

Inflammation et cerveau dans le trouble lié à l'usage d'alcool : influence du sevrage

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Nombreux travaux soutiennent un rôle majeur de l'inflammation dans le TUAL

Etudes animales

Augmentation inflammation périphérique et activation microglie quand animal exposé à l'alcool

Induction inflammation induit consommation

Plus d'interrogations chez l'humain

Inflammation dans le TUAL :

Différent des syndromes psychiatriques autoimmuns

Chronic, therapy-refractory severe mental disorders with probable immune-mediated etiology, operationalized using Pollak criteria plus NEPCAP

5 to 9 % of psychosis, OCD, MDD, Catatonia, dissociative disorders

Attended by neuronal markers of encephalopathy (MRI/EEG/CSF)

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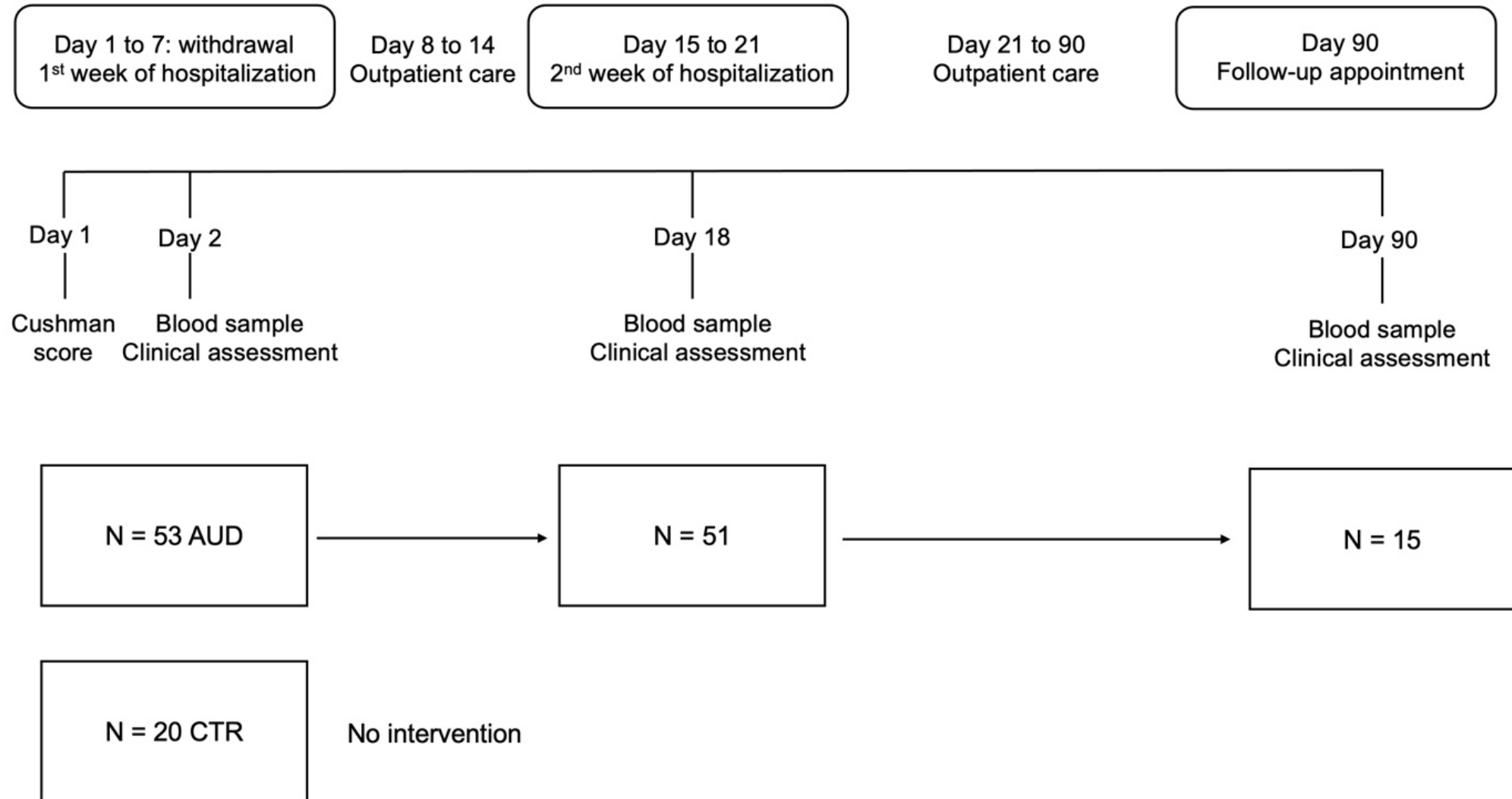
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Augmentation de la perméabilité intestinale

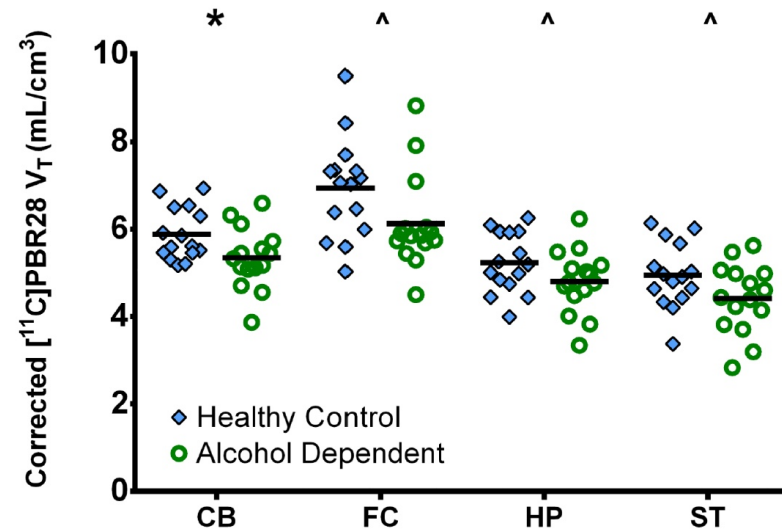
Lié au comportement de maladie

Liens inflammation symptômes dans le TUAL



Preuves du développement d'une neuroinflammation dans le TUAL (humain) ?

