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Article

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Suppression of binge alcohol drinking by an inhibitory neuronal ensemble in the mouse medial orbitofrontal cortex

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Plan

CONTEXTE

RÉSULTATS

DISCUSSIONS

ANALYSE
CRITIQUE



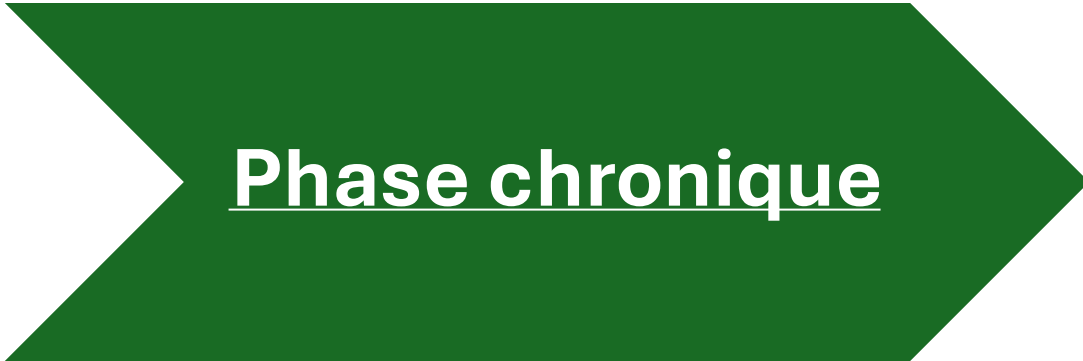
CONTEXTE

Cas clinique



Phase aiguë

- **Confusion**
- **Ataxie**
- **Ophtalmoplégie**



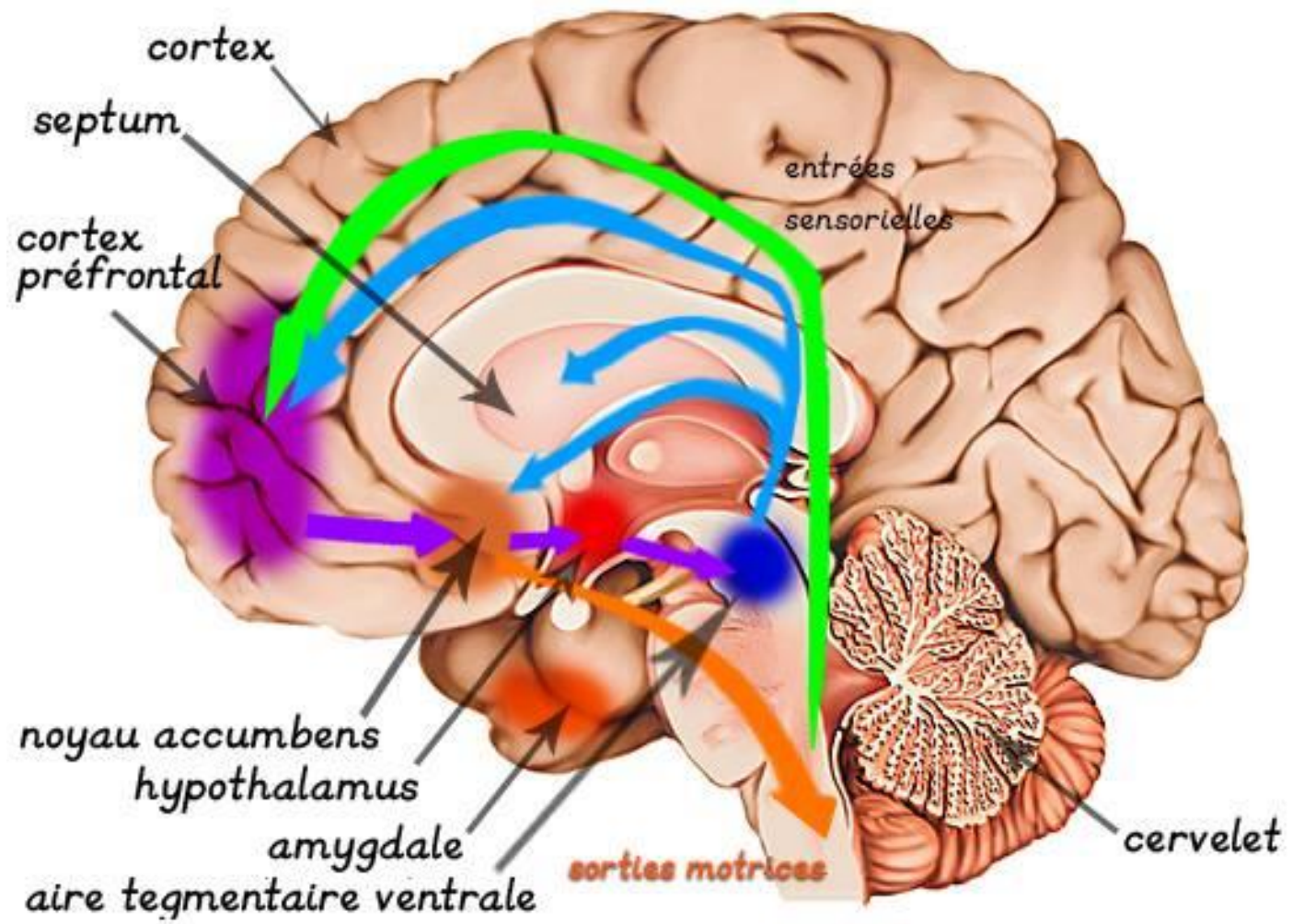
Phase chronique

- **Amnésie antérograde sévère**
- **Confabulation**
- **Irréversible**

Syndrome de Wernicke-Korsakoff



L'alcool



L'alcool



Droque la plus consommée
dans le monde (2,3 milliards)



3 millions de morts chaque
année



Lié à plus de 200 maladies

☺ La boisson la plus consommée par les étudiants en médecine ☺ (sans compter le café et le RedBull)

Cortex préfrontal

- Prise de décision
- Fonctions exécutives
- Contrôle de soi et inhibition



Objectif de l'étude

Identifier les neurones qui permettent de réduire la consommation d'alcool et caractériser leur fonctionnement



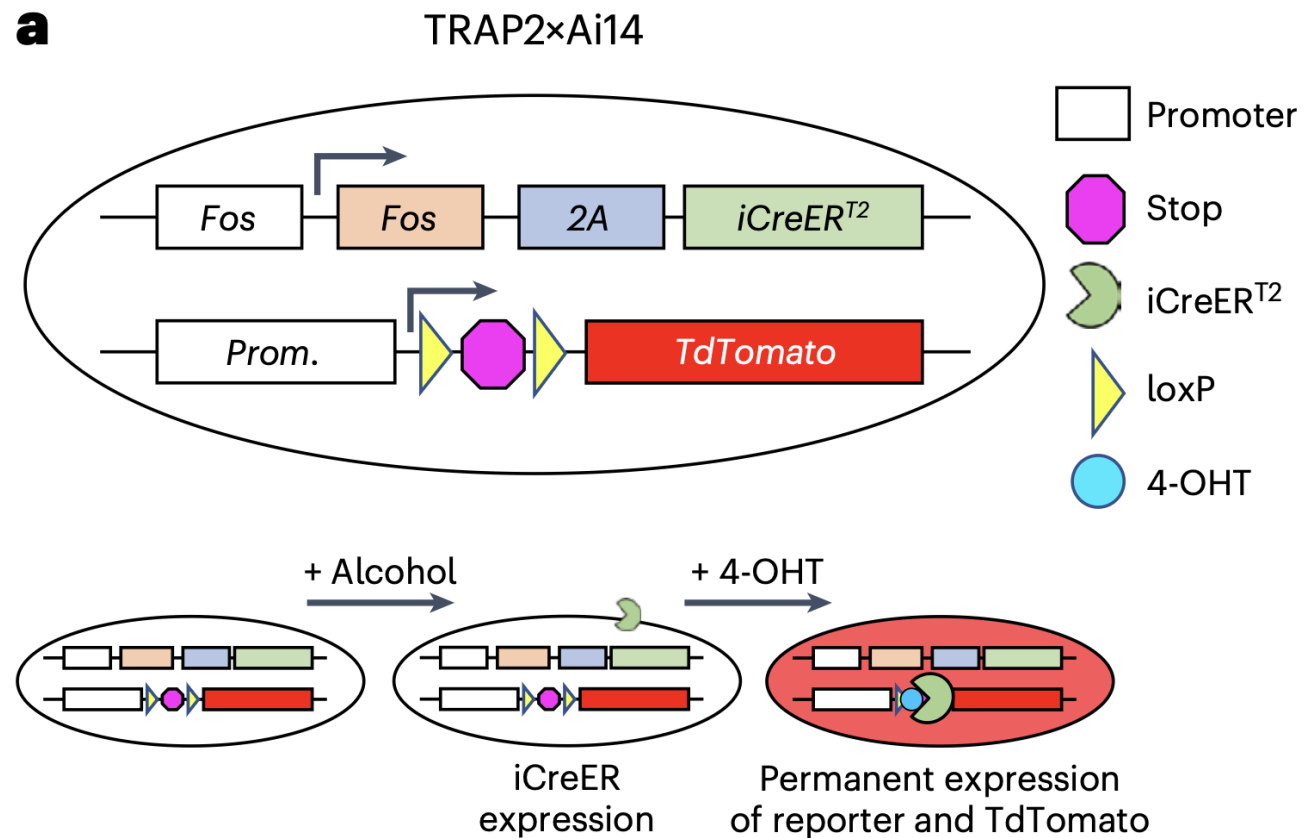
RESULTATS

A microscopic image of neurons, likely from a mouse brain, showing a dense network of axons and dendrites. A single neuron in the center is highlighted with a bright blue, textured overlay, possibly indicating calcium imaging or a specific marker. The background is dark, and the overall image has a teal/cyan tint.

