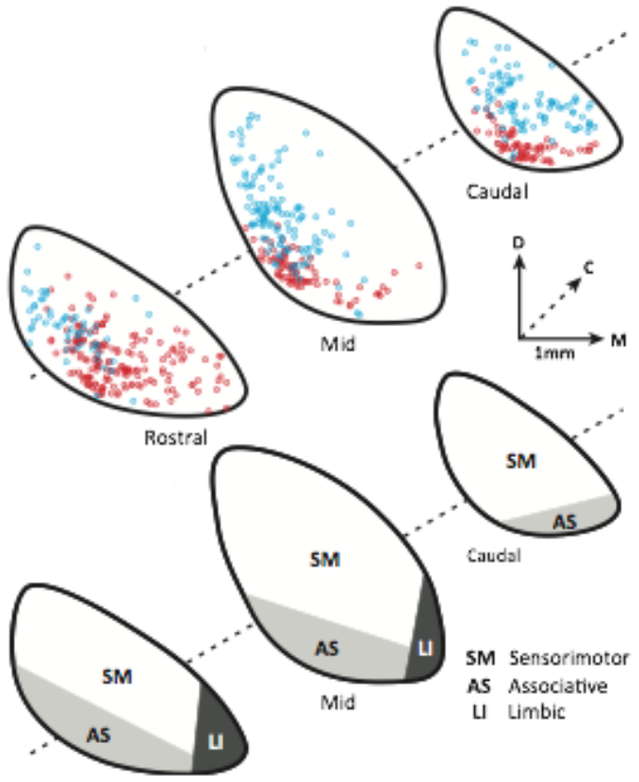
Tri-compartimentation fonctionnelle des noyaux gris centraux



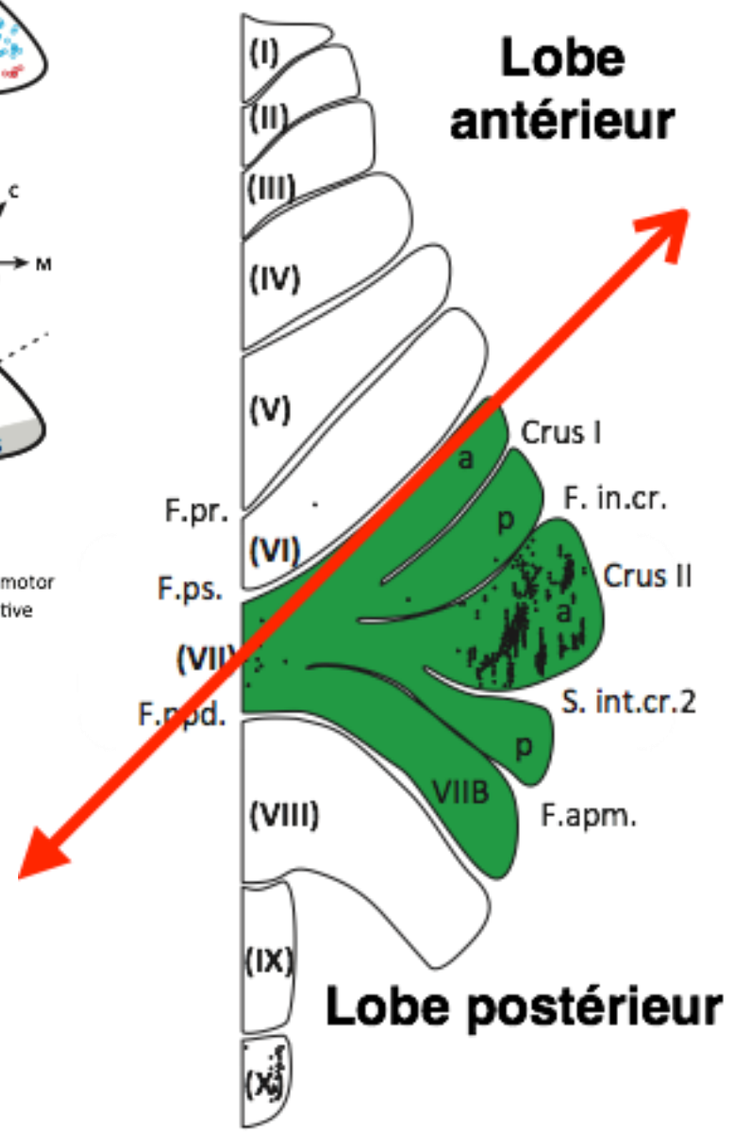
Mallet et al, PNAS 2007

Interaction cervelet & ganglions de la base?





