



SOCIETE FRANCAISE DE NUTRITION - 2013

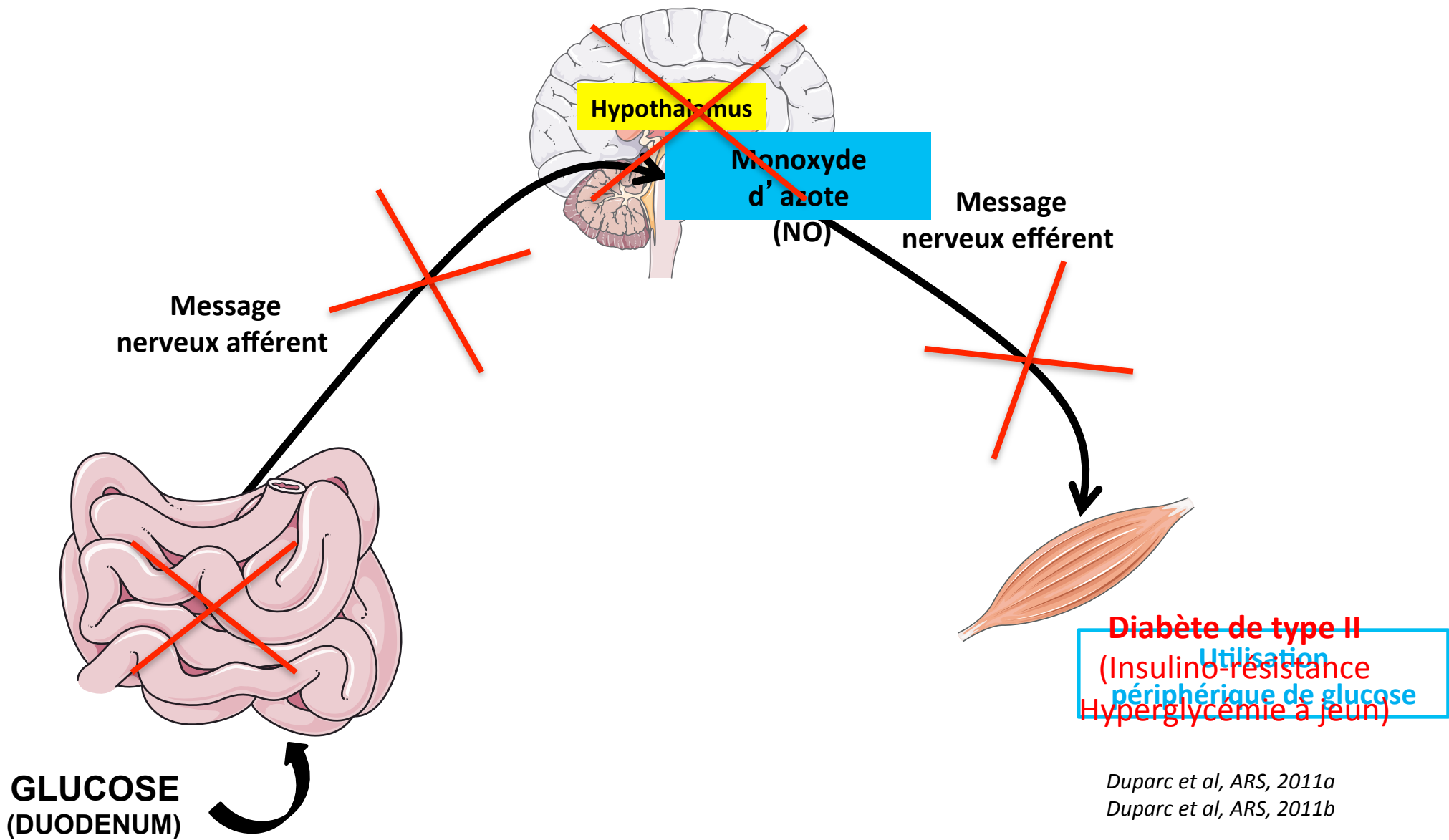


EFFET D' UN REGIME HYPERLIPIDIQUE SUR LES CONTRACTIONS DUODENALES STIMULEES PAR L' APELINE CHEZ LA SOURIS:

CONSEQUENCES SUR L' AXE « INTESTIN-CERVEAU- PERIPHERIE »

Claude KNAUF

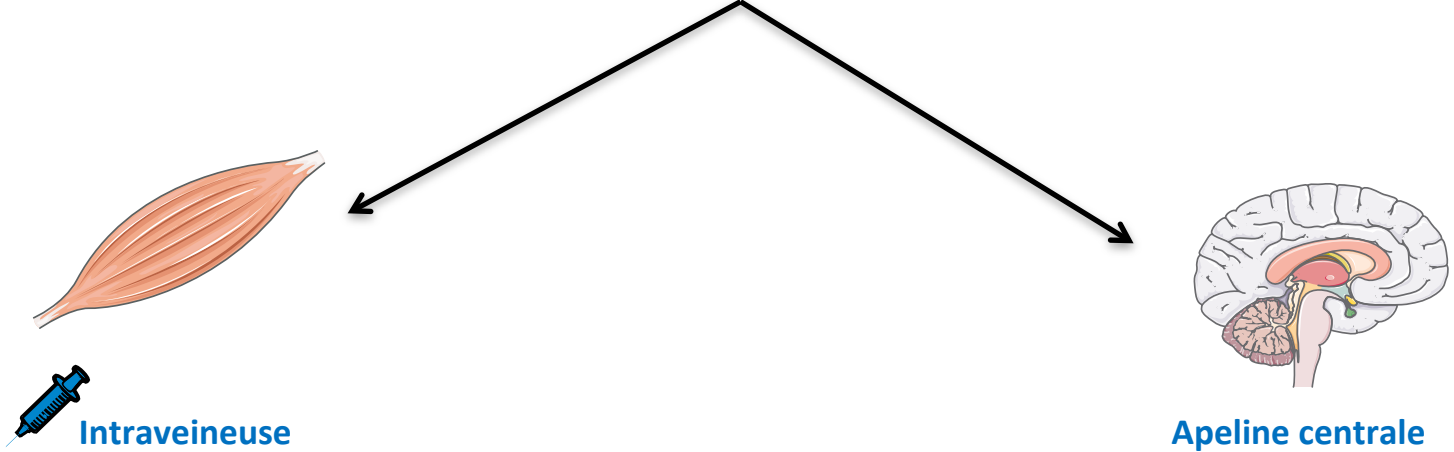
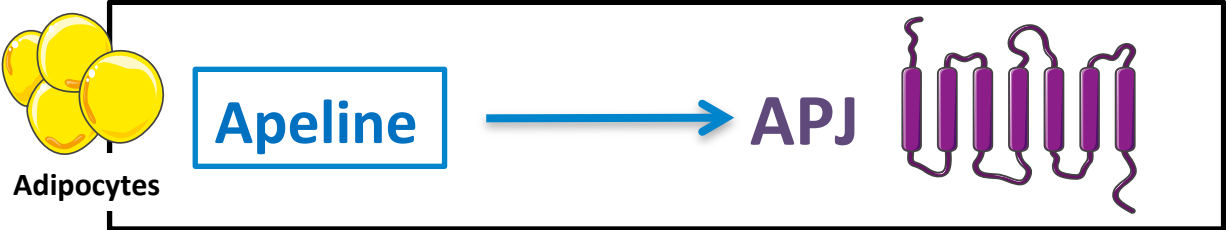
INSERM U1048/LEA NeuroMicrobiota