**Comment peut-on identifier les
neurones activés par l'alcool ?**

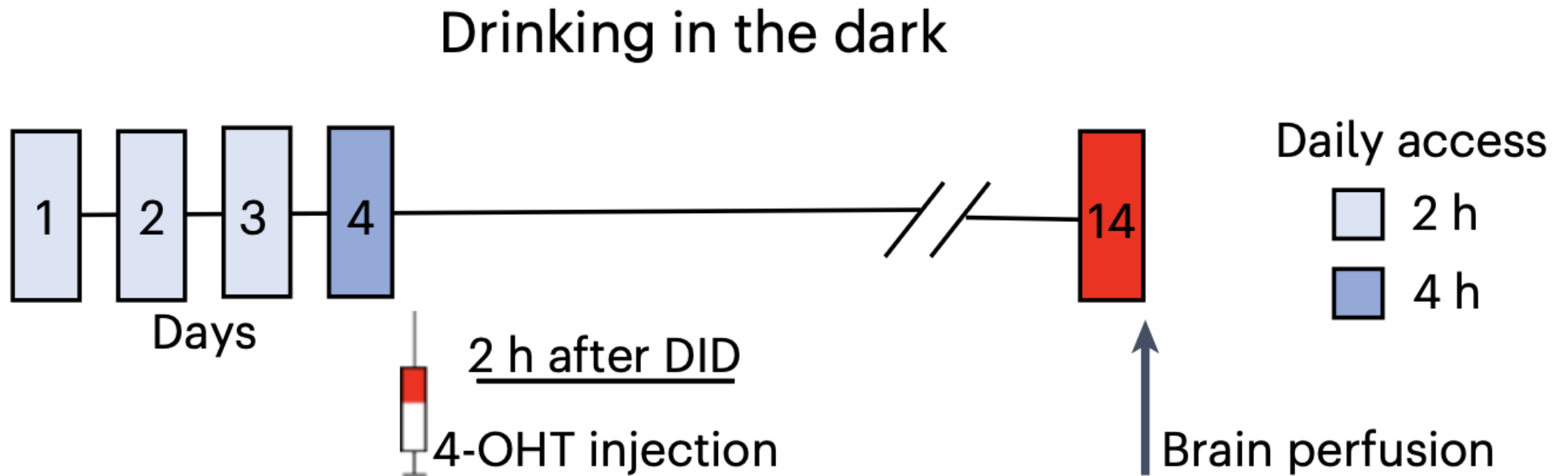
Souris transgéniques

*TRAP = Targeted Recombination
in Active Populations*



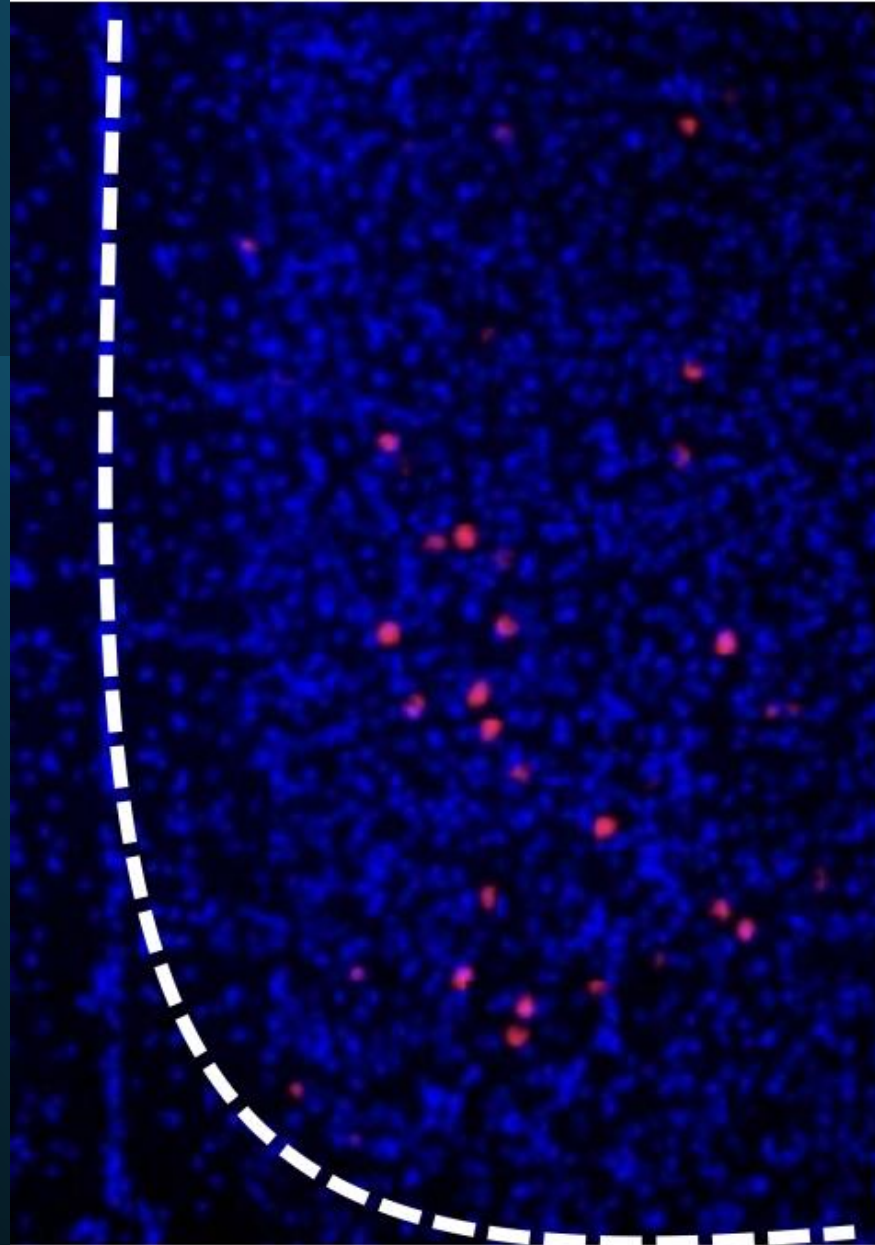
Chronologie pour le marquage des neurones