Bostan & Strick, 2003

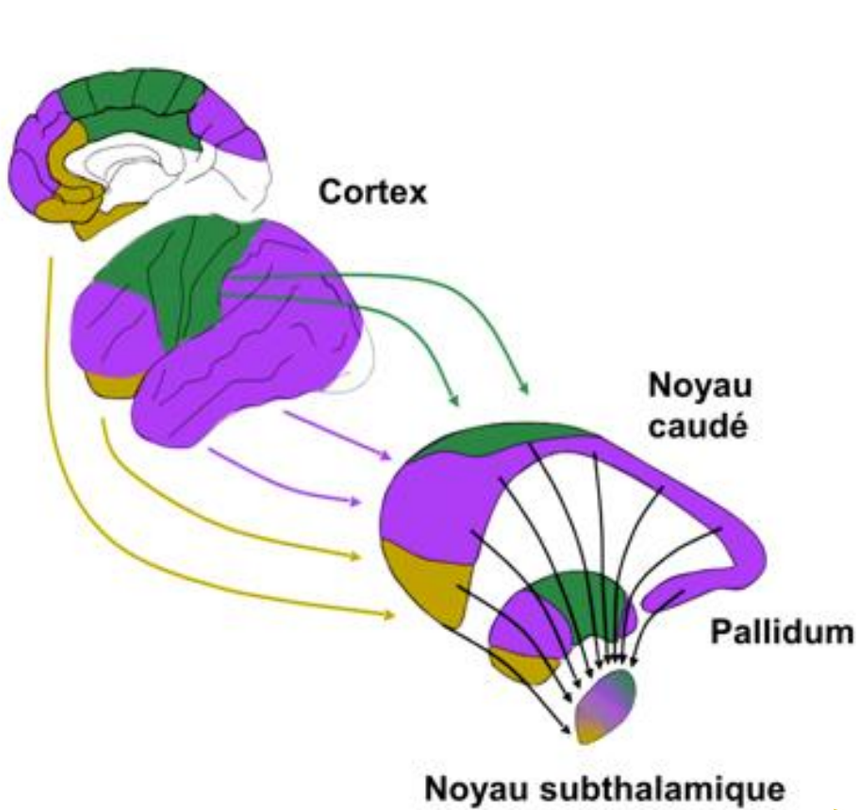


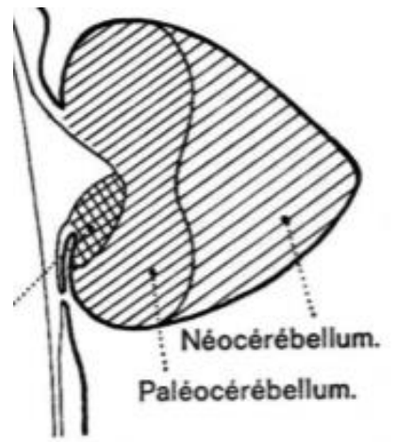
Boucles de régulation?

Projections c. de Purkinje vers cortex préfrontal

Objectifs de l'étude

- ✓ **Confirmer l'implication du cervelet dans la MP dans les fonctions non-motrice**
- ✓ **Determiner l'existence d'une connectivité fonctionnelle entre le cervelet et le cortex cérébral dans la MP**





? ? ?

Matériels et méthode

Population

- ✓ **90 patients** avec une MP idiopathique
- ✓ en bilan pré-op pour une stimulation cérébrale
- ✓ entre 2007 et 2015
- ✓ CHU Rennes

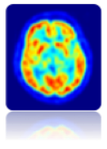
	Mean +/- SD	Range
Sex	43 F / 48 M	
Age (years)	56,97 ± 8,67	(29 - 74)
Disease Form	Akineto-hypertonic (n=41) Mixed (n=48) Tremor (n=1)	
Disease Duration (years)	10,94 ± 4,58	(4-31)
Levodopa Equivalent Daily Dose (LEDD in mg)	1293,93 ± 610,6	(150-3055)
Agoniste Daily Dose (mg)	246,35 ± 362,20	(0-1100)

Evaluations cliniques

- **Motrice**
(UPDRS 2,3,4 ; Hoehn & Yahr Scale, Schwab & England)
- **Psychiatrique**
(UPDRS 1, AES, AMDPAT, MADRS)
- **Neuropsychologique**
(MDRS, Stroop, TMT, Wisconsin, phonemic and semantic fluency)

Analyse en composante principale (PCA) sur les scores cliniques

✓ Une reflétant l'état moteur
✓ Une reflétant l'état psychique
✓ Une reflétant l'état cognitif



Analyse métabolique 18 FDG PET-Scan

SPM 8

Premier niveau d'analyse:
✓ Identifier des clusters fonctionnels cérébelleux

COMMENT ?

↳ Etude de corrélation entre le métabolisme cérébelleux et chaque PCA

Analyse statistique: régression linéaire multiple:

✓ Variable dependante: chaque PCA + métabolisme
✓ Covariable: age et LEDD

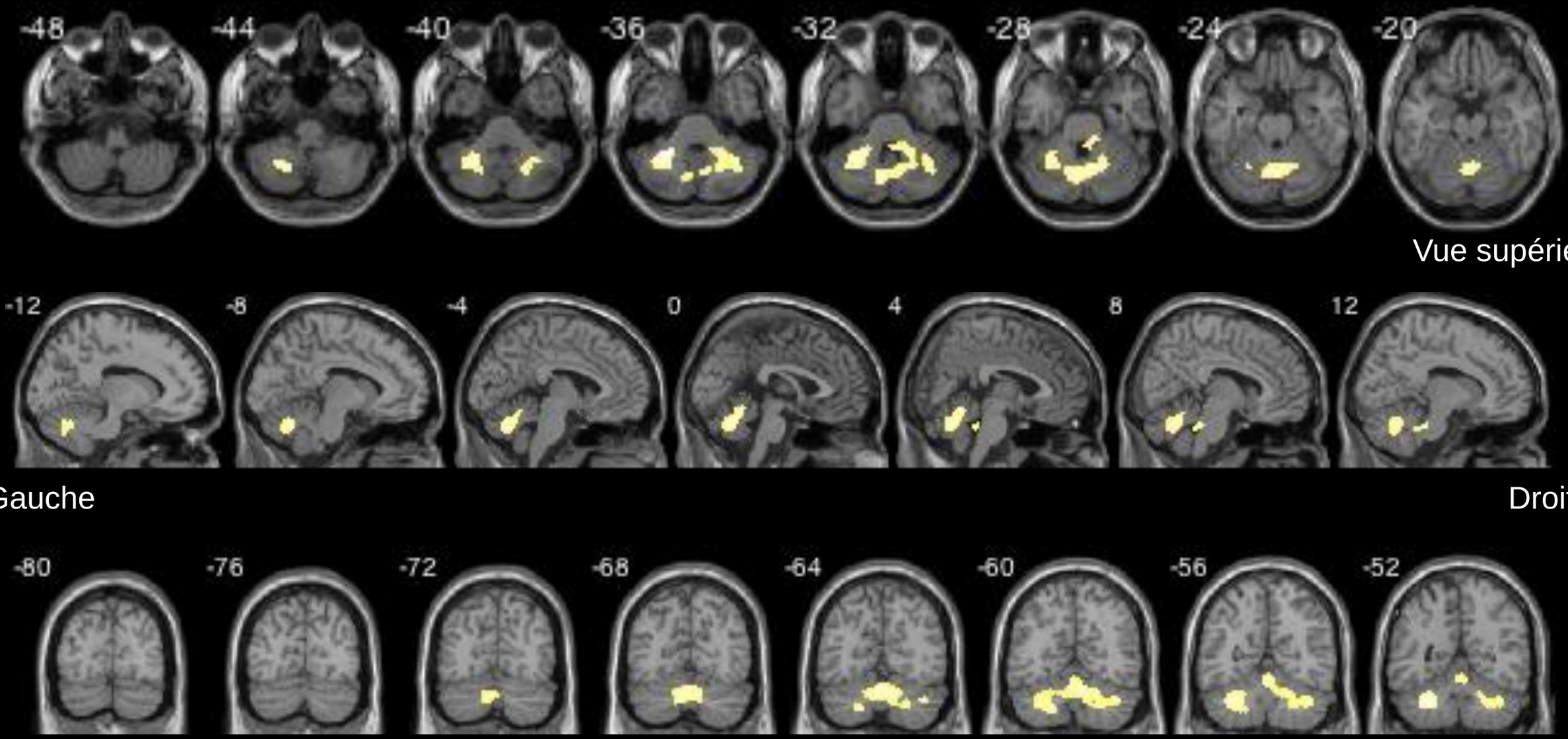
Second niveau d'analyse:
✓ Connectivité fonctionnelle cervelet - métabolisme cerebral global

COMMENT ?

↳ Par extraction de la valeur moyenne métabolique dans le cluster cérébelleux et en le corrélant avec le métabolisme cérébral global