Duparc et al, ARS, 2011a

Duparc et al, ARS, 2011b

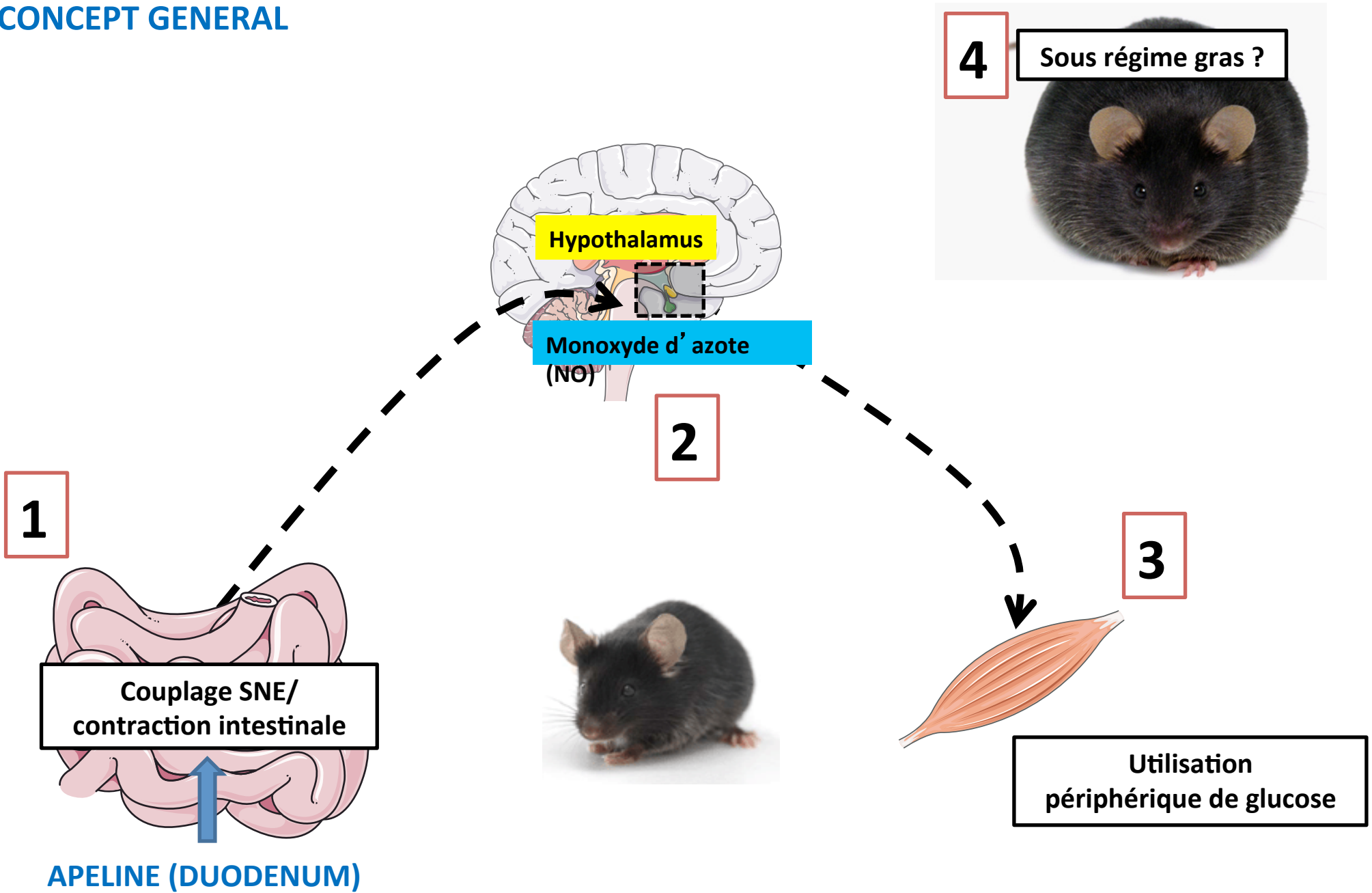
APELINE ET METABOLISME GLUCIDIQUE

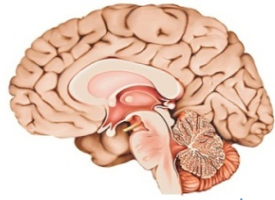
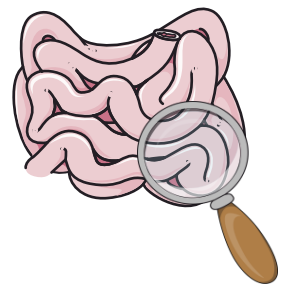


Augmentation de la sensibilité à l'insuline

Contrôle de la glycémie

CONCEPT GENERAL





**VOIES NERVEUSES
AFFERENTES**

**VOIES NERVEUSES
EFFERENTES**

Apeline ???