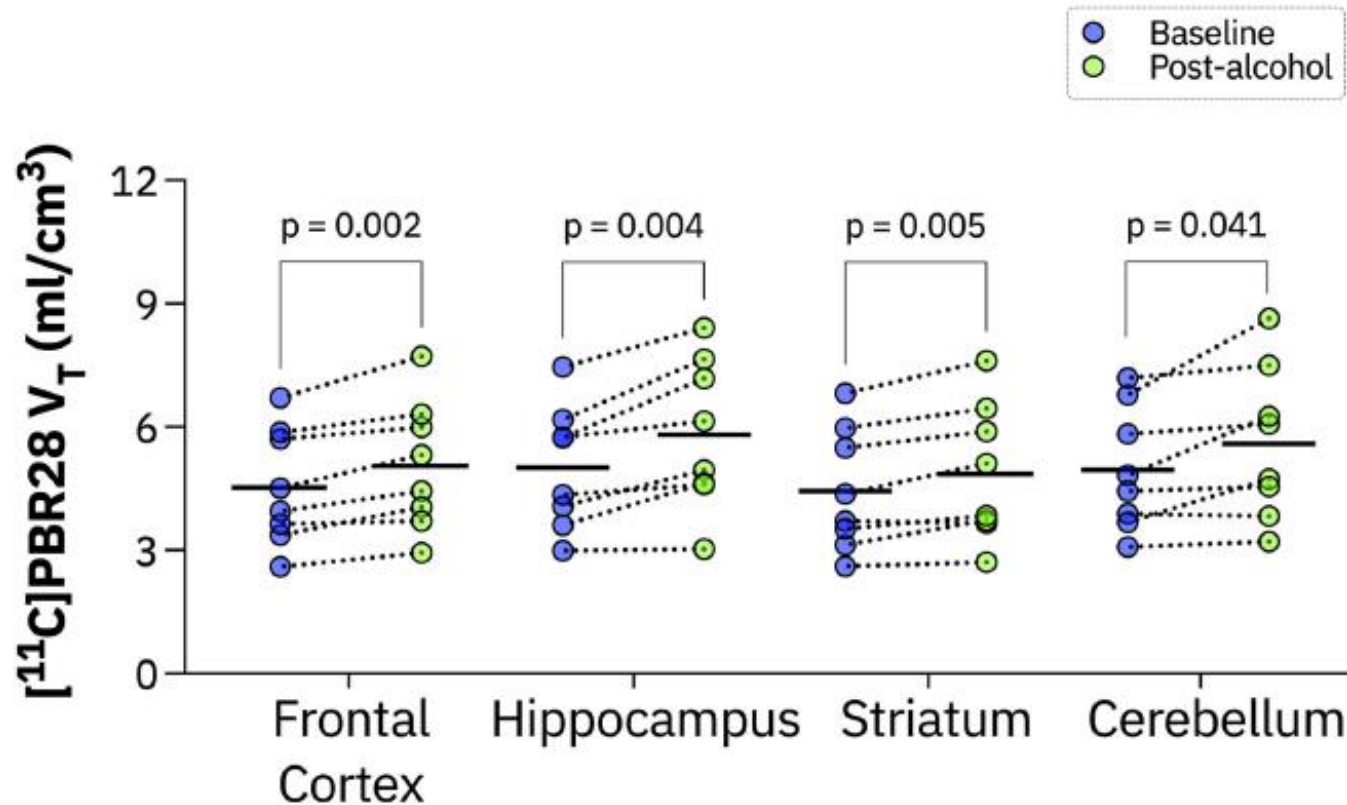
- Etudes PET scan (Tracers TSPO tracers chez des sujets détoxifiés) : **résultats contrintuitifs**



Hillmer et al. 2017

Les niveaux de microglie active est plus bas chez les sujets alcoolo-dépendants que chez les contrôles.

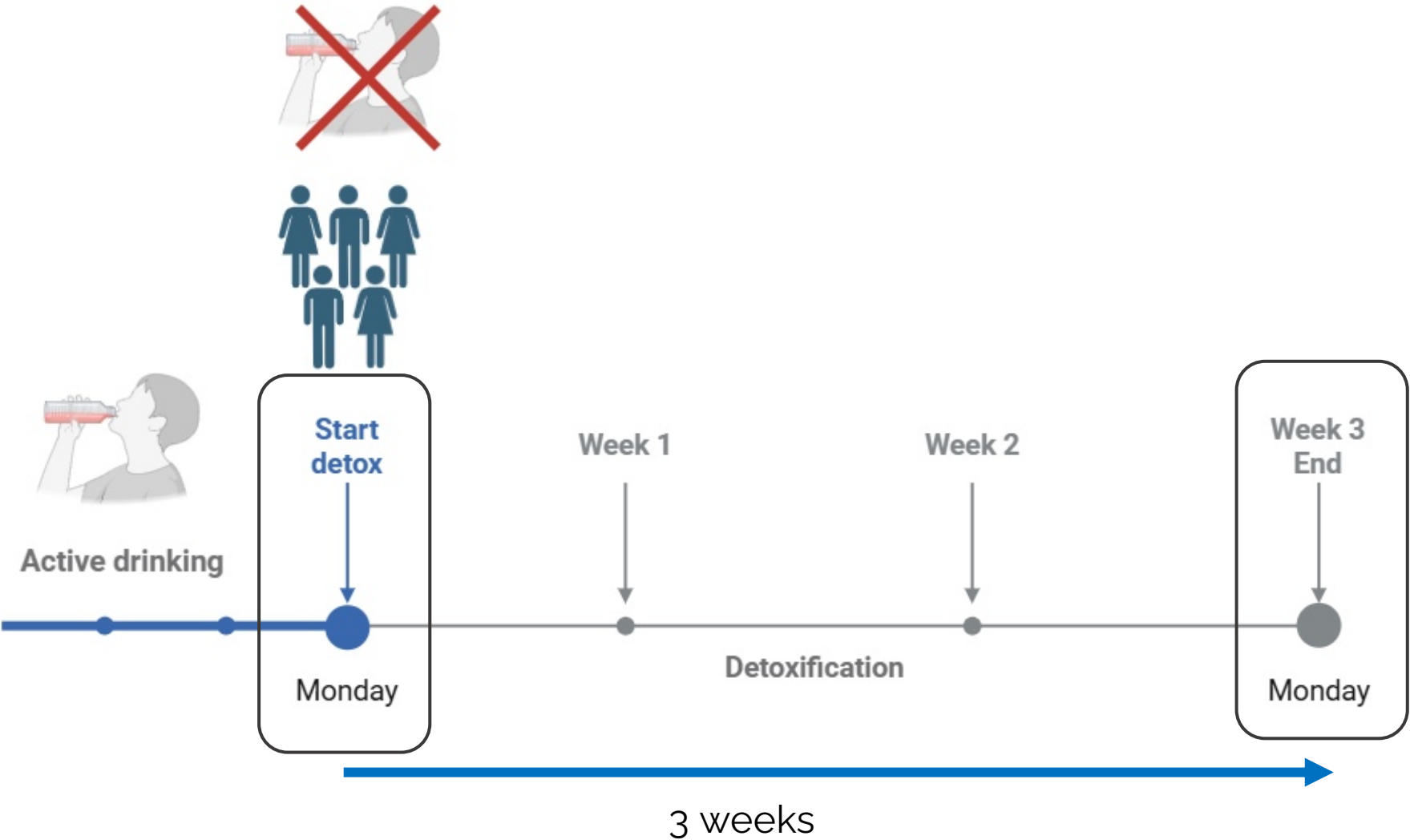
Exposition aigue à l'alcool → marquage accru par le TSPO



Raval et al. 2023

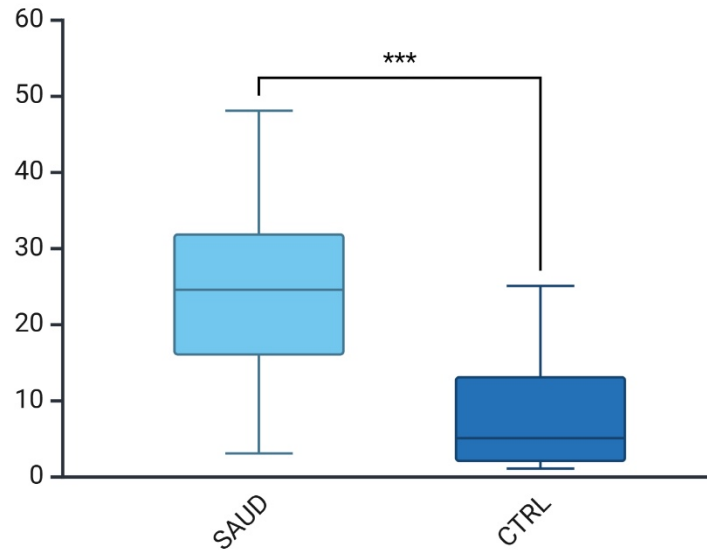
TSPO levels, increased in all regions after the laboratory alcohol challenge.

→ Quels modifications de l'inflammation systemique, du volume cerebral et du comportements pendant le sevrage?