Partie I: Analyse métabolique cérébelleuse

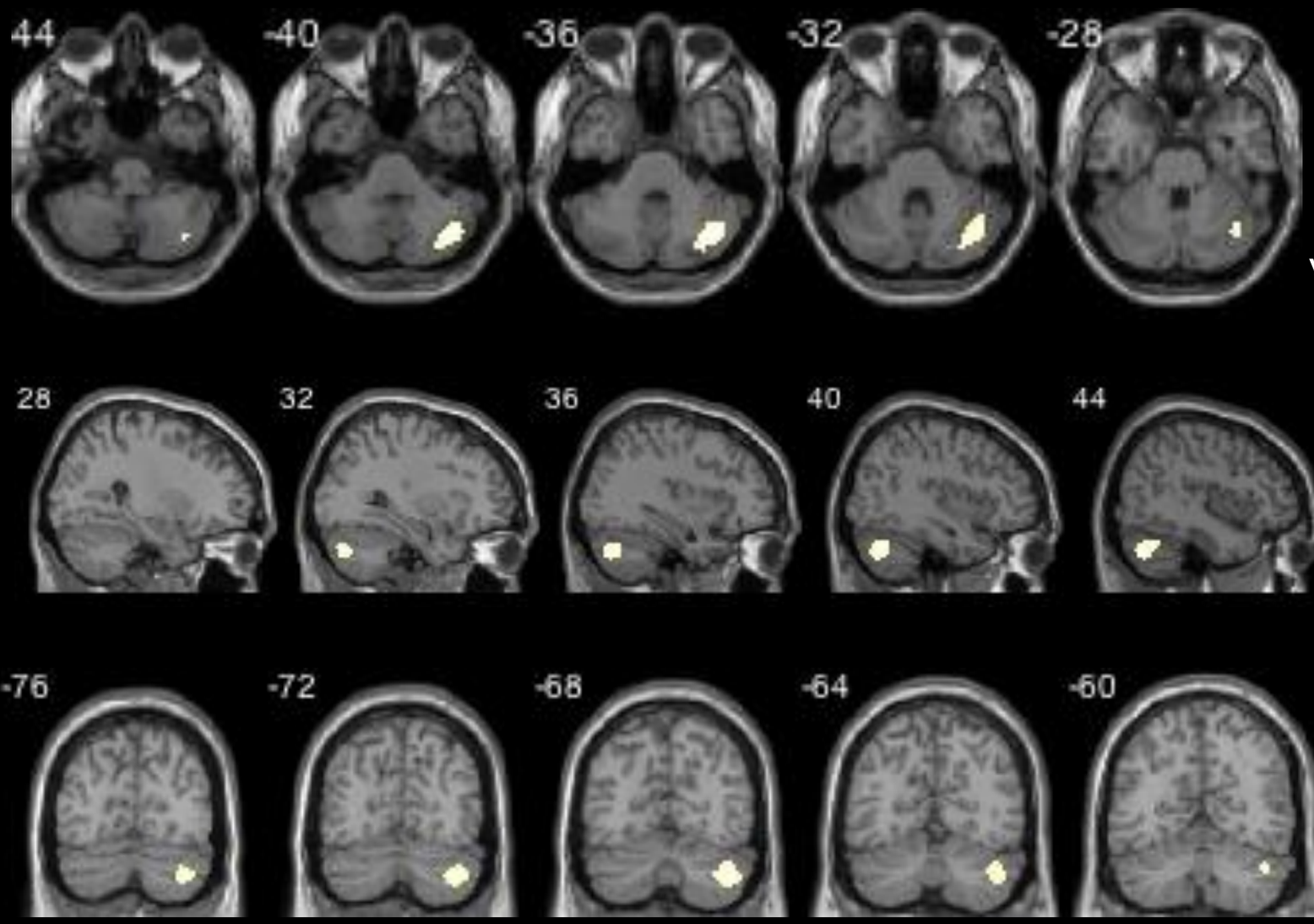
Résultats: moteur



corrélation positive
p<0,001

score ↟
sévérité maladie ↟
métabolisme ↟

Résultats: psychique



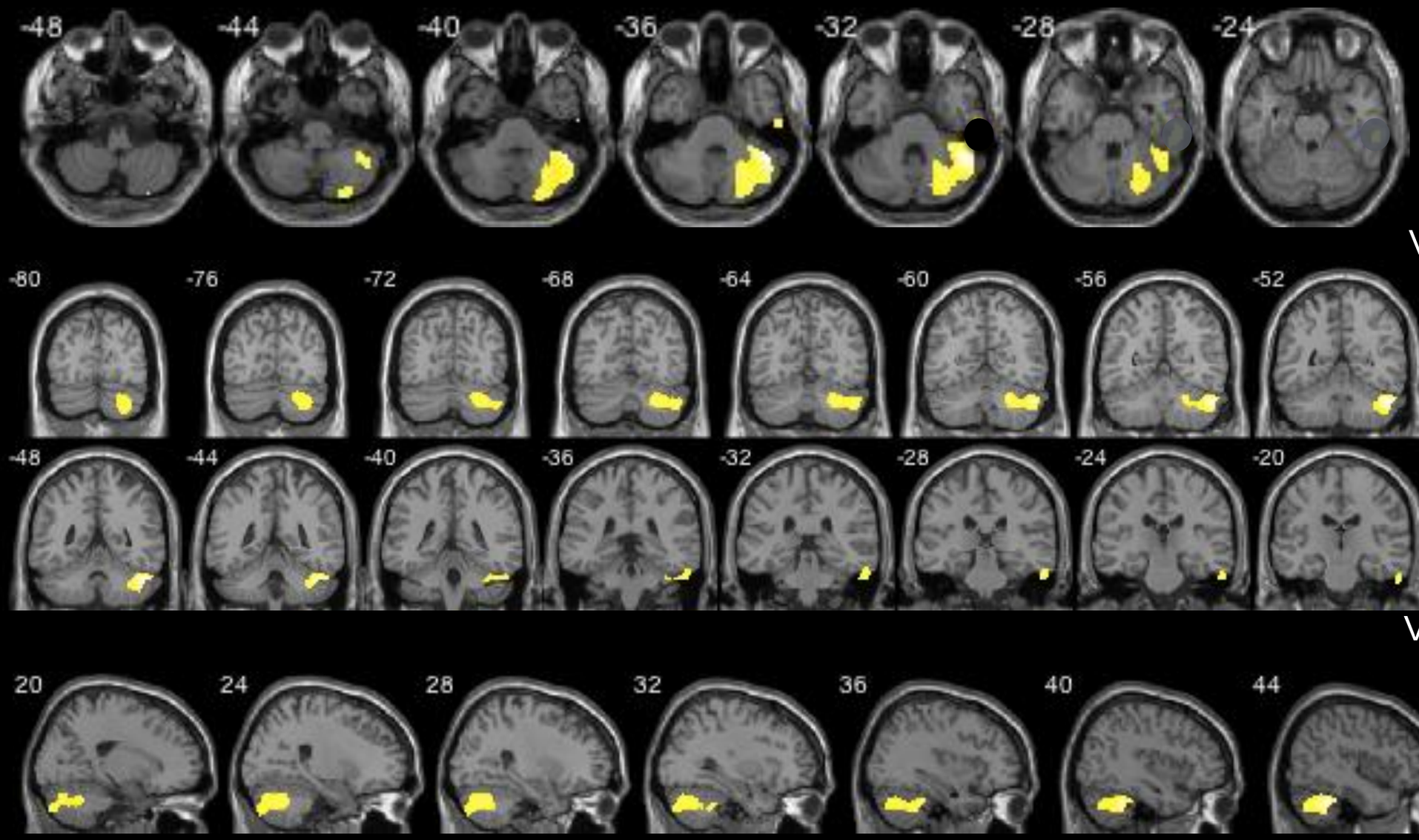
Vue supérieure

Vue postérieure

corrélation positive
p<0,05

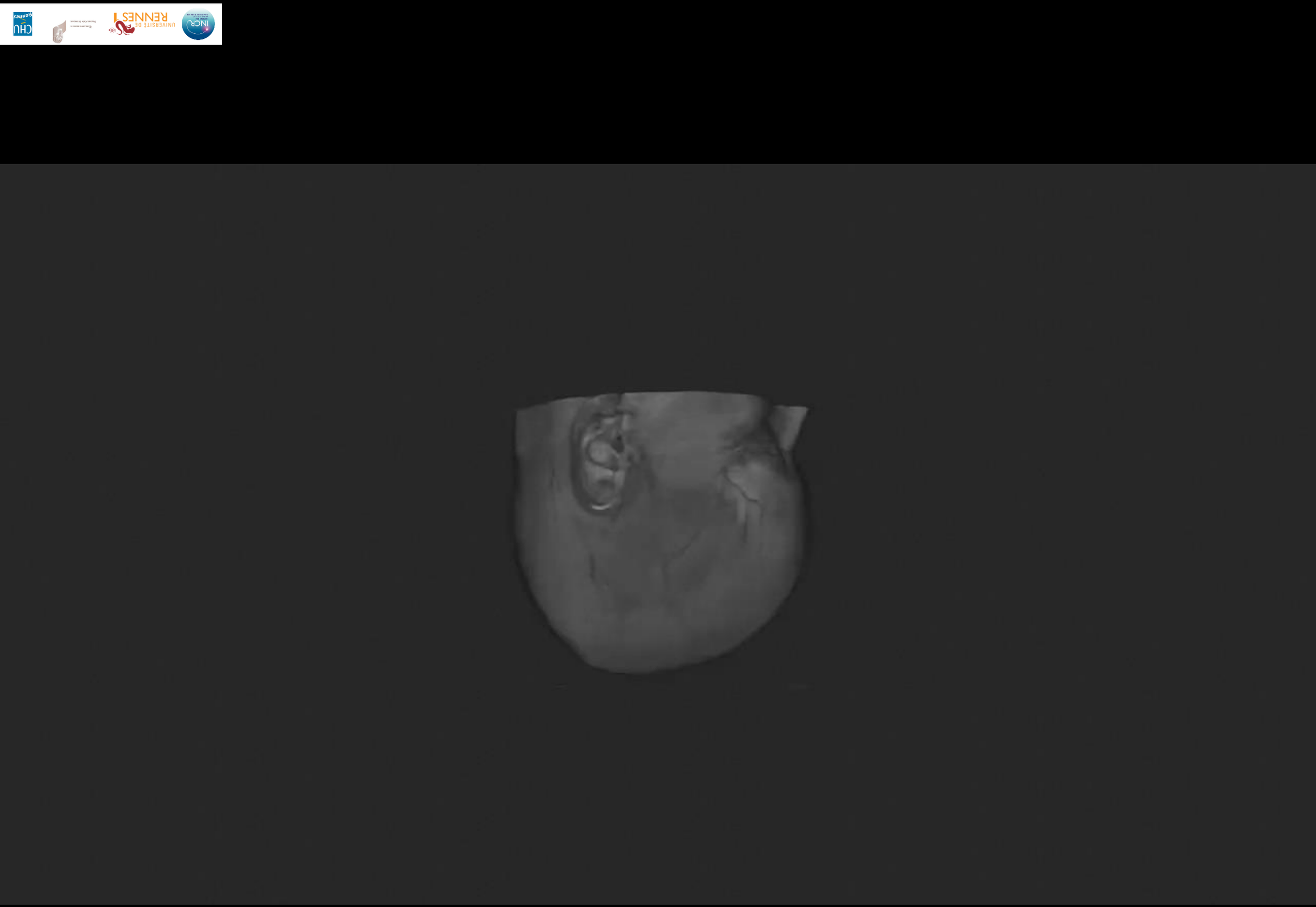
score ↟