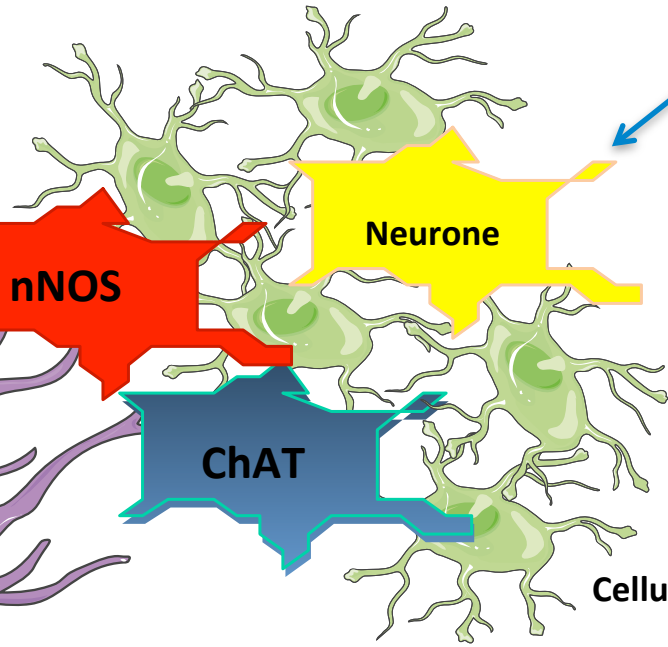


**Cellules musculaires
lisses**

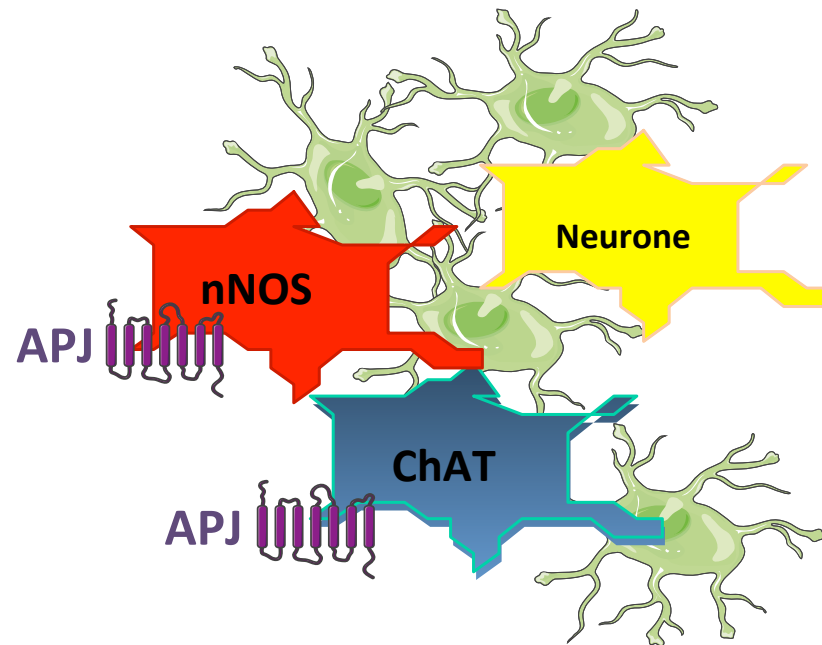
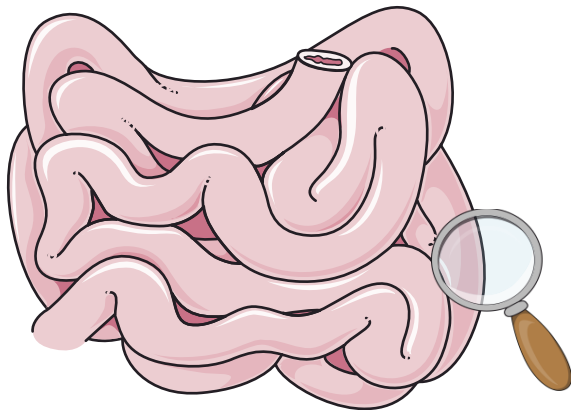
Cellules gliales