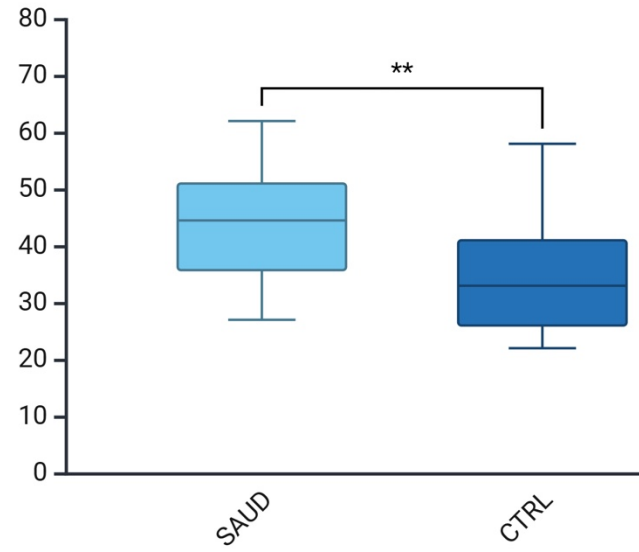
Symptômes à l'admission

Depressive symptoms



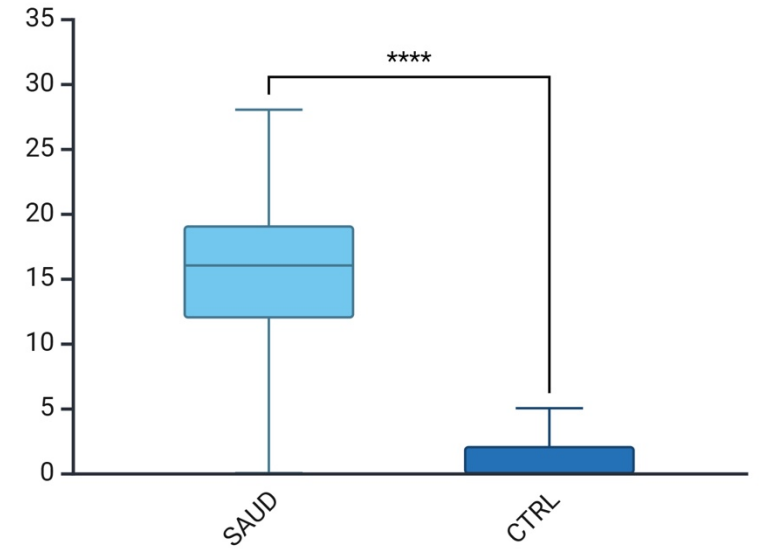
◆ Moderate

Anxiety symptoms



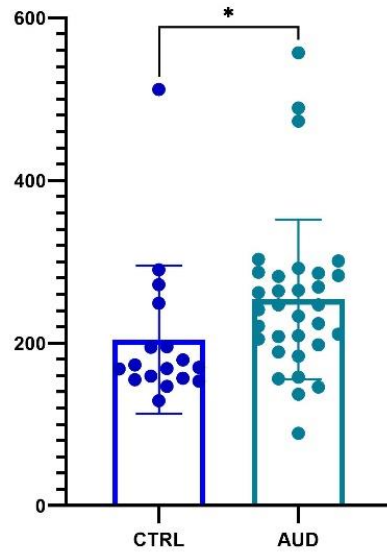
◆ Moderate to high

Craving

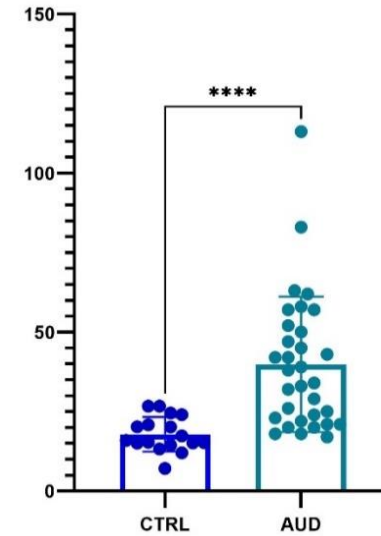


◆ High

Inflammation à l'admission

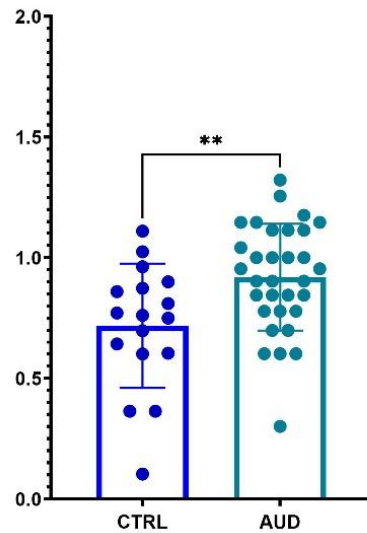


Inflammation
périphérique de bas
grade

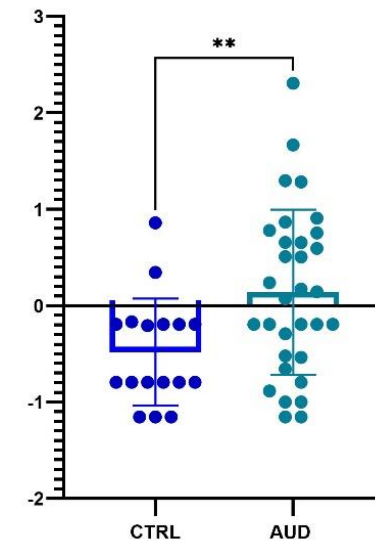


Monocyte chemoattractant protein 1 (MCP-1)/CCL2