sévérité maladie ↟
métabolisme ↟

Résultats: cognitif



corrélation négative
p<0,001

score ⇣
sévérité maladie ⇡
métabolisme ⇡



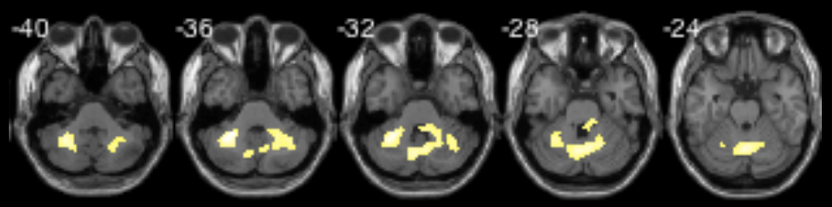
Partie II: Analyse de connectivité fonctionnelle

Results

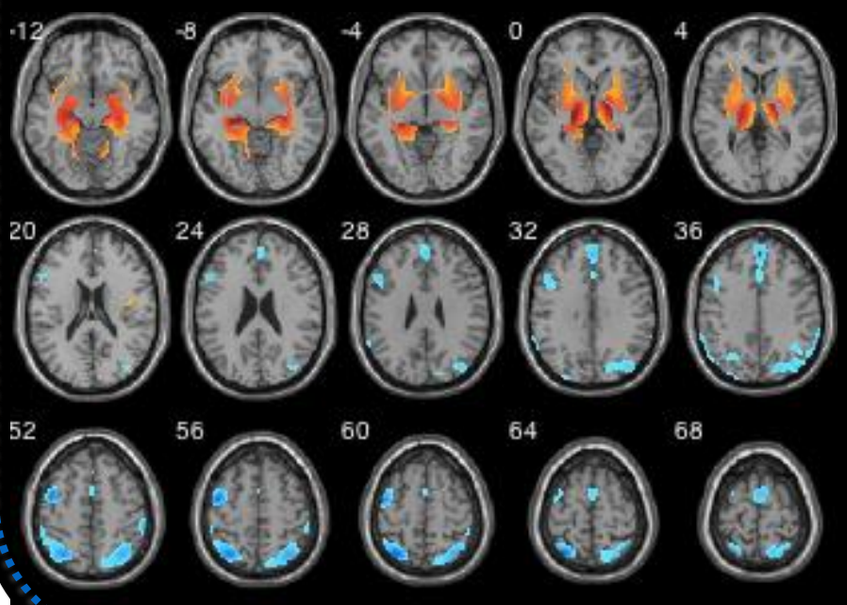
Motor

✓ **Correlation** between PD motor symptoms and cerebellar metabolism *(p<0,001)*