b

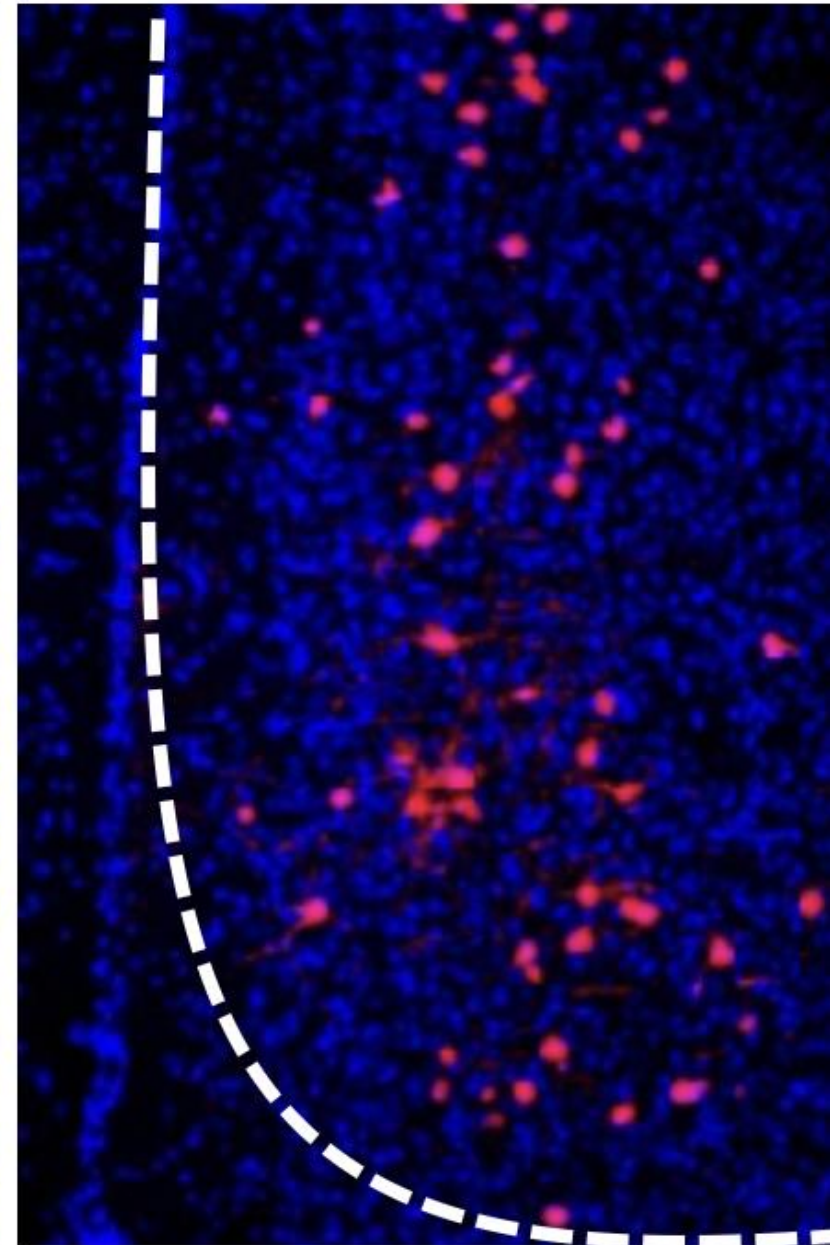


**Neurones
activés par
l'alcool**

Sacch



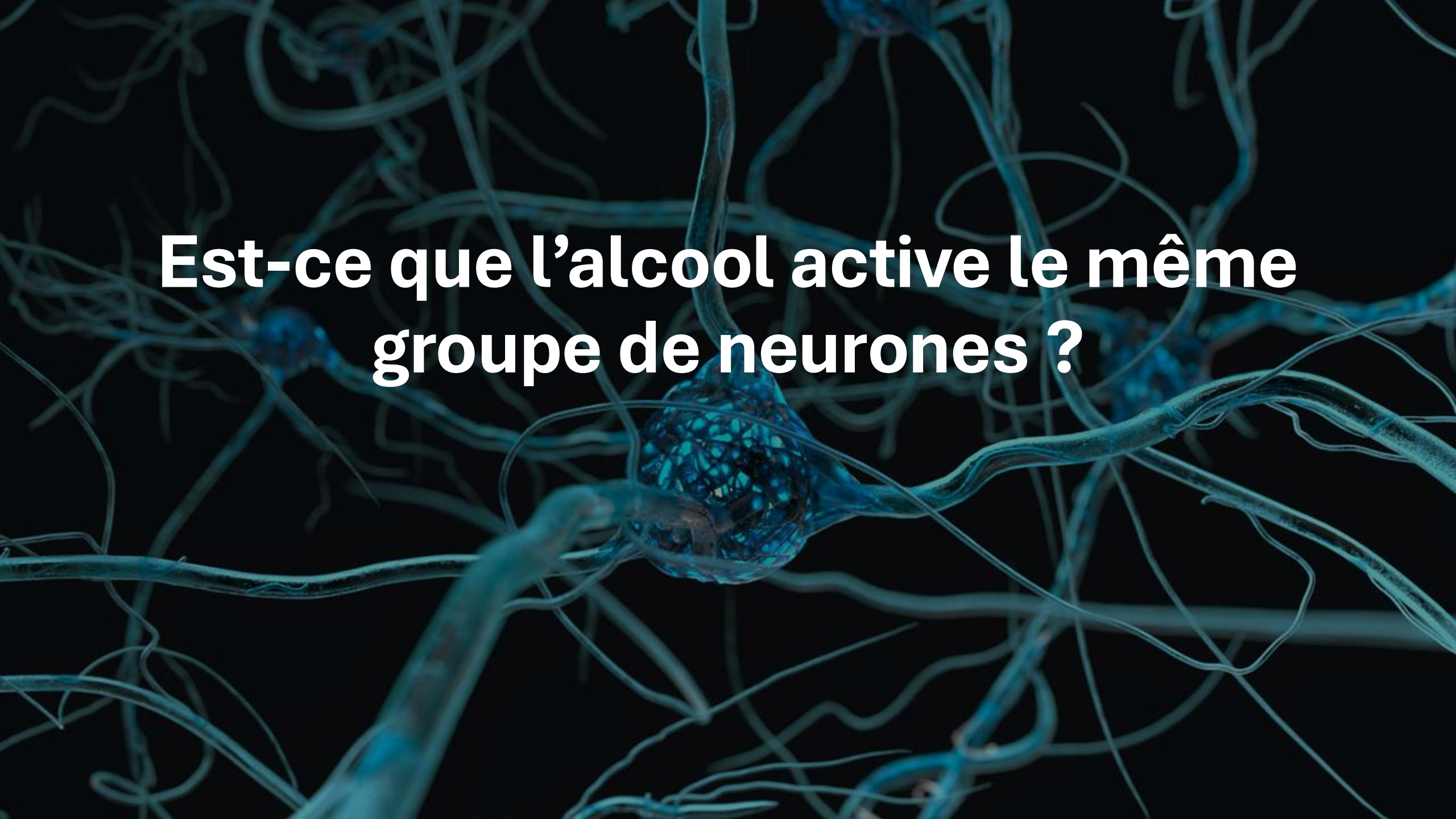
Alcohol



Résultat n°1 :

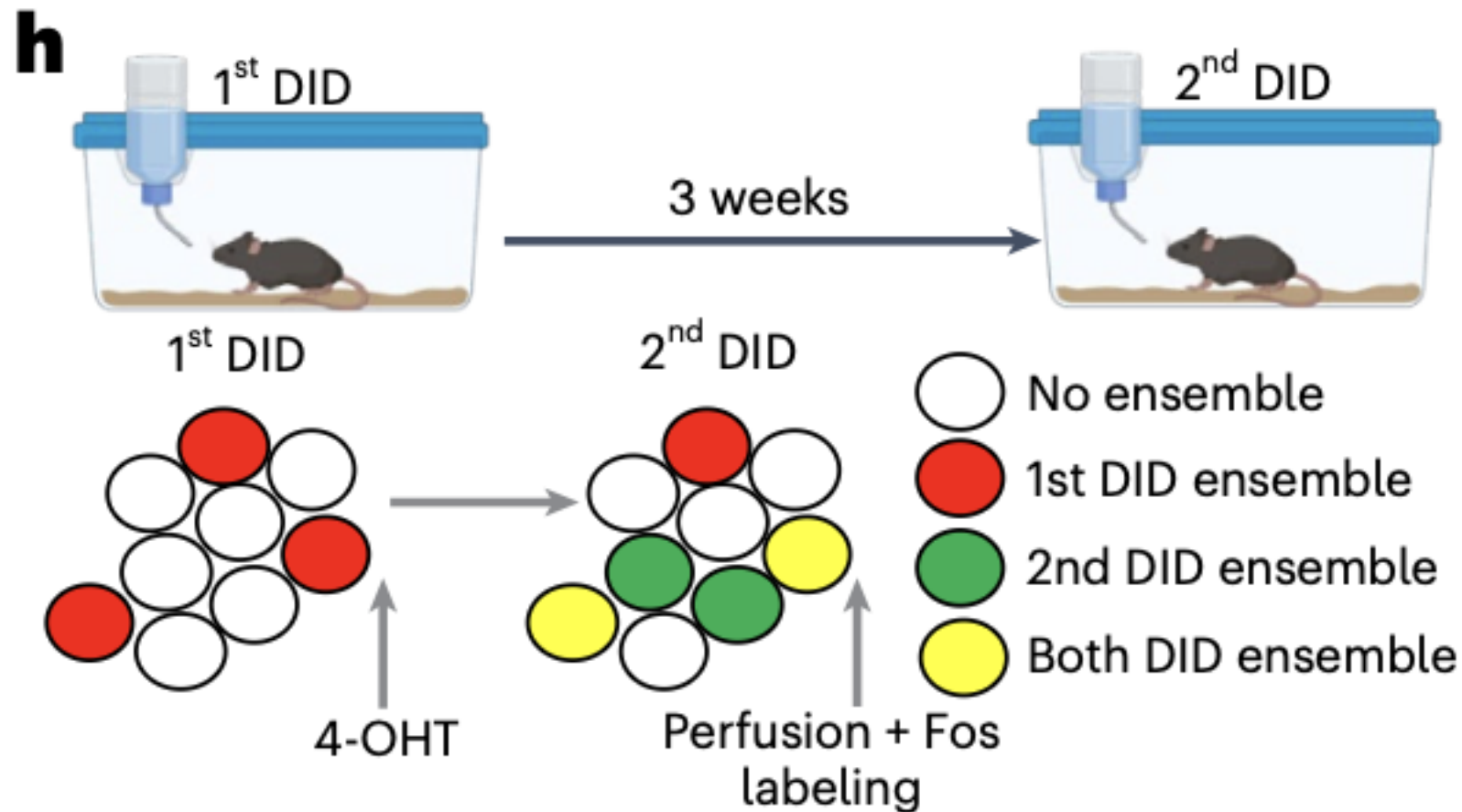
**Une population de neurones
s'active dans le mOFC après une
consommation d'alcool**



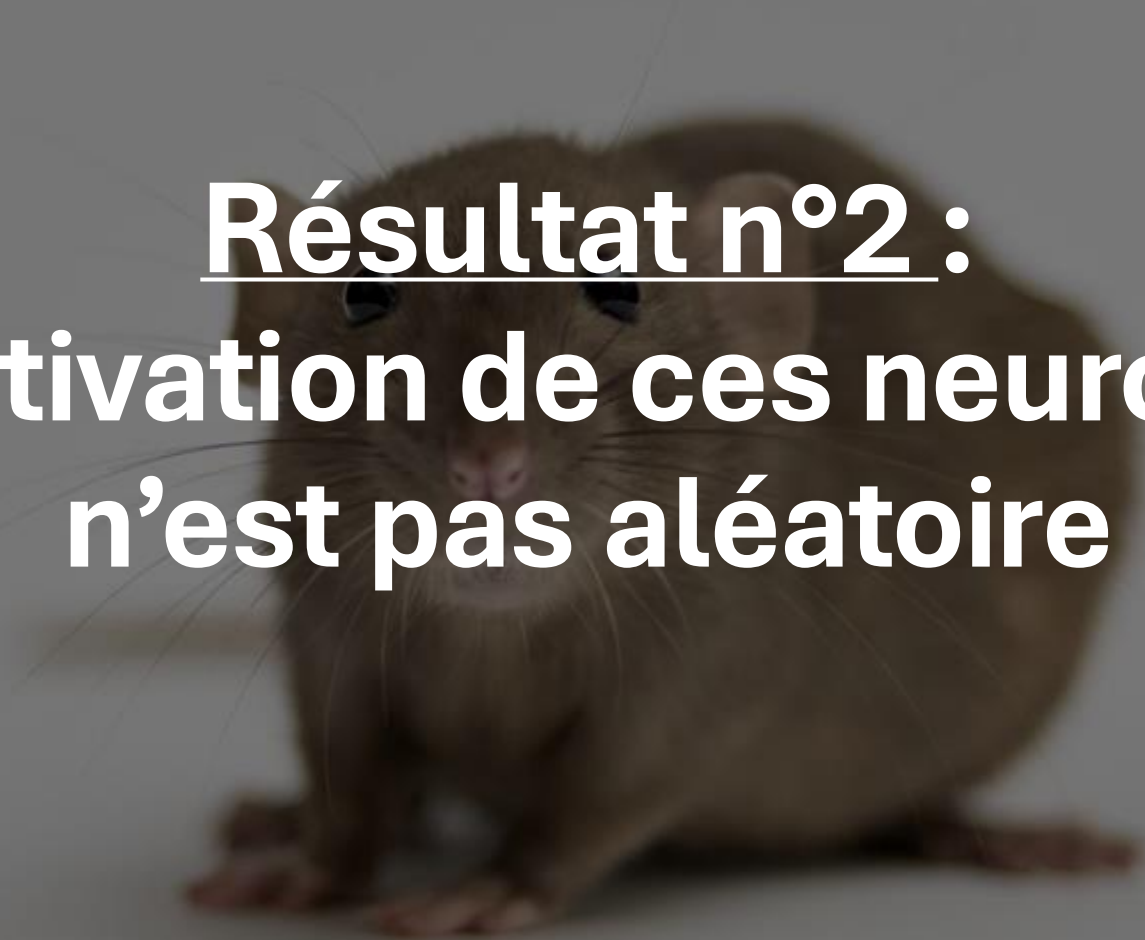
A microscopic image of neurons, showing a central cell body (soma) with a dense network of internal organelles, surrounded by a complex web of branching processes (dendrites and axons). The image has a cyan/blue color cast.