Macrophage inflammatory protein 1 beta (MIP-1β)/CCL4



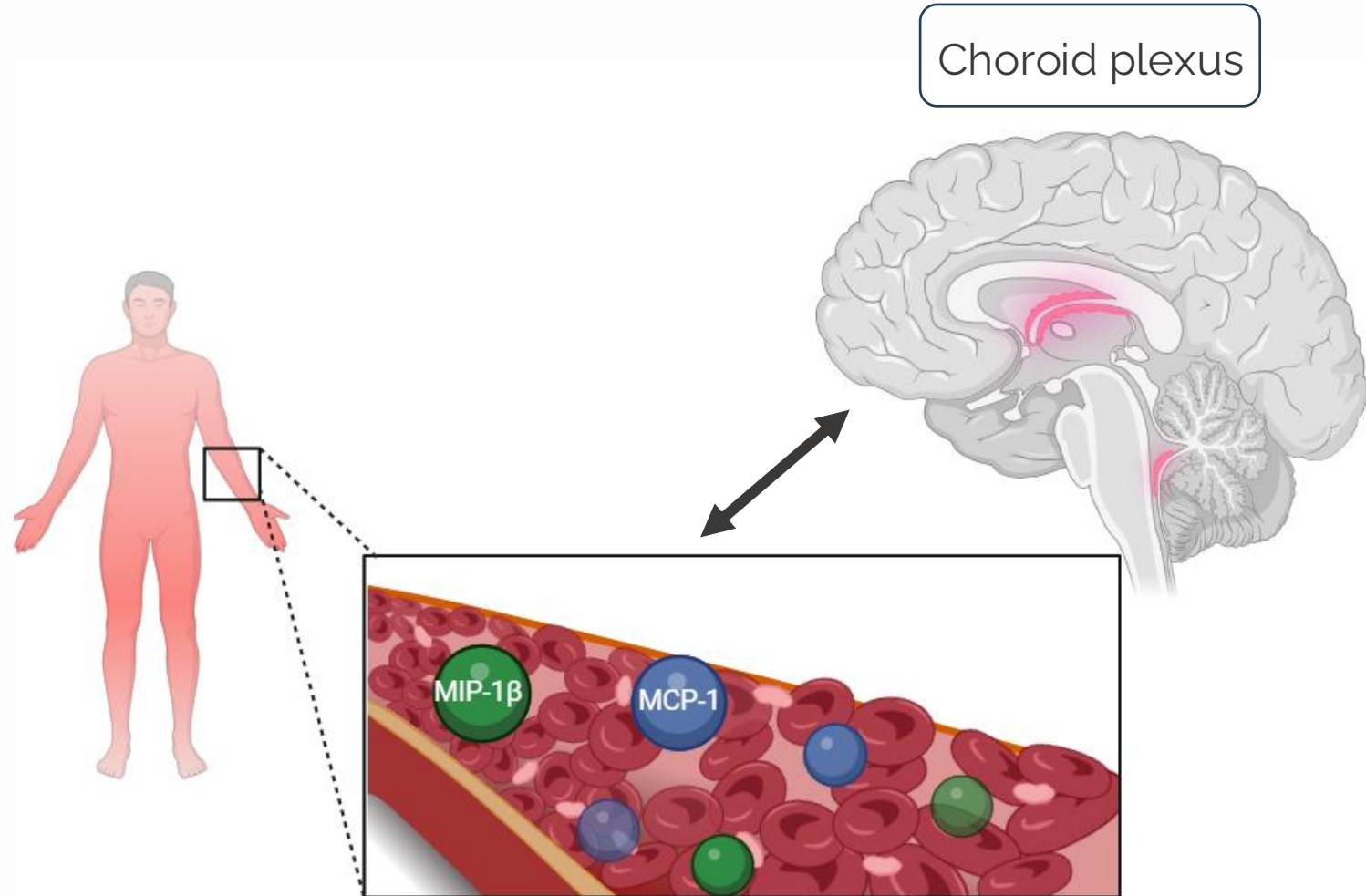
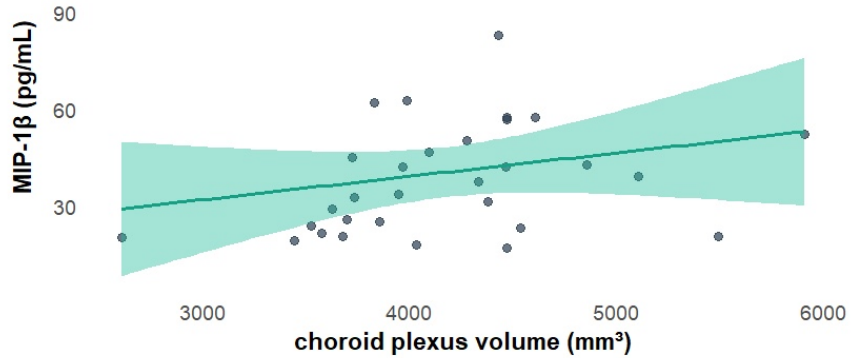
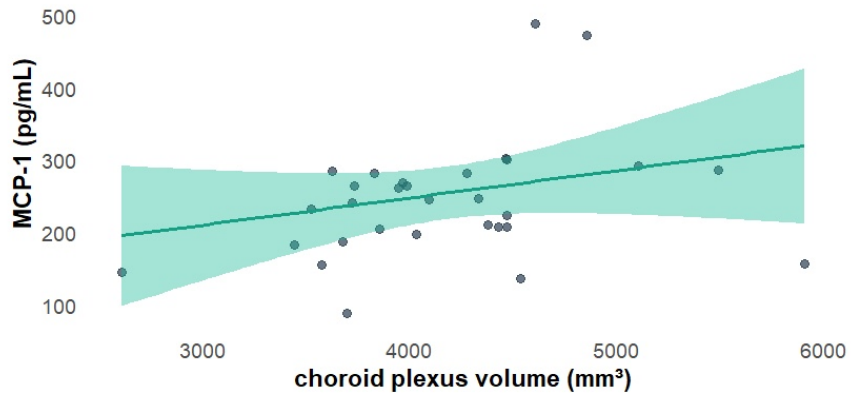
Tumor necrosis factor alpha (TNF-α)



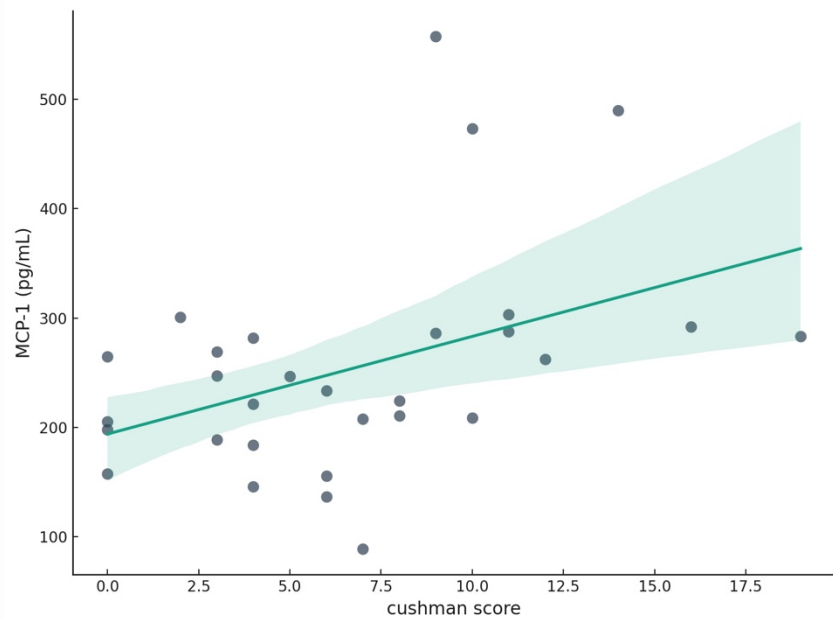
Interleukin-8 (IL-8)

Les niveaux de MCP-1 et de MIP-1 β corréle avec le volume des plexus choroides

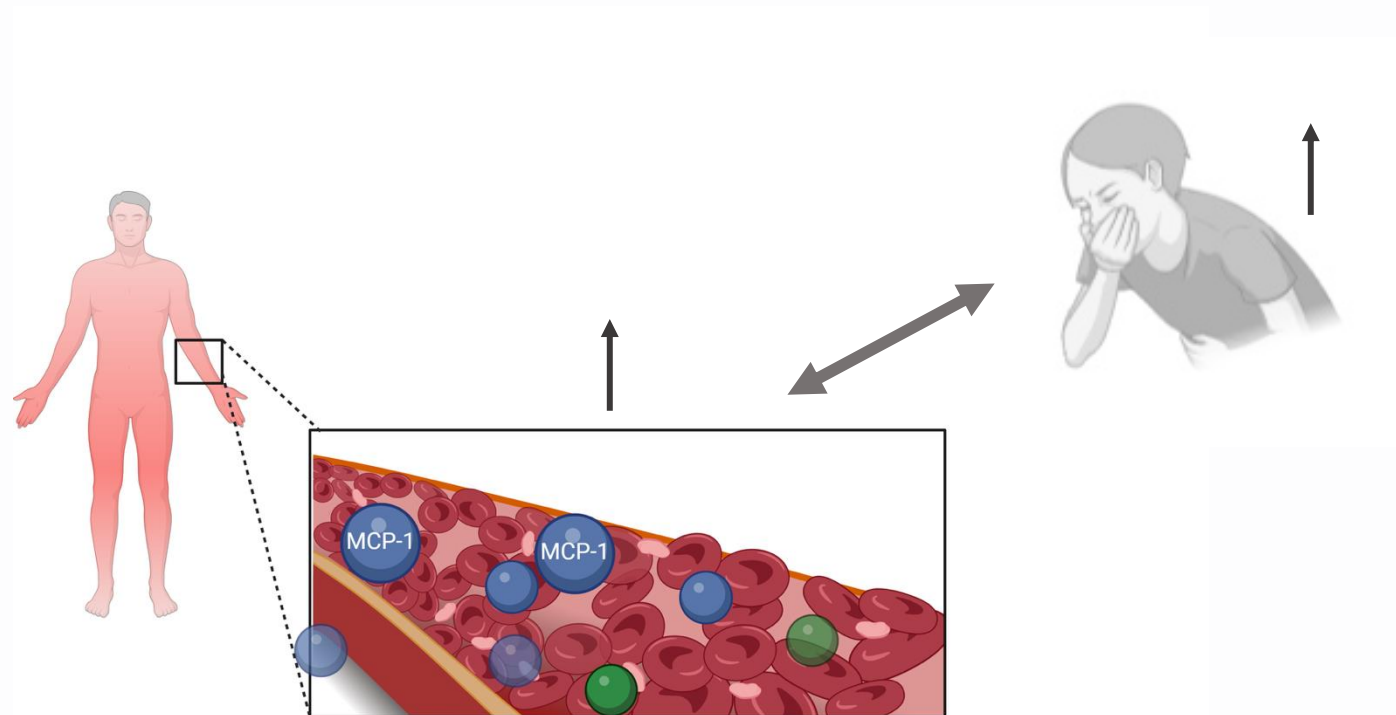
MCP-1 : $\rho=0.364$, $p=.040$
MIP-1 β : $\rho=0.378$, $p=.033$