Motor PCA score⇡
Disease severity ⇡
Metabolism ⇡



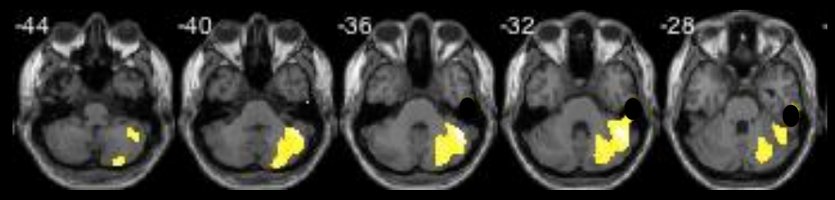
Functional connectivity
(p=0.001 FWE corrected)



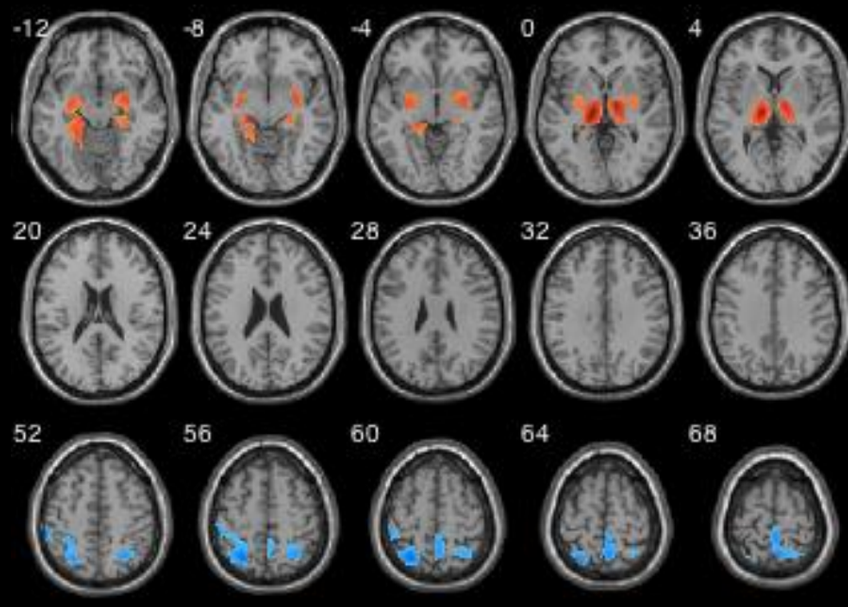
Cognitive

✓ **Correlation** between PD cognitive symptoms and cerebellar metabolism *(p<0,001):*

Cognitive PCA score ⇣
Disease severity ⇡
Metabolism ⇡



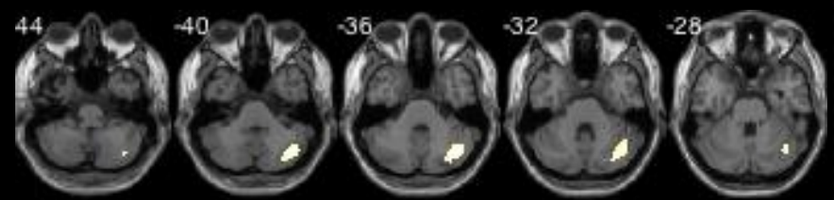
Functional connectivity
(p=0.001 FWE corrected)



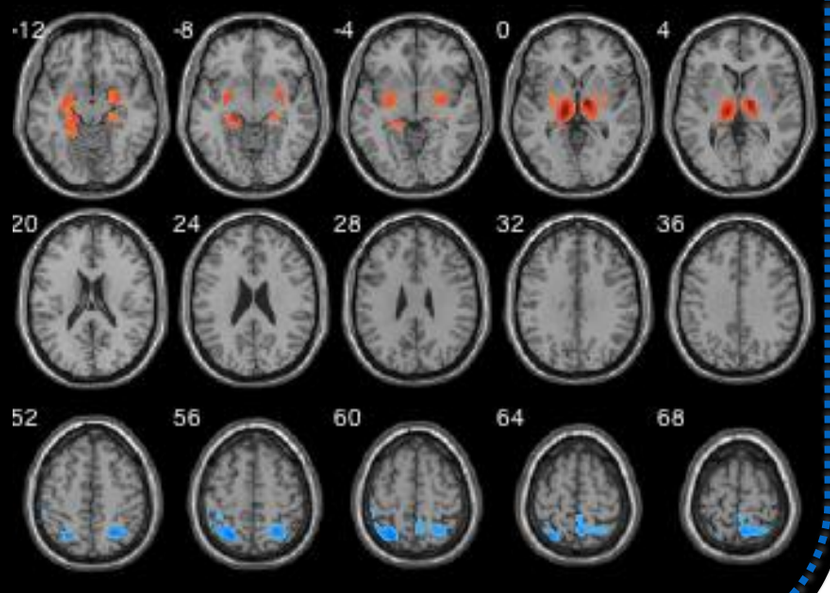
Psychic

✓ **Correlation** between PD psychic symptoms and cerebellar metabolism *(p<0,05):*

Psychic PCA score ⇡
Disease severity ⇡
Metabolism ⇡



Functional connectivity
(p=0.001 FWE corrected)



Right hemisphere is illustrated on the right
Positive correlation = red ; negative correlation = blue