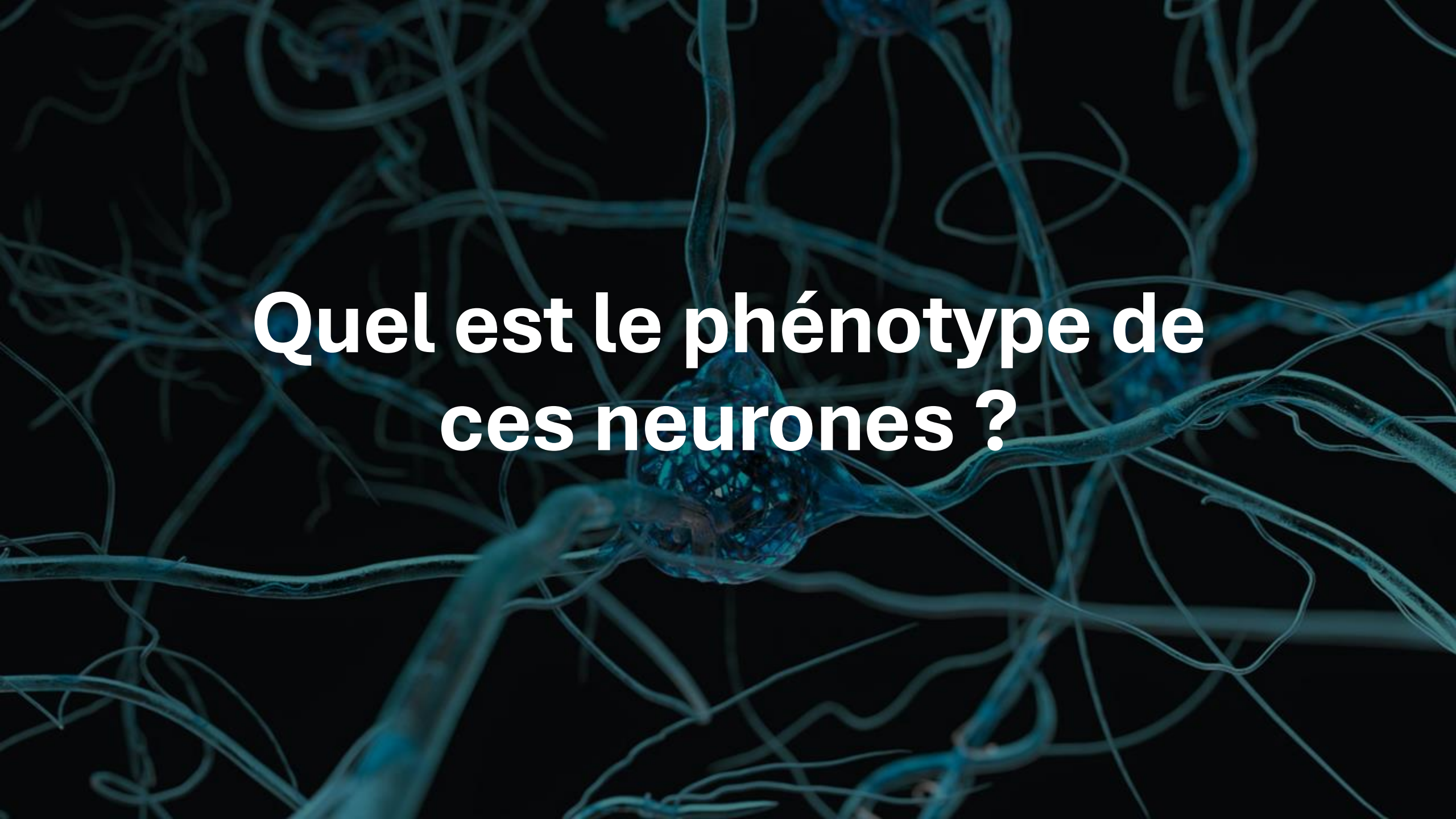
**Est-ce que l'alcool active le même
groupe de neurones ?**

Stratégie pour étudier la stabilité de l'ensemble neuronal



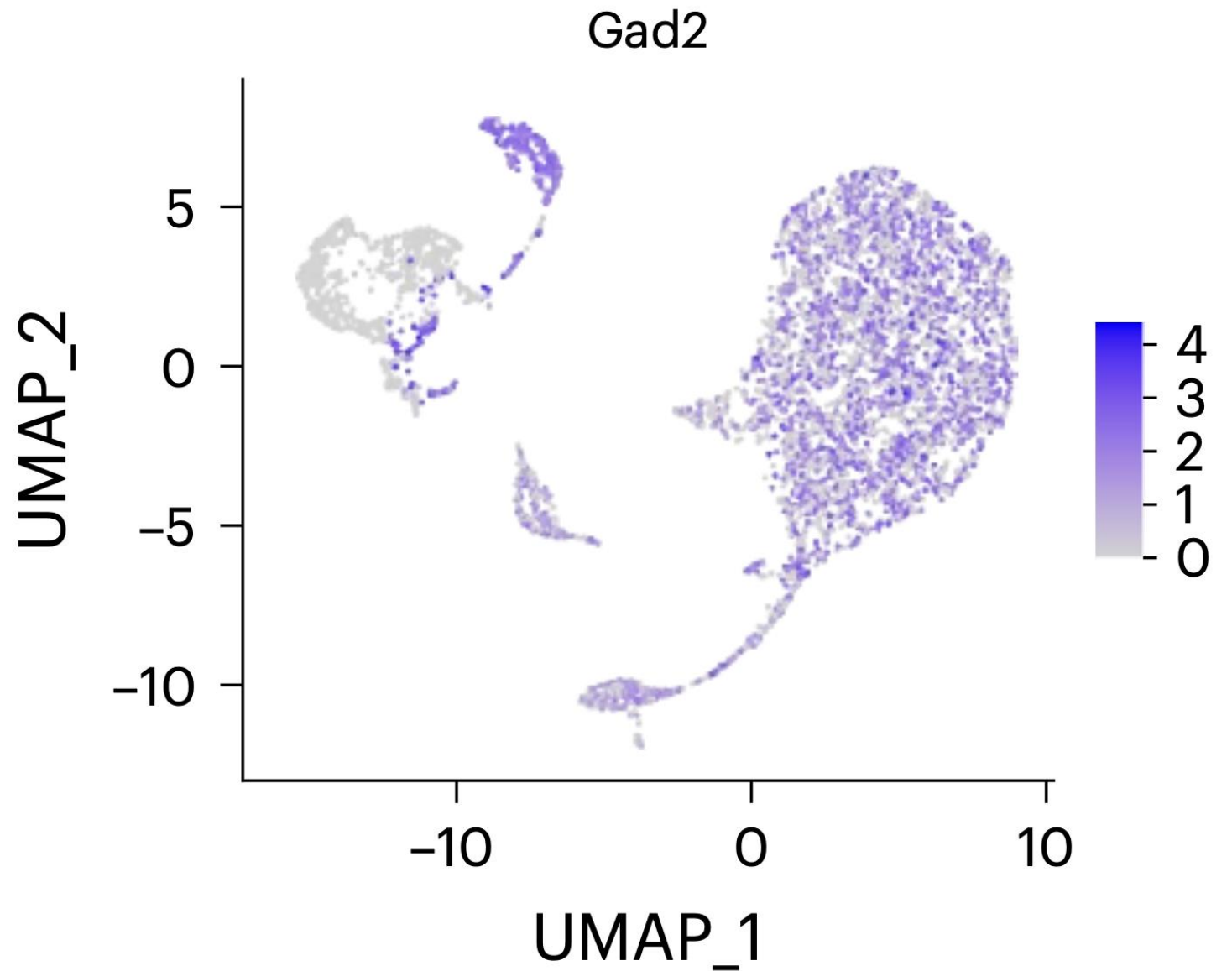
Résultat n°2 :
L'activation de ces neurones
n'est pas aléatoire



A microscopic image of neurons, showing a central cell body (soma) with a dense network of internal organelles, surrounded by a complex web of branching processes (dendrites and axons). The entire image is tinted with a cyan/blue color. The text is overlaid in the center in white.

**Quel est le phénotype de
ces neurones ?**

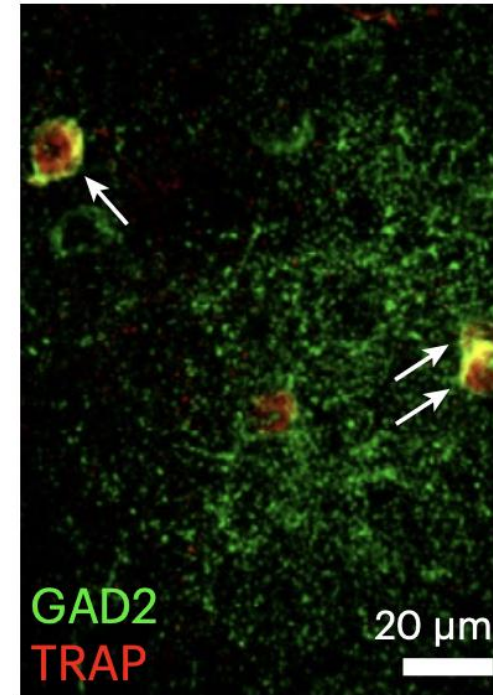
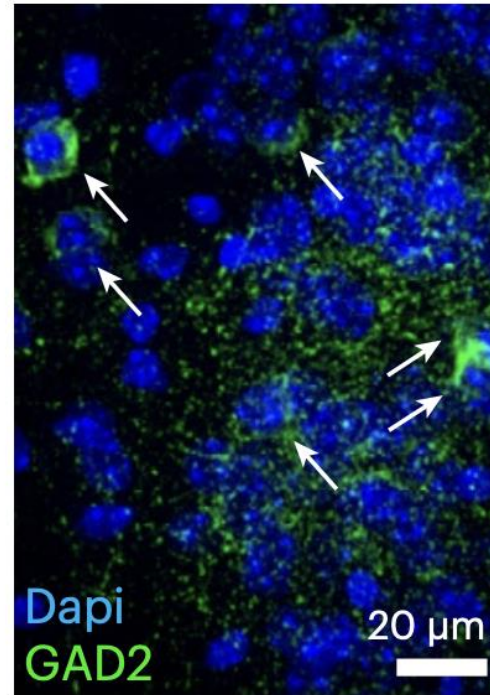
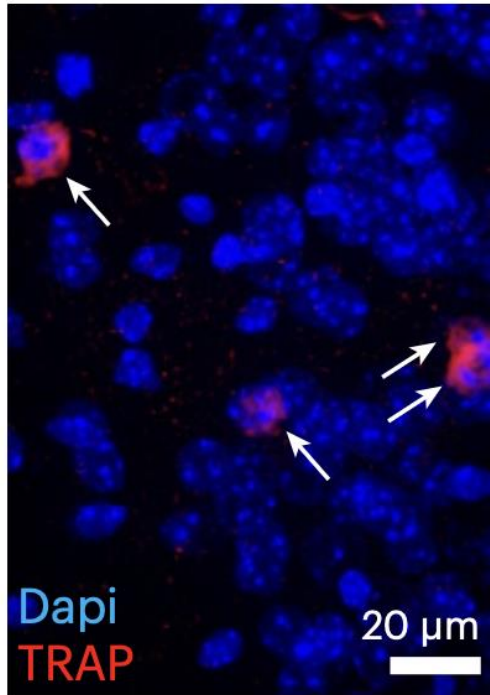
**Séquençage
d'ARN à
cellule
unique
(scRNA-séq)**