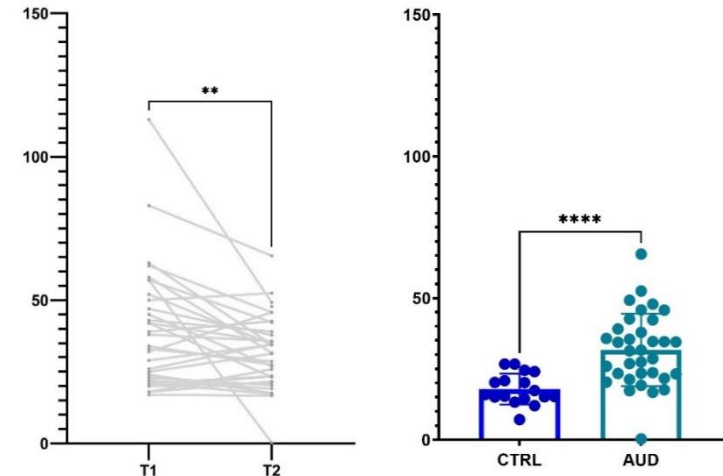
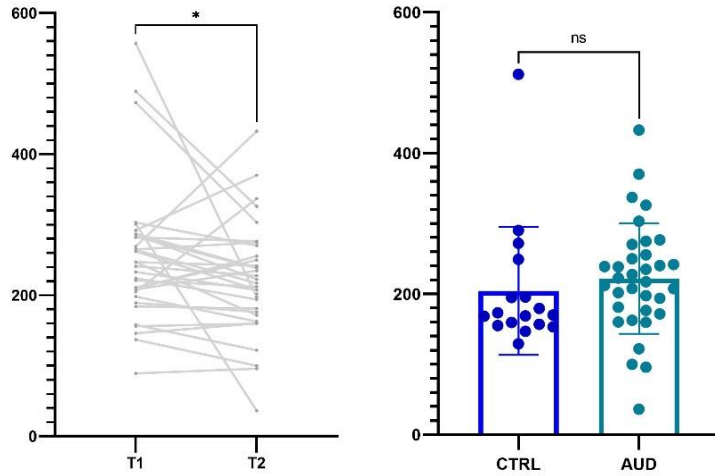
Le MCP-1 corréle avec la sévérité du sevrage



$\rho = .469$, $p = .009$, FDR-corrected $p = .036$

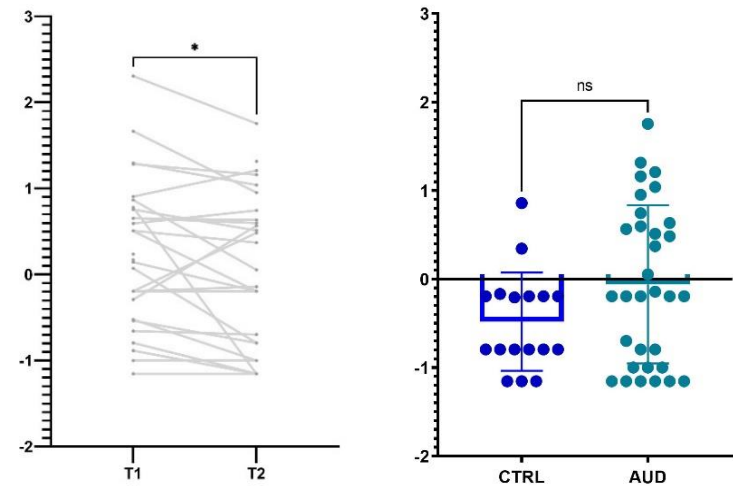
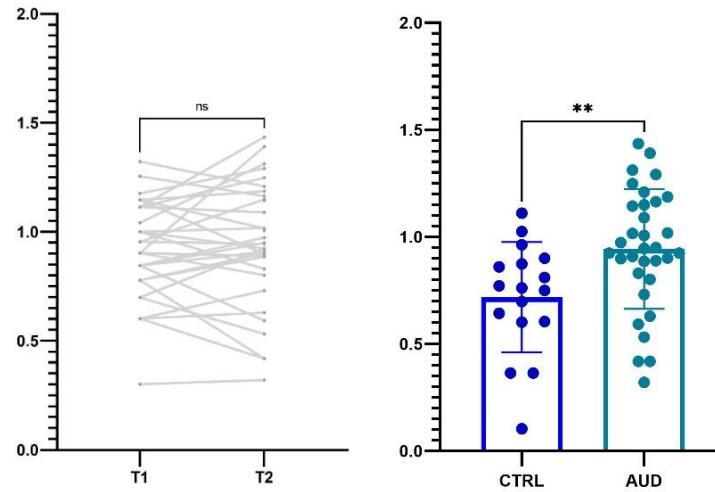


Inflammation post-détoxication



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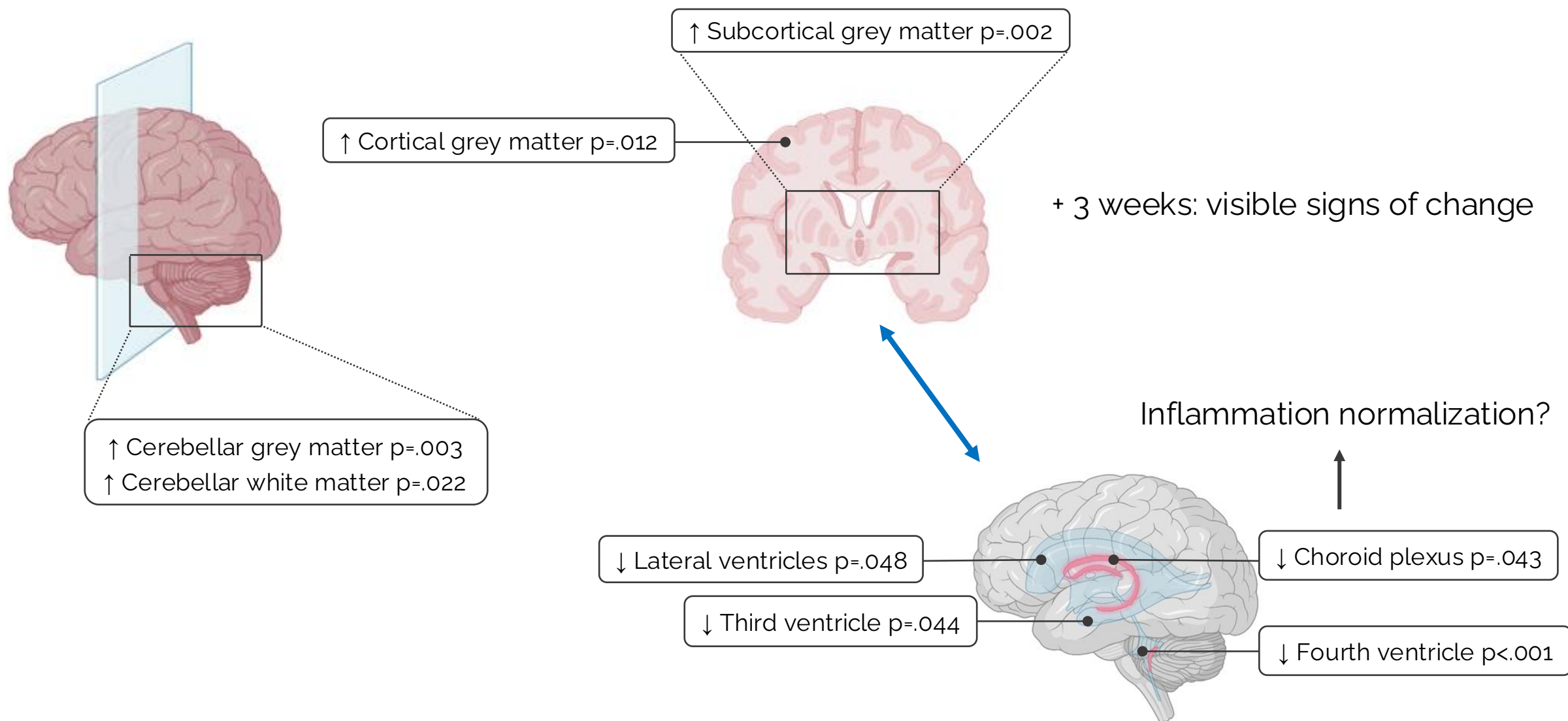
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Tumor necrosis alpha (TNF-α)

