

Student number.....

## UE BODY MIND INTERACTION (M Darnaudéry, A Nadjar)

You can answer in French or English at your convenience. Be concise in your answers

1- Explain what are microglia and what are their physiological functions? (2pts)

2. In this article (Borovikova et al., Nature 2000), the authors explore the bi-directional communication between body and brain, in a context of systemic inflammation. Endotoxins, produced by all Gram-negative bacteria, activate the immune system, including macrophages, leading to the release of cytokines that can have lethal effects at very high dose. In preclinical research, bacterial infection is often simulated by injecting lipopolysaccharide (LPS) into animals, which recapitulates the macrophage-mediated cytokine production. This inflammatory response, in turn, influences brain activity, partly through afferent fibers of the vagus nerve. This cranial nerve being bi-directional, the study investigates whether the brain, in response, can regulate systemic inflammatory responses to endotoxins by modulating macrophage activity. Specifically, it examines whether efferent vagal fibers play a role in controlling inflammation in the body. Below is presented the first figure of the article, indirectly addressing this question.

### FIG1.

In a first series of experiments, the authors tested the effect of cholinergic agonists on the production of the pro-inflammatory cytokine TNF- $\alpha$  by macrophages in culture exposed to LPS (*in vitro* experiments).

*Ach: Acetylcholine: binds to both nicotinic and muscarinic cholinergic receptors*

*Muscarine: cholinergic agonist specifically activating muscarinic receptors only*

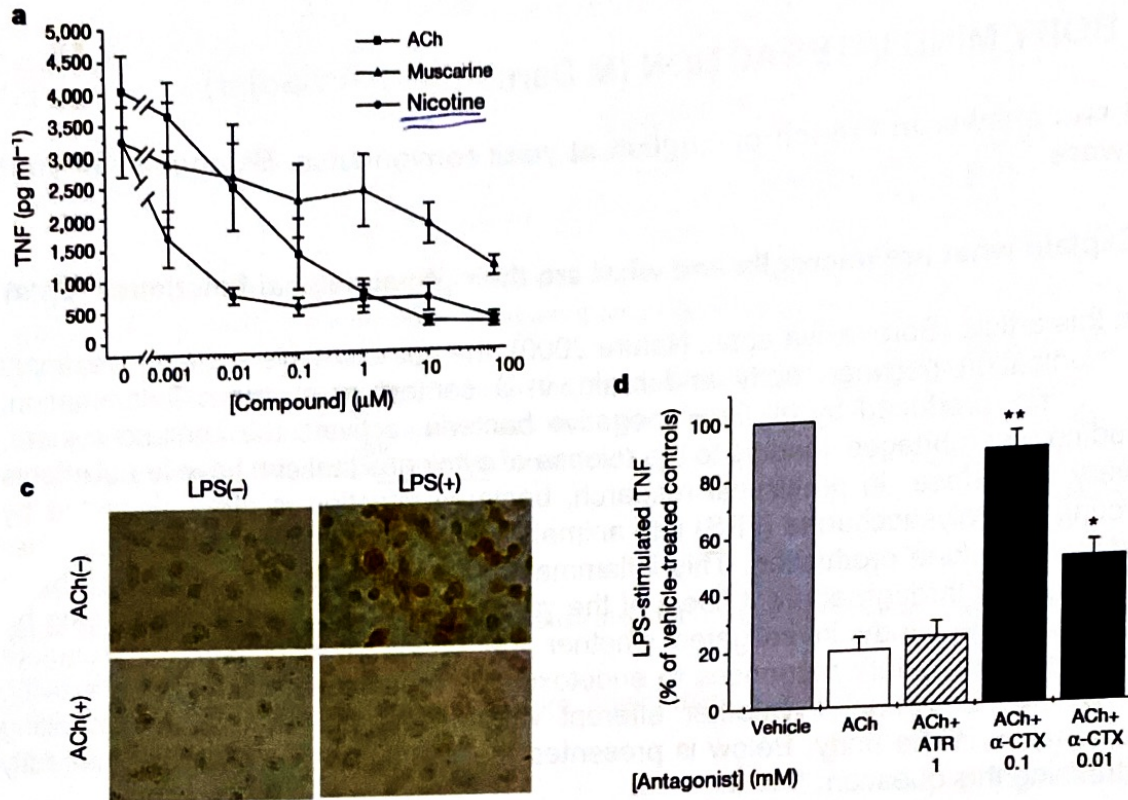
*Nicotine: cholinergic agonist specifically activating nicotinic receptors only*