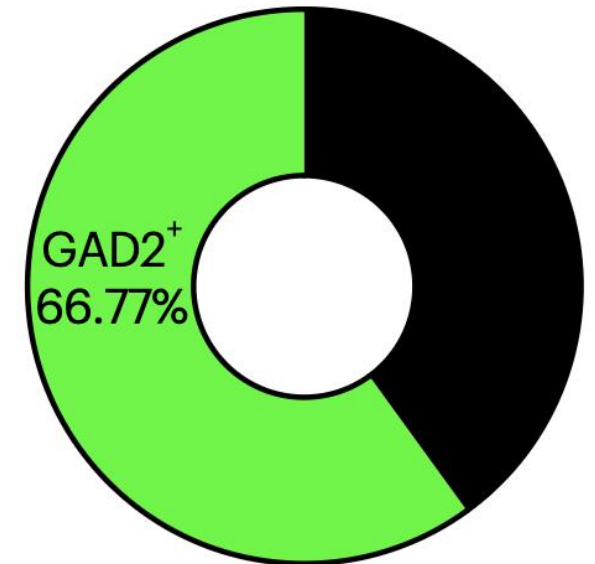
Validation par immunofluorescence

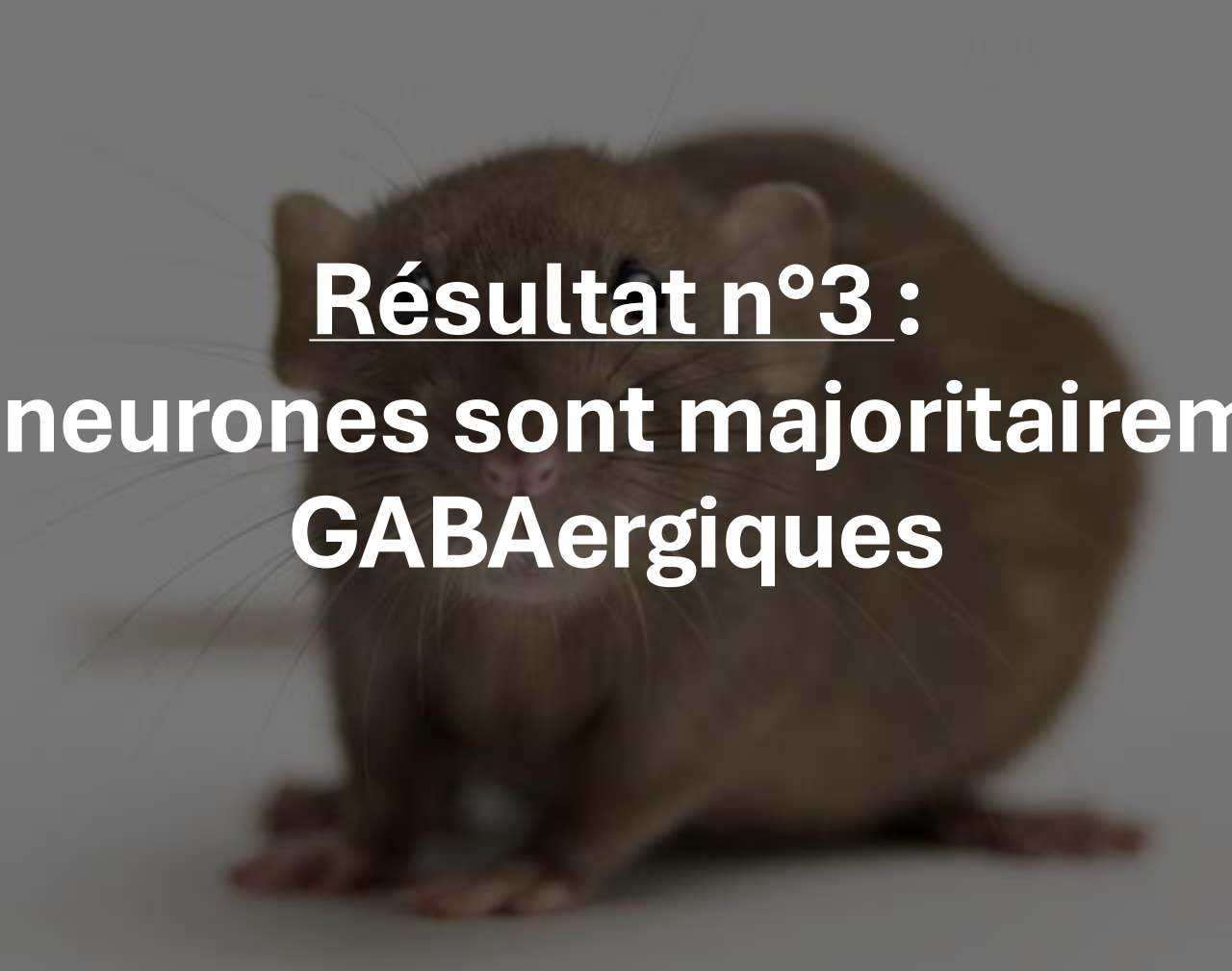
GAD2 = Glutamate Decarboxylase 2

f



GAD2+ (% TRAP)



A brown mouse is sitting on a light-colored surface. The mouse is facing forward, and its body is slightly hunched. The text is overlaid on the mouse's body, centered horizontally and vertically.

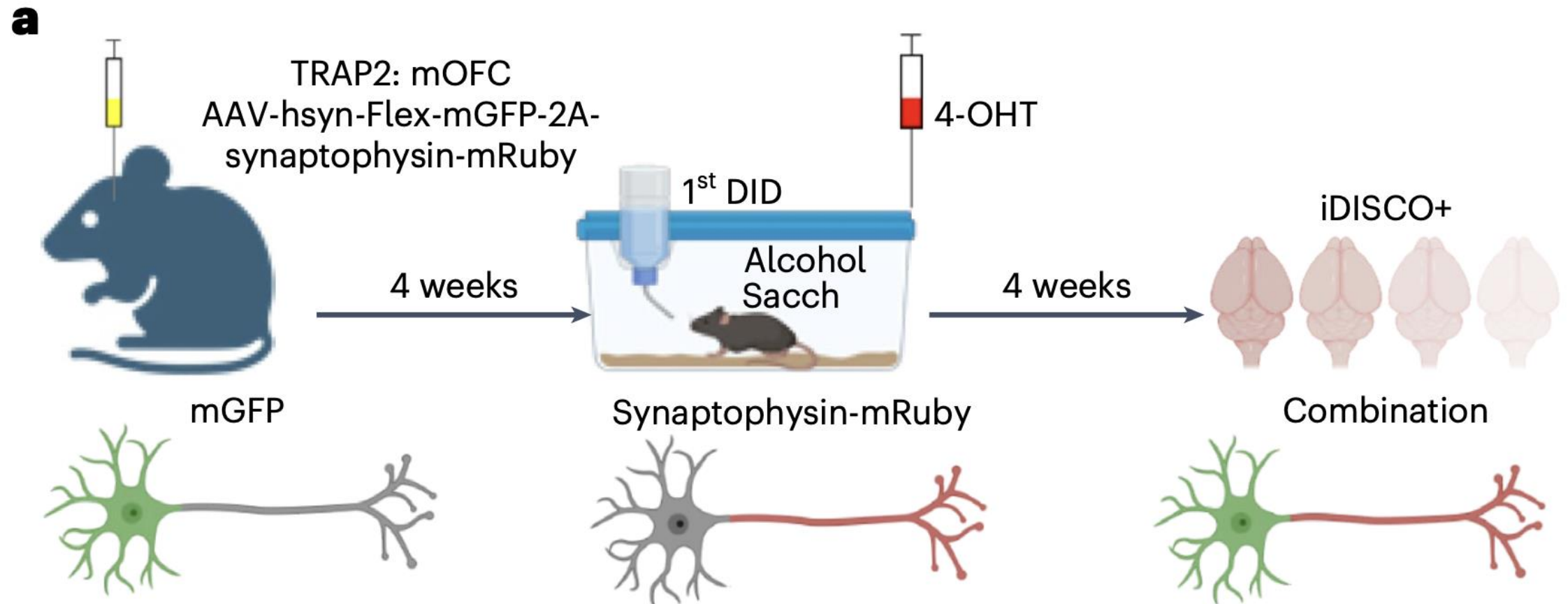
Résultat n°3 :
Les neurones sont majoritairement
GABAergiques

A microscopic image of neurons, likely from a developing brain. The image shows a dense network of thin, branching processes (dendrites and axons) against a dark background. A single neuron in the center is highlighted with a bright cyan color, showing its cell body (soma) and a prominent, textured nucleus. The text "Quelles sont les projections de ces neurones ?" is overlaid in white, bold font, centered on the image.