Discussion

- Confirme **compartimentation fonctionnelle du cervelet et** **son rôle moteur et non-moteur dans la maladie de Parkinson**

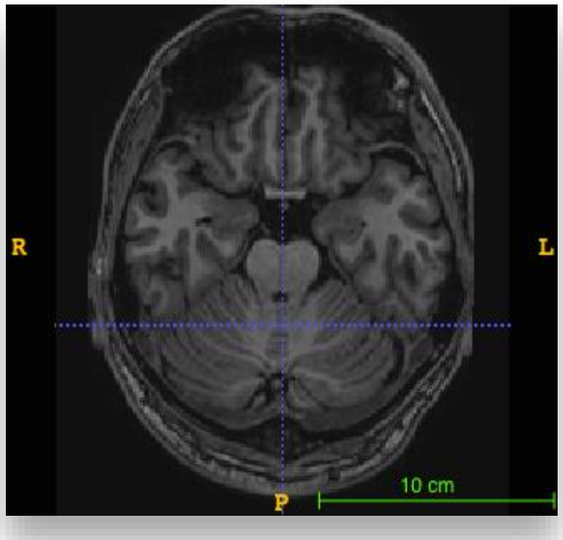
- **Confirme une forte implication cervelet / noyaux gris centraux**

- **Forte puissance** :
  - **nombre** de patients inclus (90 versus en moyenne 30 patients / publication)
  - première étude **centrée uniquement** sur le cervelet
  - exploration **clinique exhaustive / PCA**

Arguments pour un rôle compensateur du cervelet dans la maladie de Parkinson

ou dysfonction primitive?

Perspectives: volumétrie cérébelleuse

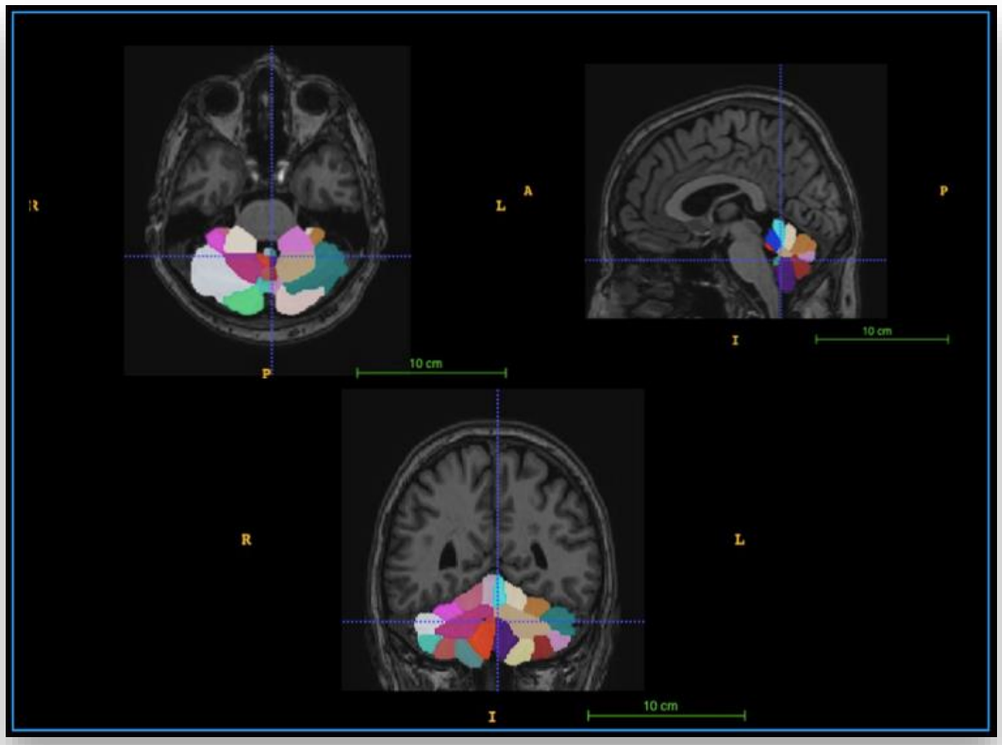


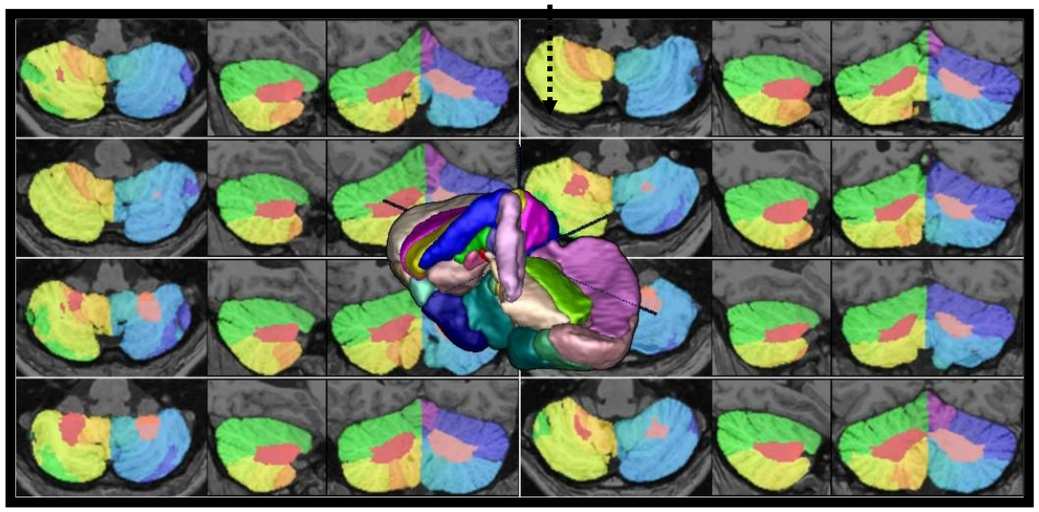
RASCAL

Rapid Automatic Segmentation of the Human Cerebellum and its Lobules (RASCAL)—Implementation and Application of the Patch-based Label-fusion Technique With a Template Library to Segment the Human Cerebellum