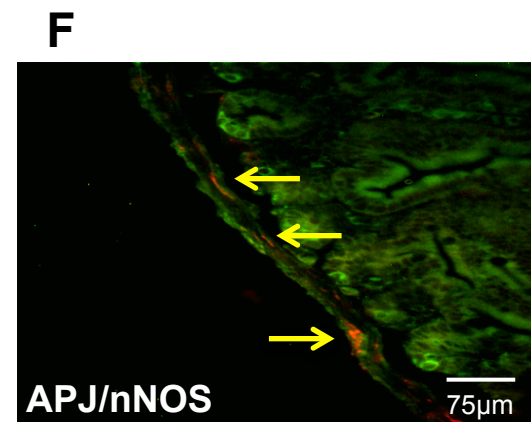
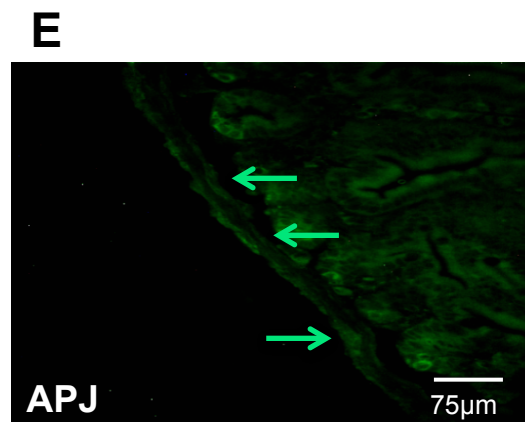
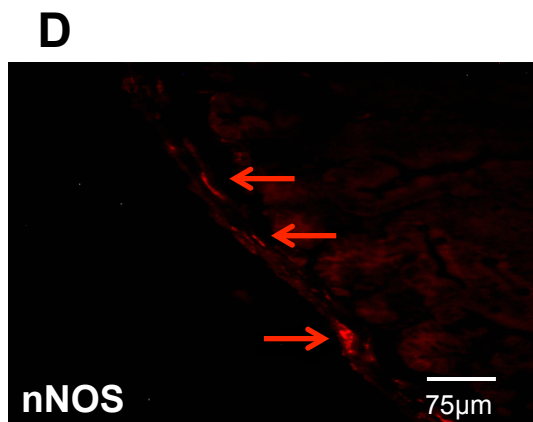
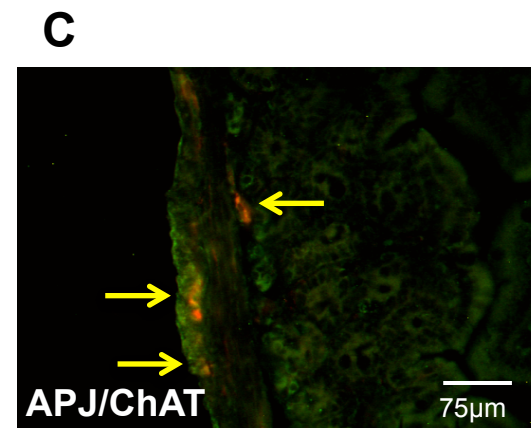
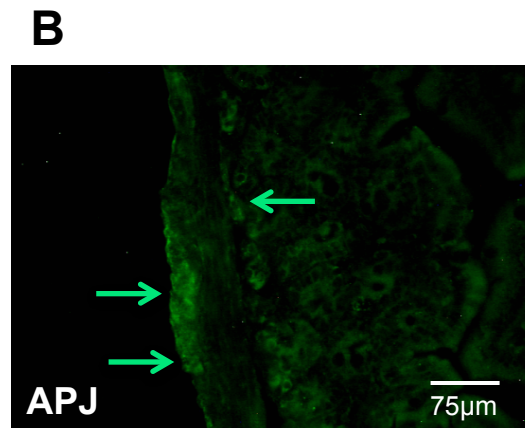
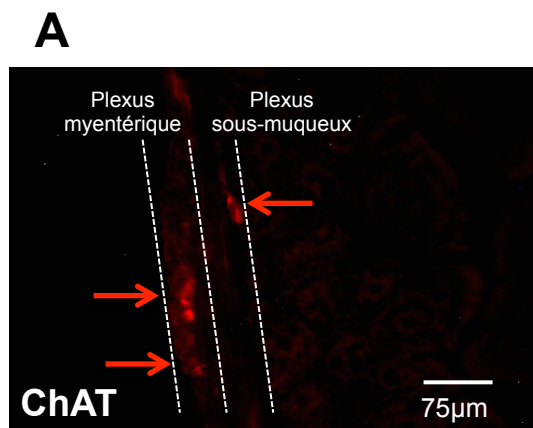
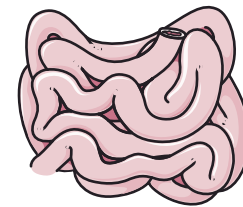
**SYSTÈME NERVEUX
ENTERIQUE (SNE)**