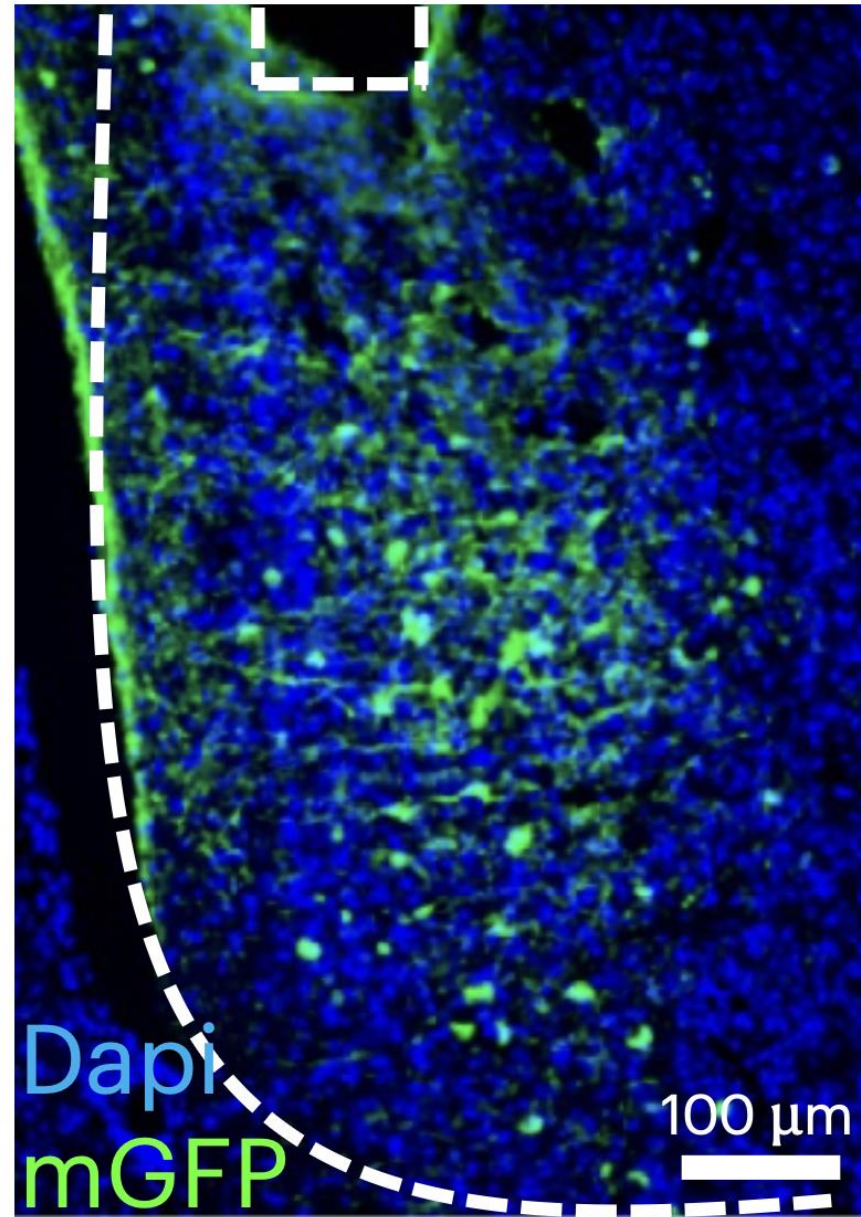
**Quelles sont les projections de
ces neurones ?**

Vecteur viral pour marquer les projections

AAV = Adéno-Associated Virus



Corps cellulaires des neurones

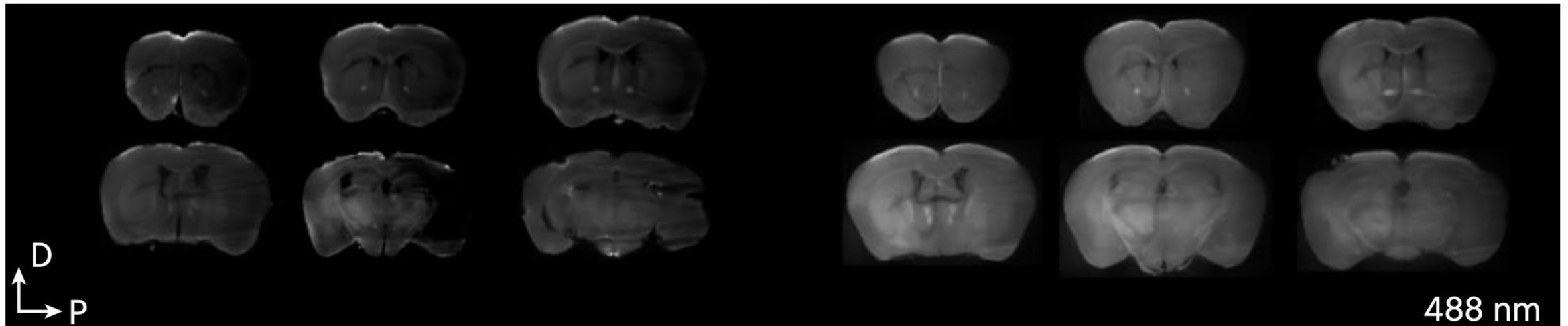


Light sheet microscopy

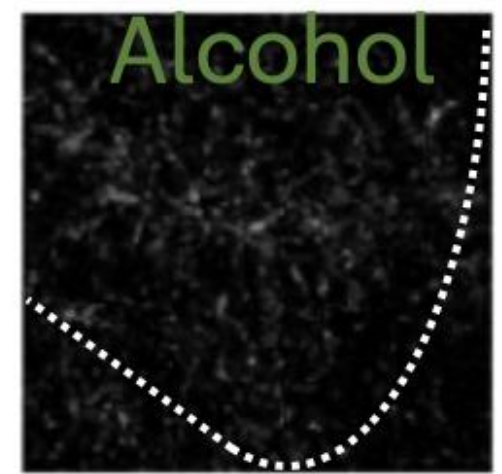
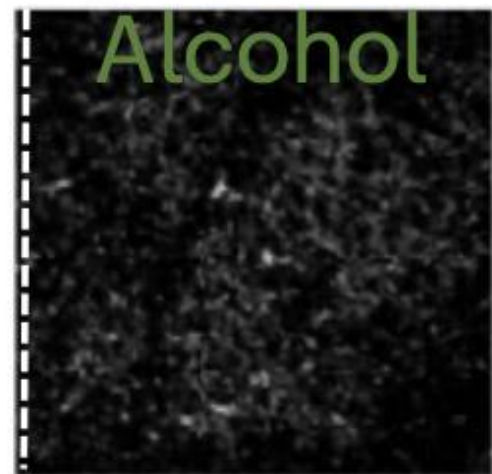
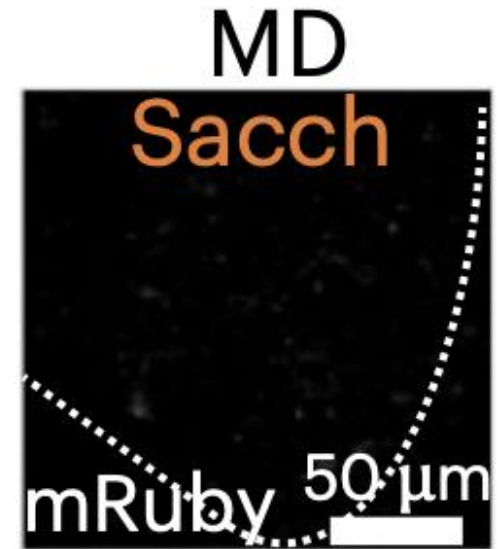
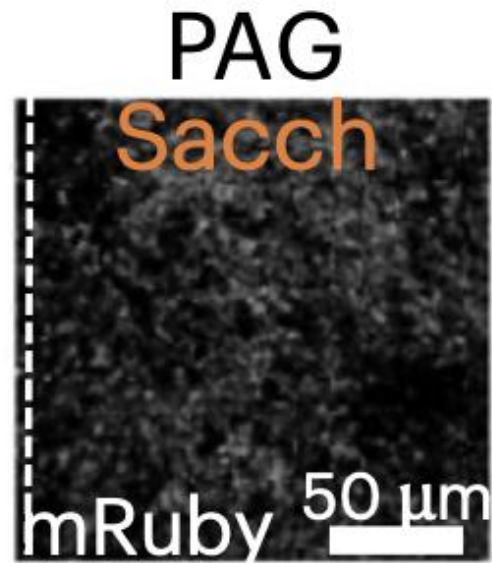
f