Katrin Weier,[1,2] Vladimir Fonov,[1] Karyne Lavoie,[3] Julien Doyon,[4] and D. Louis Collins[1,2]*

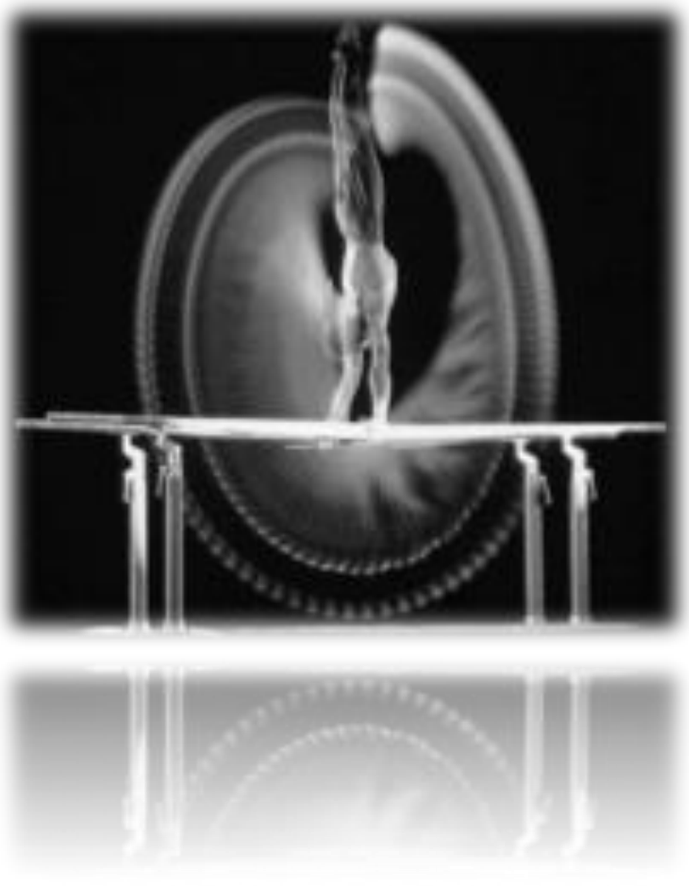
[1]*McConnell Brain Imaging Center, Montreal Neurological Hospital and Institute, McGill University, Montreal, Canada*
[2]*Department Biomedical Engineering, McGill University, Montreal, Canada*
[3]*Research Centre in Neuropsychology and Cognition, University of Montreal, Montreal, Canada*
[4]*Functional Neuroimaging Unit and Department of Psychology, University of Montreal, Montreal, Canada*

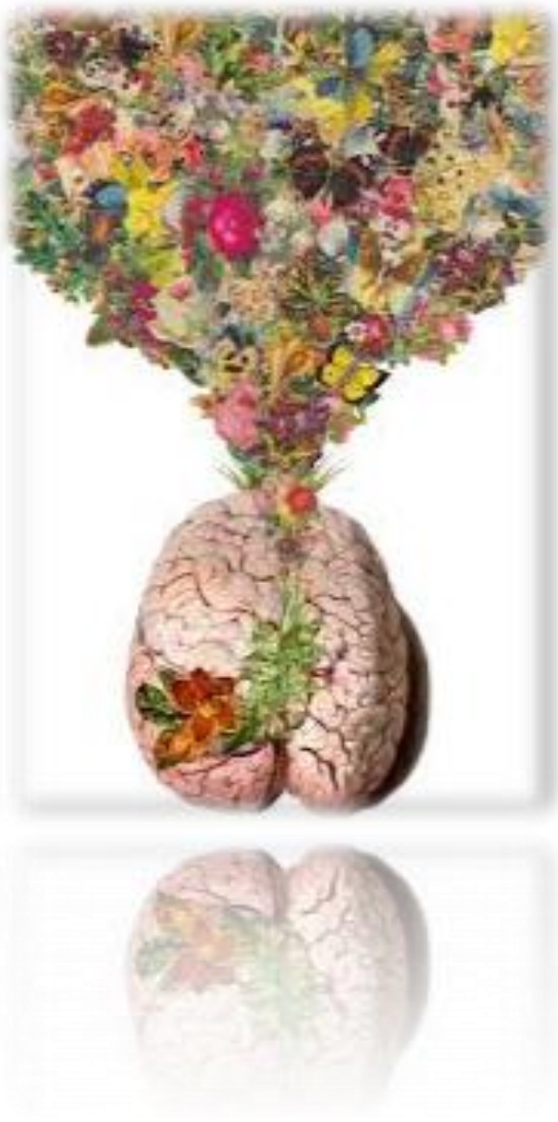




Conclusion

« Missing link »?





Modulateur global?

MERCI

A ceux qui ont rendu possible ce projet

NIST NeuroImaging & Surgical Technologies Lab

McGill

INCR INSTITUT DES NEUROSCIENCES CLINIQUES DE RENNES

UNIVERSITÉ DE RENNES 1

EA 4712

Comportement et Noyaux Gris Centraux