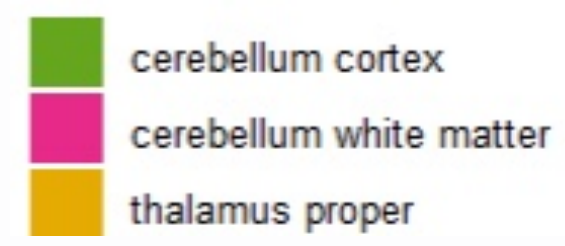
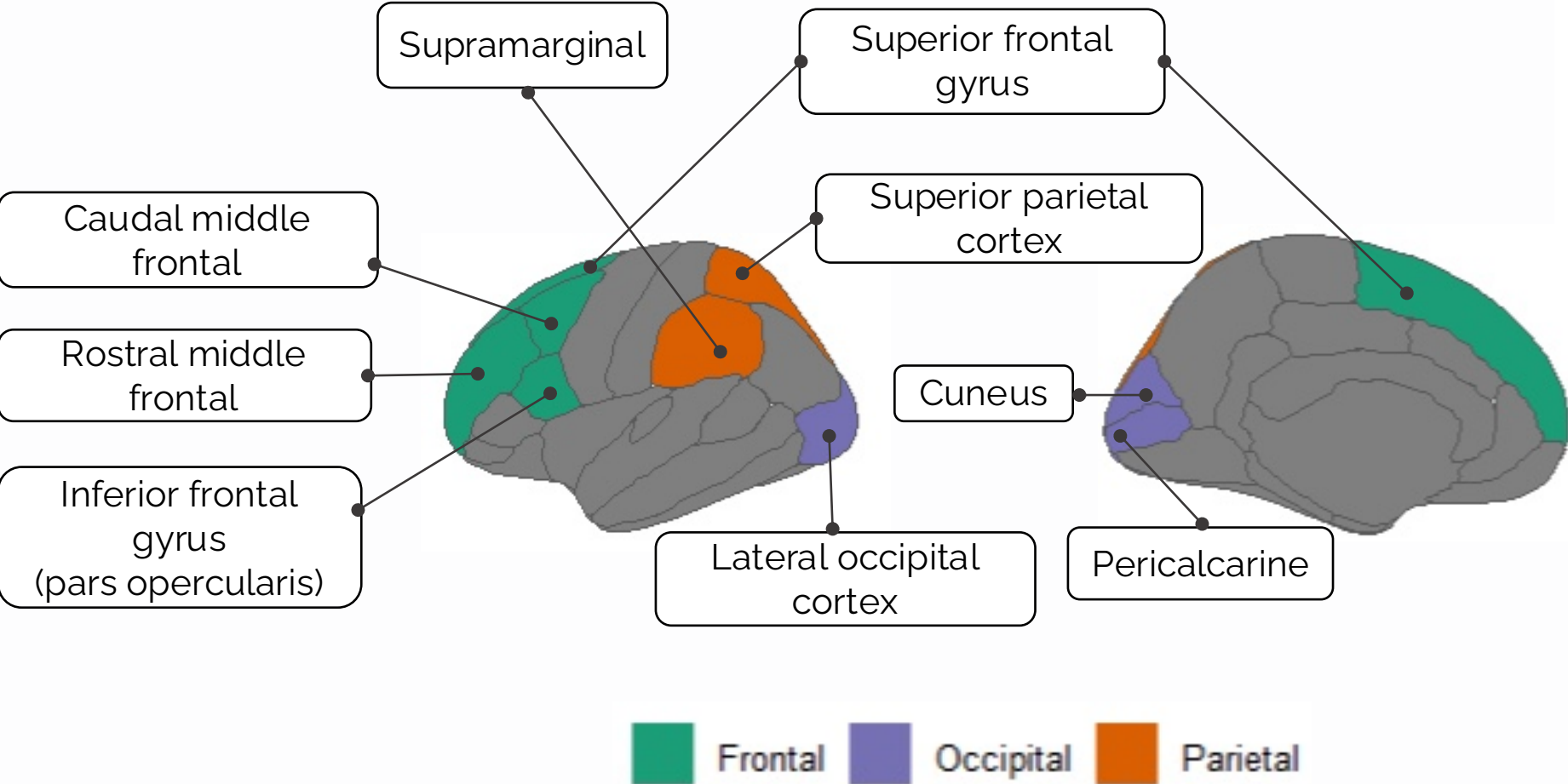
Interleukin-8 (IL-8)