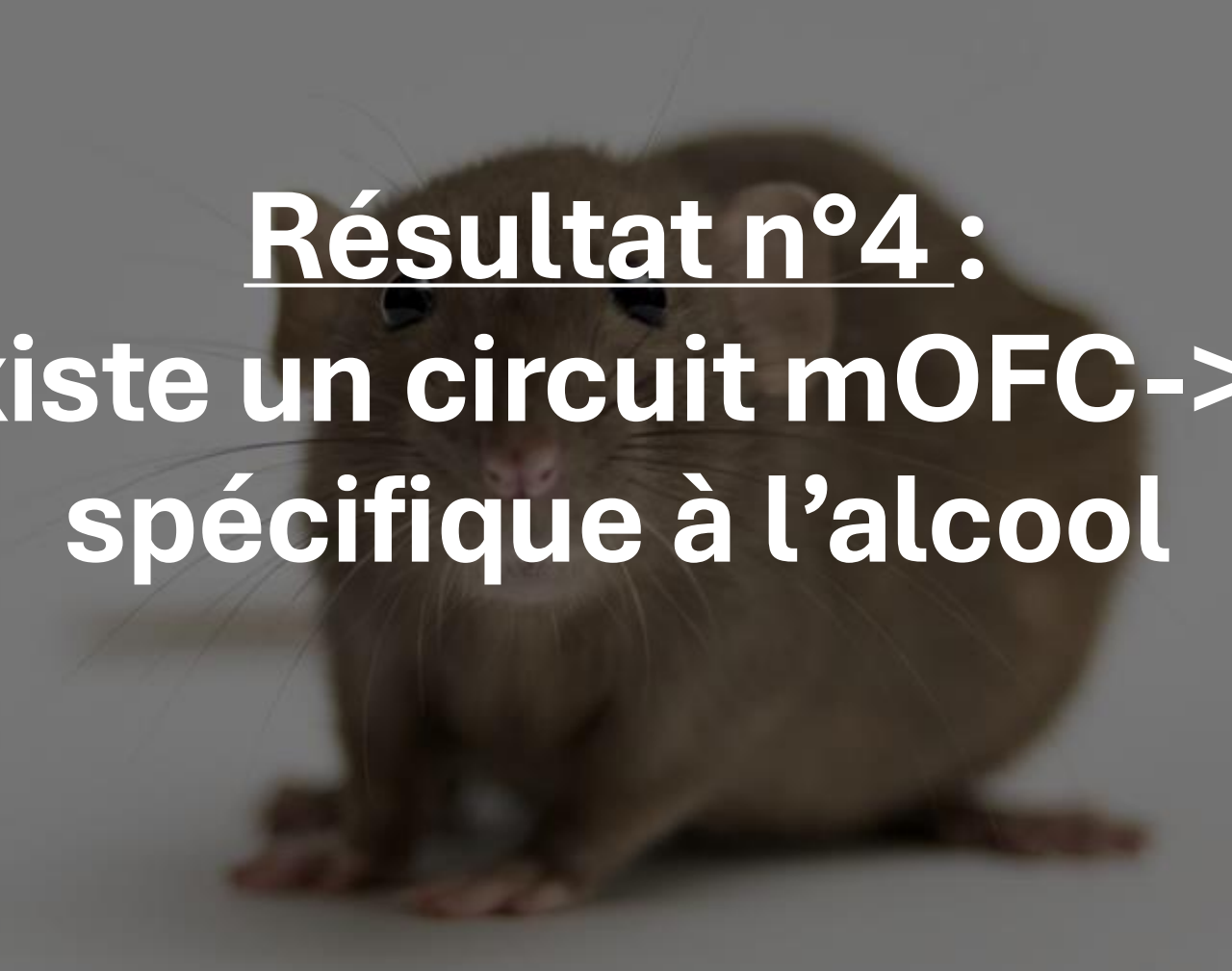
Sacch

Alcohol

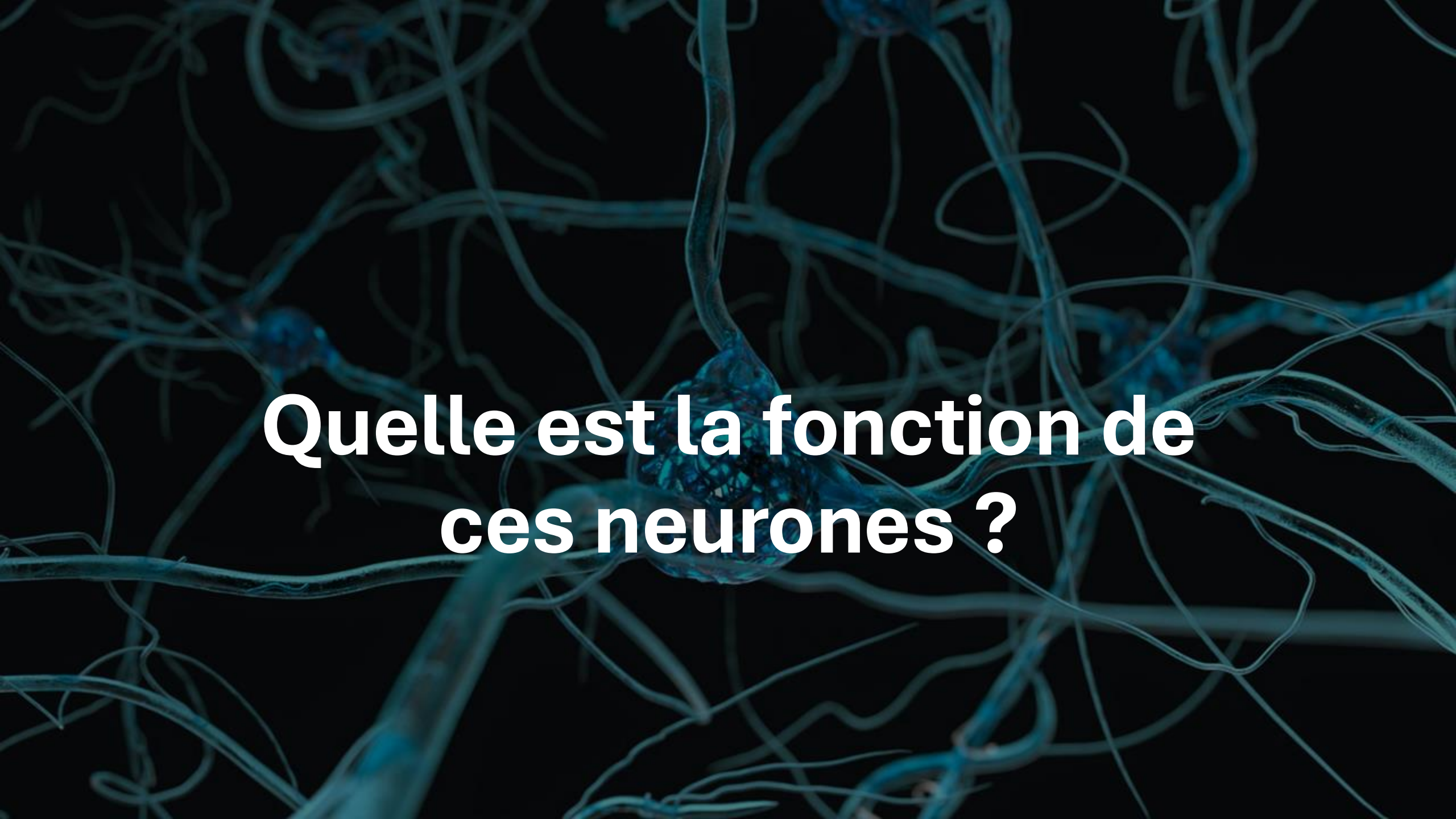


Projections axonales dans la PAG et le thalamus



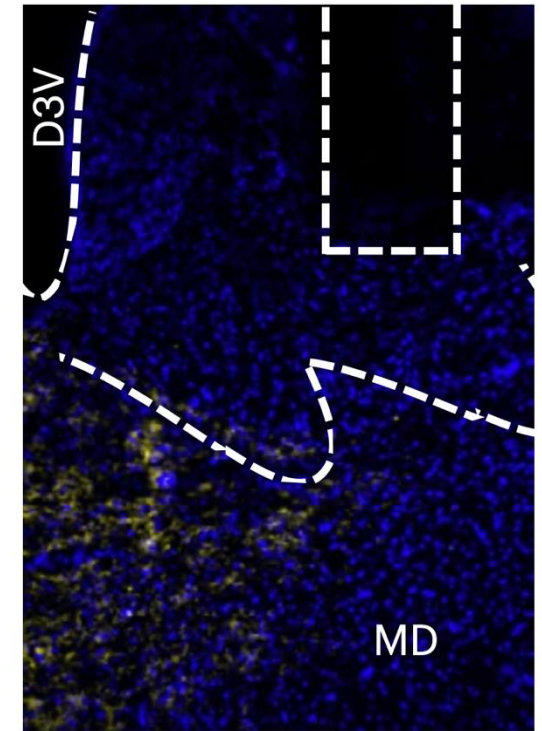
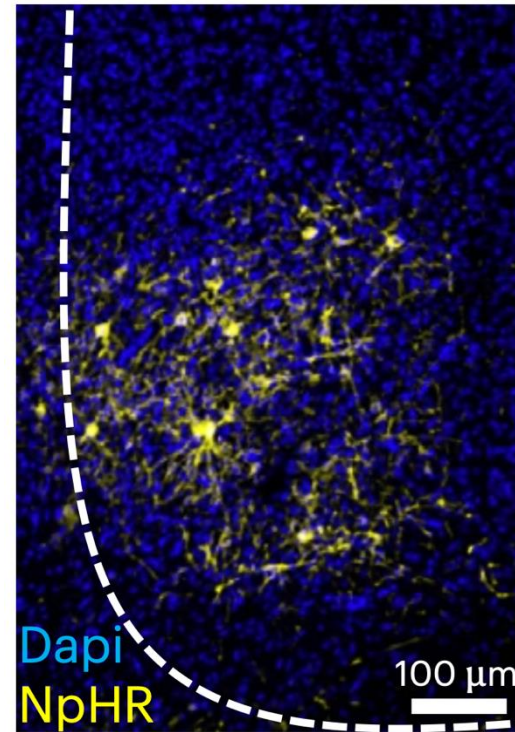
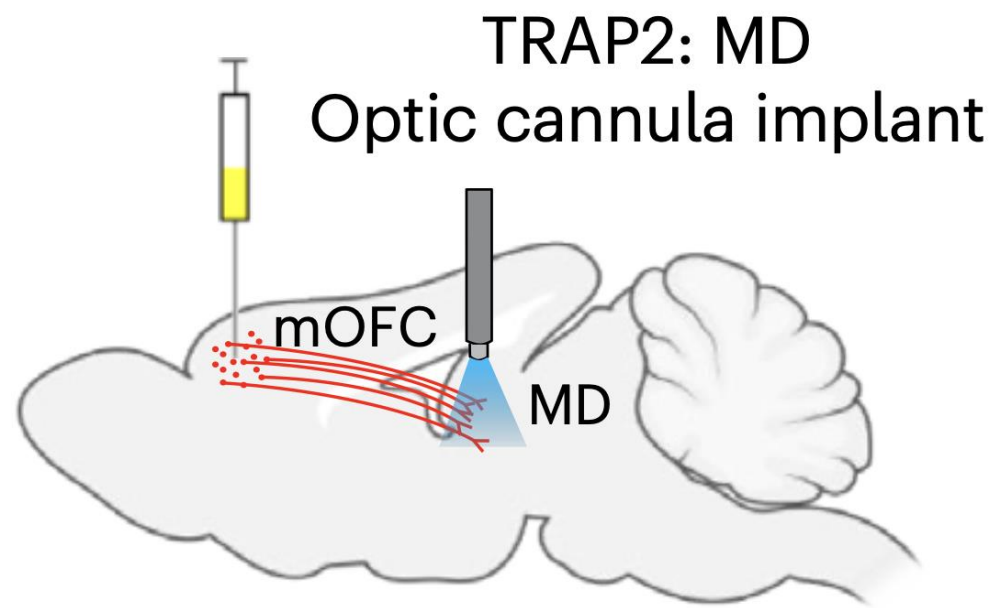


Résultat n°4 :
Il existe un circuit mOFC->MD
spécifique à l'alcool

A microscopic image of neurons, showing a central cell body (soma) with a prominent nucleus, surrounded by a dense network of branching processes (dendrites and axons). The image is rendered in a dark blue/cyan color scheme. The text "Quelle est la fonction de ces neurones ?" is overlaid in white, bold font.