2.1 FIG1.a. What are the dependent and independent variables? Briefly explain the purpose of the experiment (2pts)

2.2. Explain why the authors use 2 different cholinergic agonists in Figure 1a (1pt)

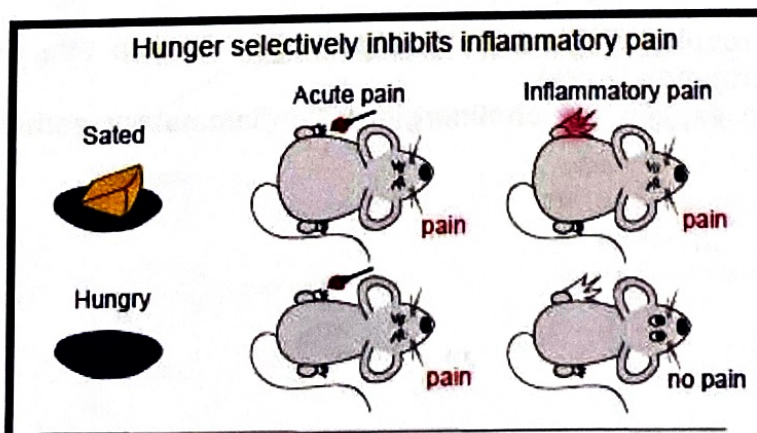
2.3 Briefly describe the results of Figure 1 and conclude. Give a title that summarizes the main information (2 pts)

2.4 Propose a schema to explain the cholinergic anti-inflammatory pathway (3pts)

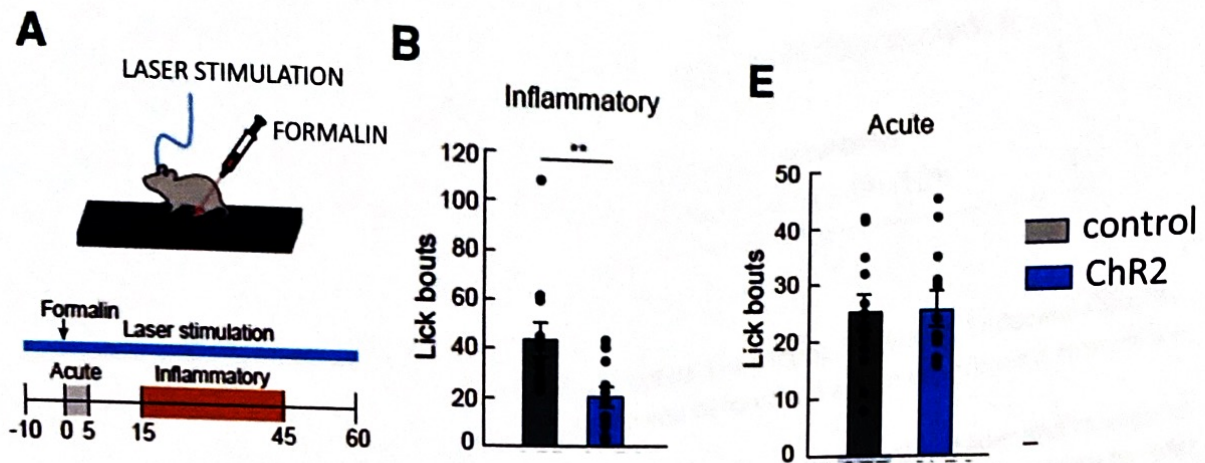


**Figure 1.** a. TNF- $\alpha$  protein production by macrophages in culture, exposed to LPS, in association with Achetylcholine (ACh), Muscarine or Nicotine. b. Immunohistochemical staining of TNF- $\alpha$  production by macrophages, in response to LPS +/- Achetylcholine. c. TNF- $\alpha$  protein quantification in response to LPS +/- cholinergic antagonist atropine (ATR) et  $\alpha$ -conotoxine ( $\alpha$ -CTX). *Nota Bene*: Atropine: muscarinic receptors antagonist;  $\alpha$ -conotoxin: nicotinic receptor antagonist

### 3. On the article from Alhadeff et al., Cell, 2018



3.1. With the help of the graphical abstract, explain the objective of the study and the main results (3pts)



**Figure 3:** A) Experimental design: Laser light pulses delivered to AgRP neurons of AgRP GFP and AgRP-ChR2 mice began 10 min before formalin injection and continued while formalin-induced paw licking was quantified. B) Inflammatory phase formalin-induced lick bouts in AgRP-GFP and AgRP-ChR2 mice (unpaired t test,  $p < 0.01$ ). D) Time spent paw licking during acute phase of formalin test in AgRPGFP and AgRPChR2 mice (unpaired t test,  $p = ns$ ). ChR2 =channelrhodopsin-2

- 3.2. Briefly explain the protocol of the study (2pts)
- 3.3. What is the main aim of this experiment? (2pts)
- 3.4. What are the dependent and independent variables? (1pt)
- 3.5. Describe the results and conclude. (2pts)