Augmentation du volume cérébral → matière grise

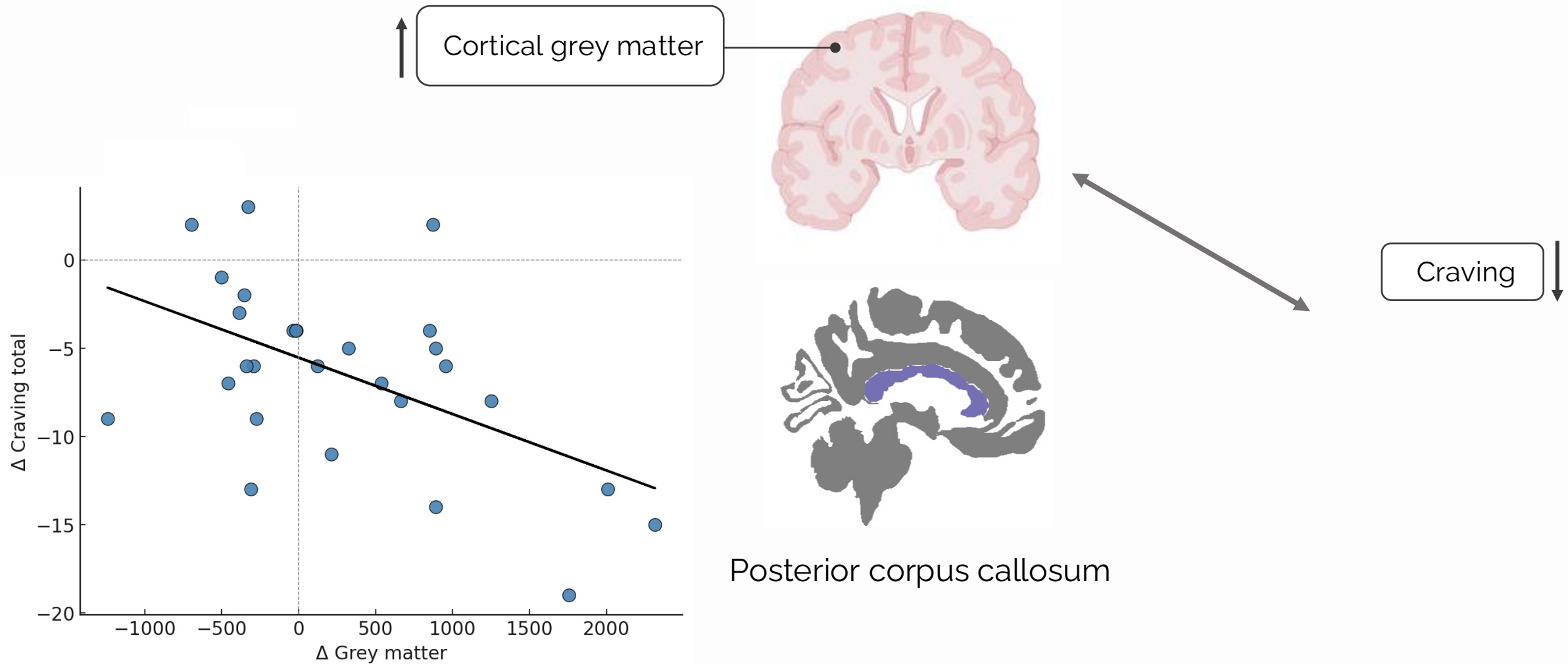


Plus les ventricules diminuent de volume → plus grande est l'augmentation des volumes sous-corticaux/cérébelleux

Regions où il existe une augmentation significative du volume (T1 → T2)

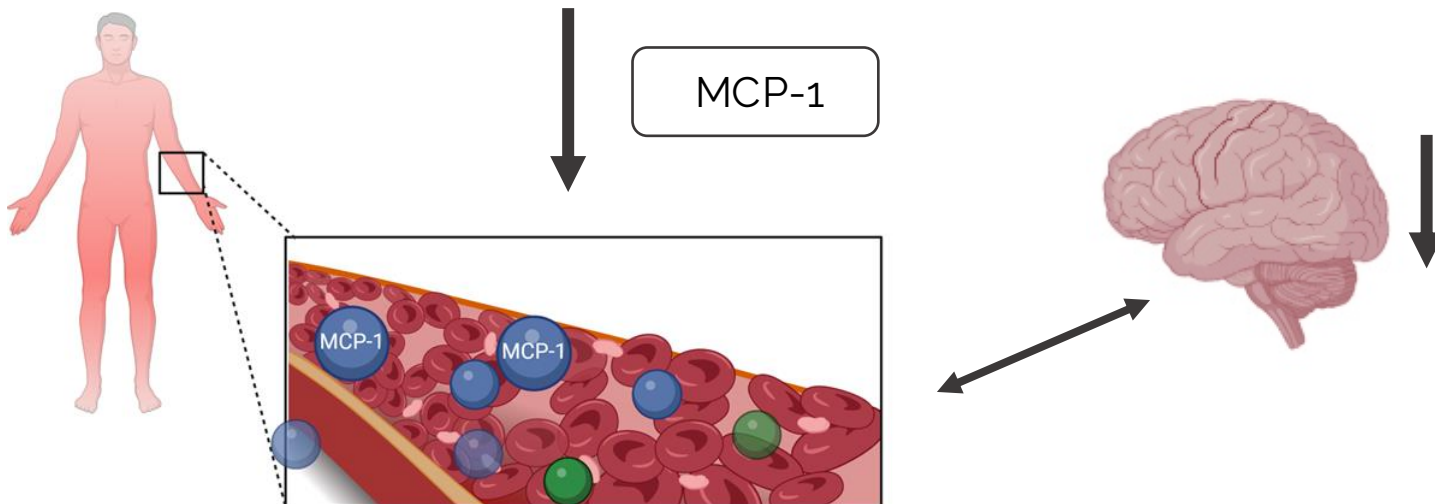
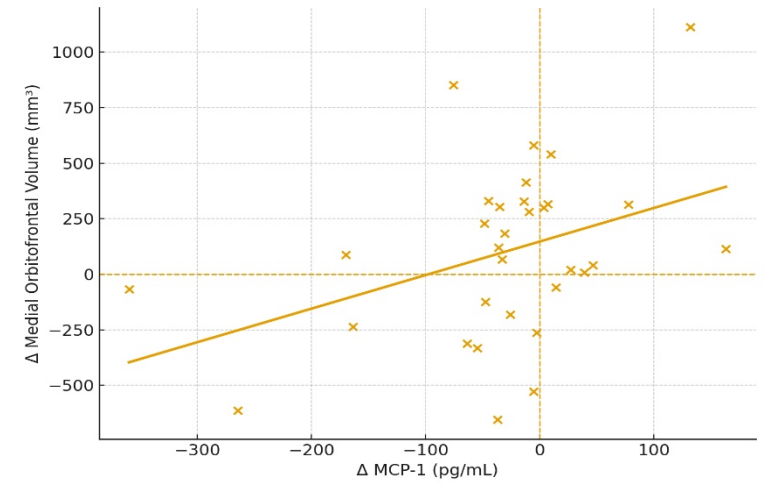


Corrélation négative entre les changements de volume de matière grise et du craving