**Quelle est la fonction de
ces neurones ?**

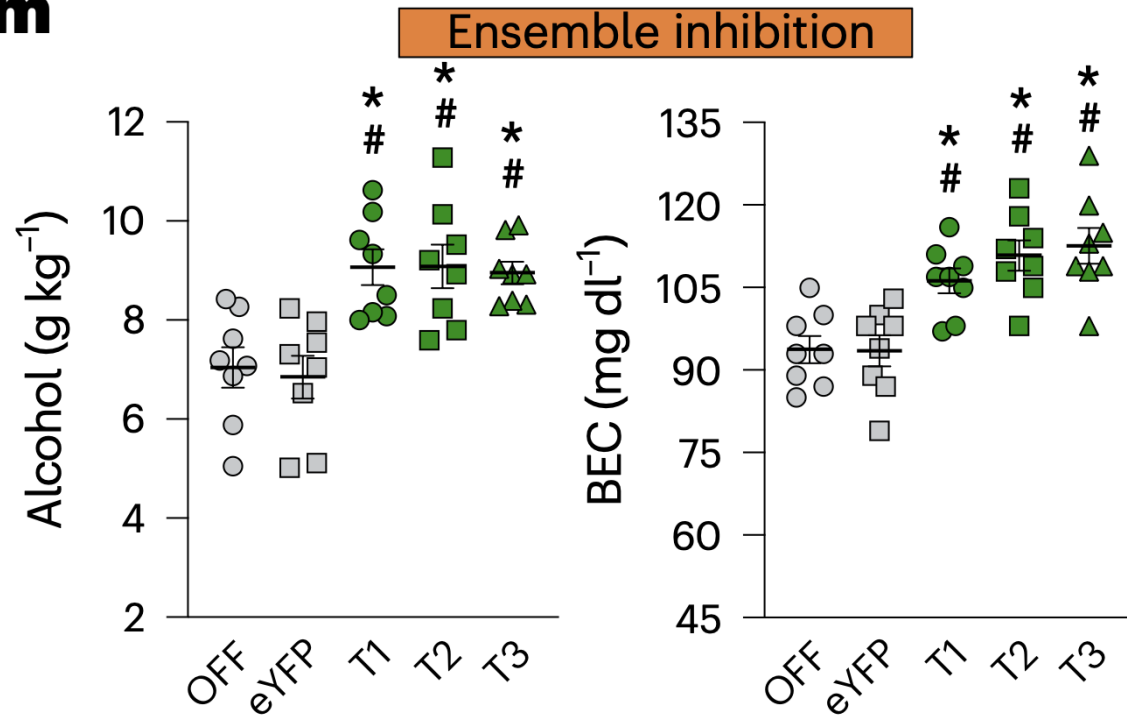
Optogénétique



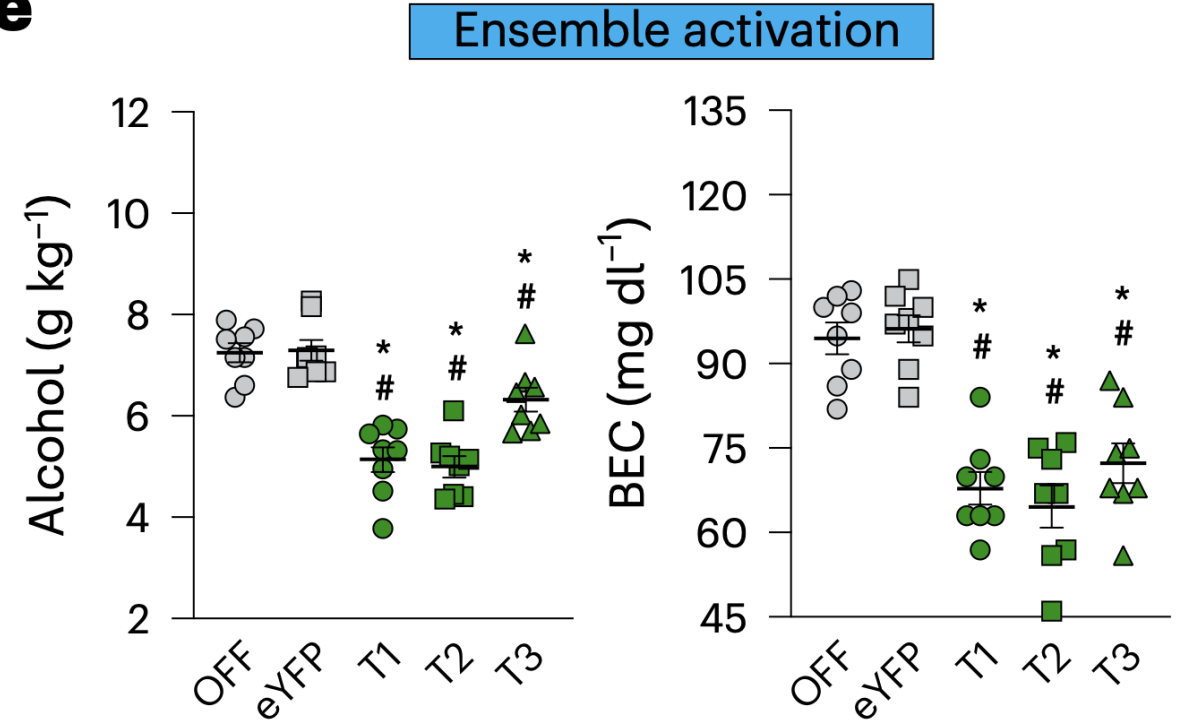
Consommation après activation/inhibition de l'ensemble

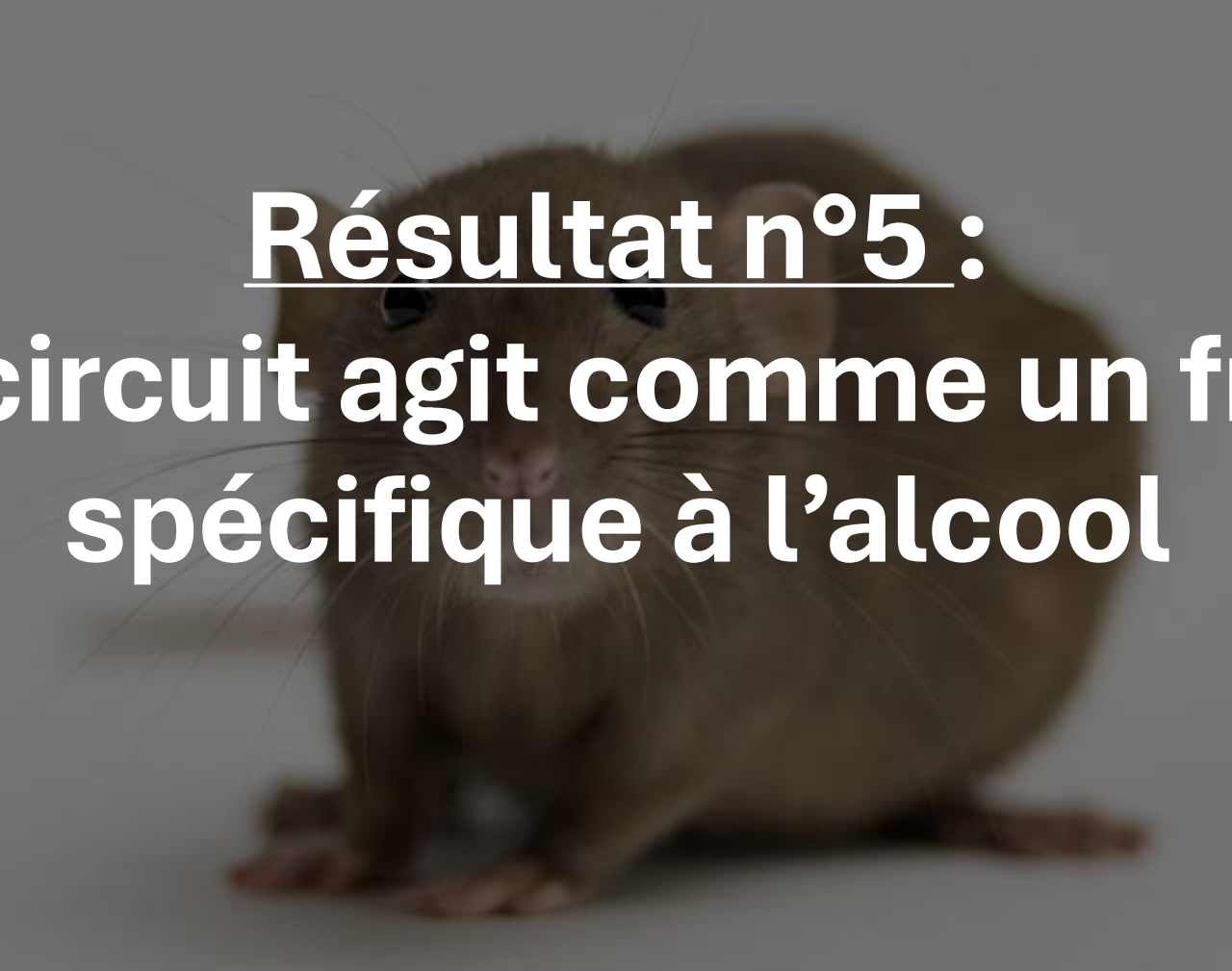
*BEC = Blood Ethanol
Concentration*

m



e





Résultat n°5 :
**Le circuit agit comme un frein
spécifique à l'alcool**

DISCUSSIONS

Messages clés

L'alcool active un groupe de neurones dans le cortex orbitofrontal médian

L'activation de ce groupe n'est pas aléatoire et dépend de l'alcoolémie

Ces neurones sont majoritairement GABAergique et ont des projections vers le thalamus (MD)

Cet ensemble neuronal permet d'inhiber la consommation d'alcool

ANALYSE CRITIQUE

Analyse critique

Points forts :

- Approche multimodale complète
- Étude longitudinale avec effets persistants démontrés
- Sujet d'intérêt majeur en santé publique

Limites :

- Modèle murin ≠ comportements humains réels
- Manque d'exploration d'autres circuits (hippocampe, amygdale, etc...)

Questions ouvertes

Peut-on mettre en évidence un ensemble neuronal équivalent dans le mOFC chez l'humain ?

Est-ce qu'il existe d'autres circuits spécifiques à d'autres drogues ?

Comment la fonction de ces neurones est supprimée chez les patients intoxiqués ?

Comment on pourrait prévenir la consommation addictive ?

A white mouse is shown standing on its hind legs, looking upwards and to the right. The mouse has pinkish-red eyes and ears. The word "MERCI" is written in large, white, bold, sans-serif capital letters across the middle of the image, partially overlapping the mouse's body. The background is a blurred, light-colored interior space with vertical lines, possibly from a window or door frame.

MERCI