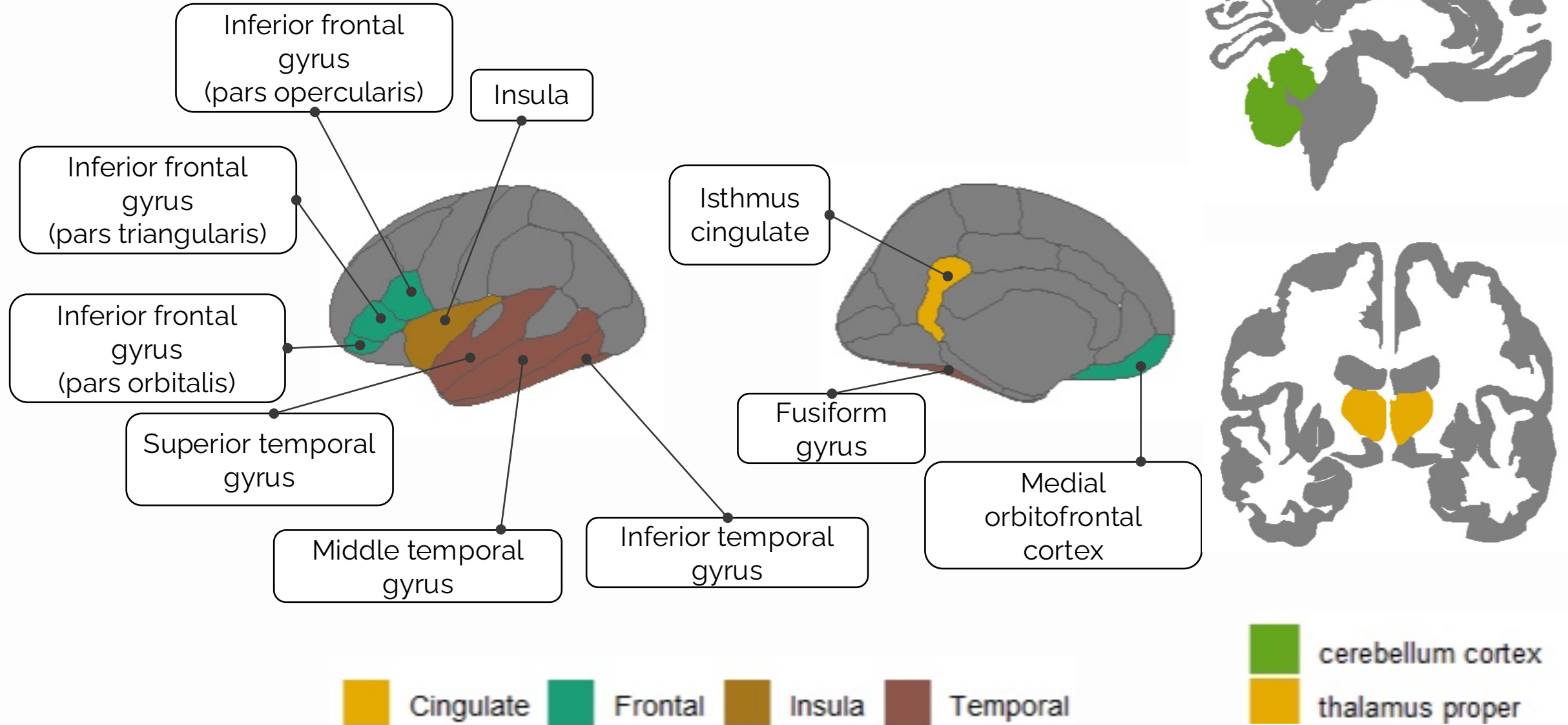


Régions cérébrales qui ne montrent pas d'augmentation significative des volumes mais une corrélation positive avec la baisse du MCP-1

Lower inflammation linked to volume loss?
Inflammation resolution ?



Régions qui corrent avec la baisse du MCP-1



Immune activation

Damage → normalization

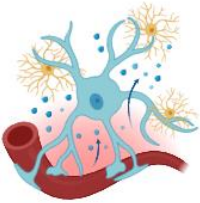
Glial activation



Swollen brain



BBB changes



Oedema



Inflammation



↓ Swelling
↓ Volume



Start detox

Week 1

Week 2

Week 3 End

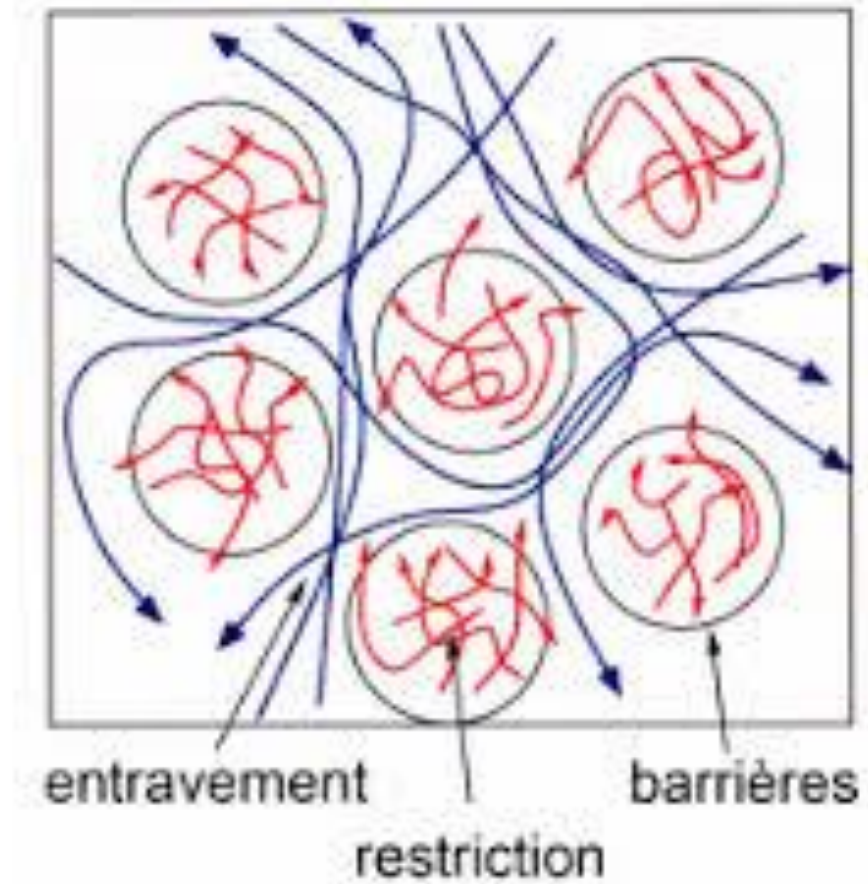


Monday

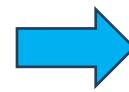
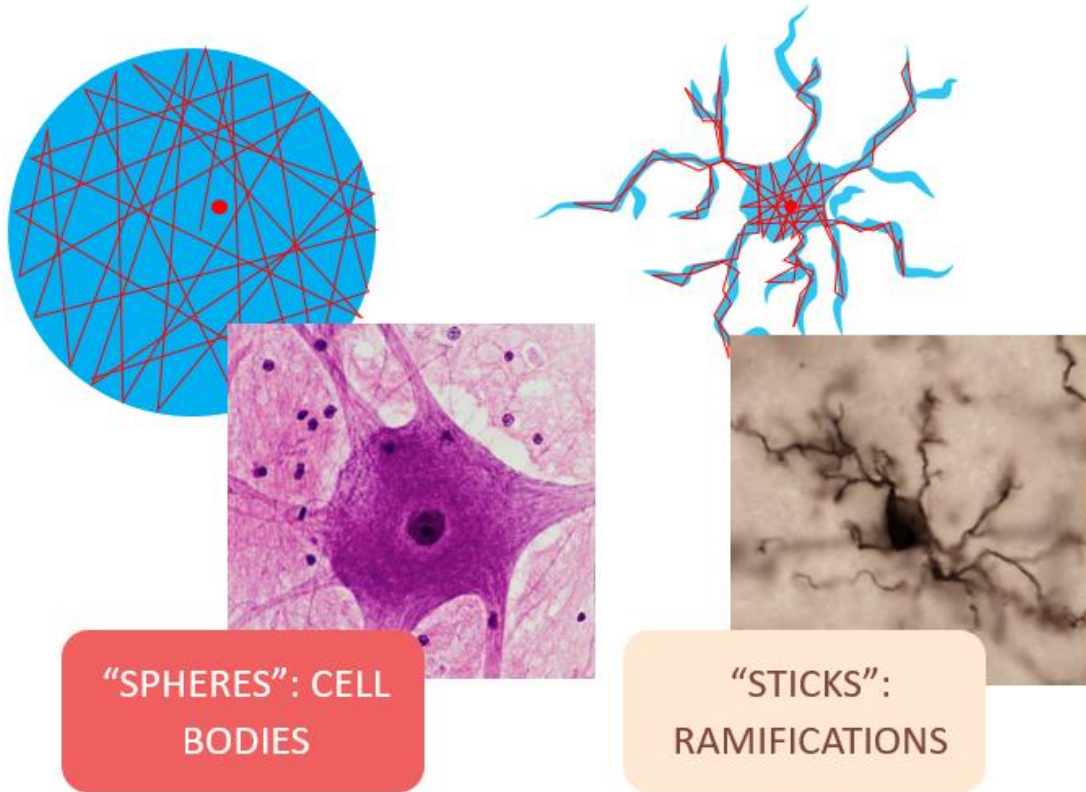
Detoxification

Monday

Essais mesures en imagerie de diffusion



Modeling microglie par la dw-MRI



We used the **CHARMED** model with a diffusion sequence derived from Garcia-Hernandez et al., 2022

- **CHARMED FR**: fraction of water movement restricted by microglial ramifications
- **CHARMED disp**: dispersion of directions of restricted water movements



Sophie Leclercq



Laurence Dricot



Melissa Salavrakos



Arnaud Leroy



Camille Amadiou



Ron Kupers



Géraldine Petit



Jérôme
Delforge

Merci