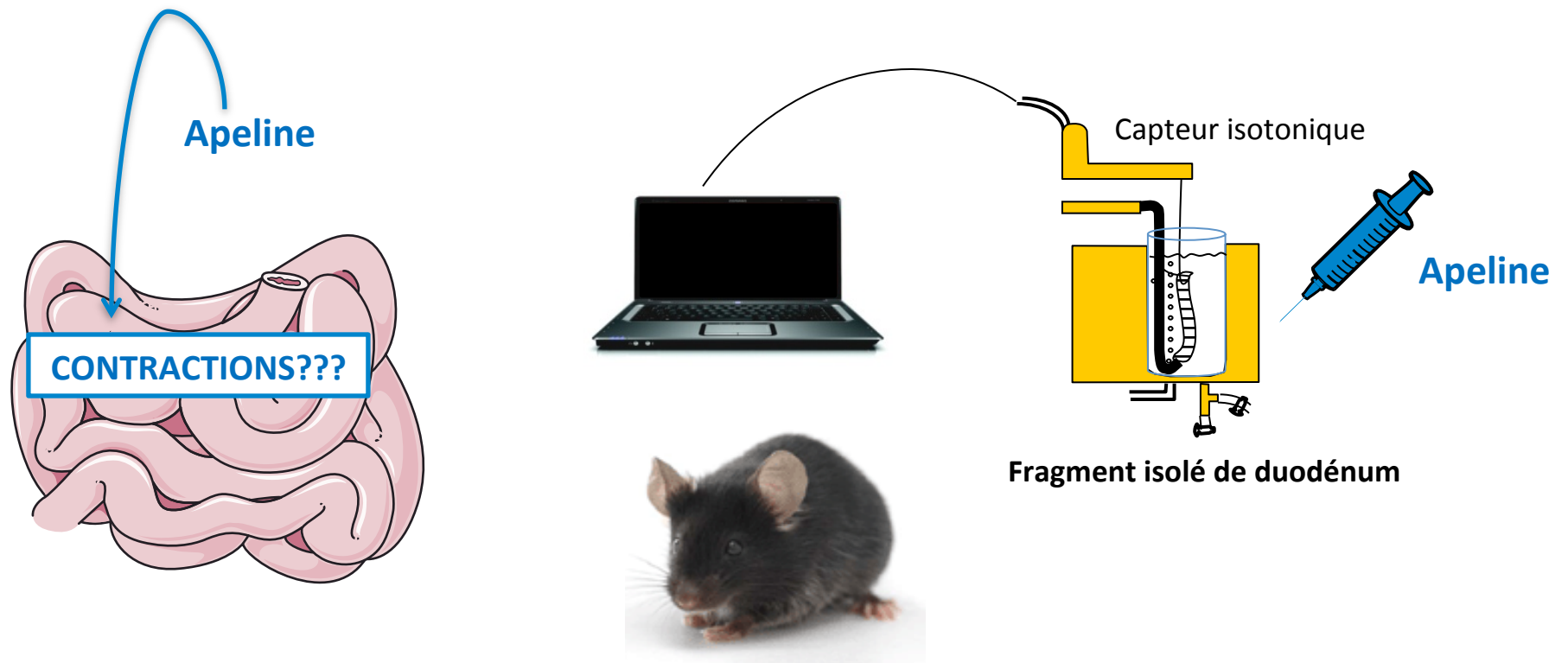
1- LE RECEPTEUR APJ EST-IL EXPRIME DANS LES NEURONES DU SNE nNOS et/ou ChAT DANS LE DUODENUM ?



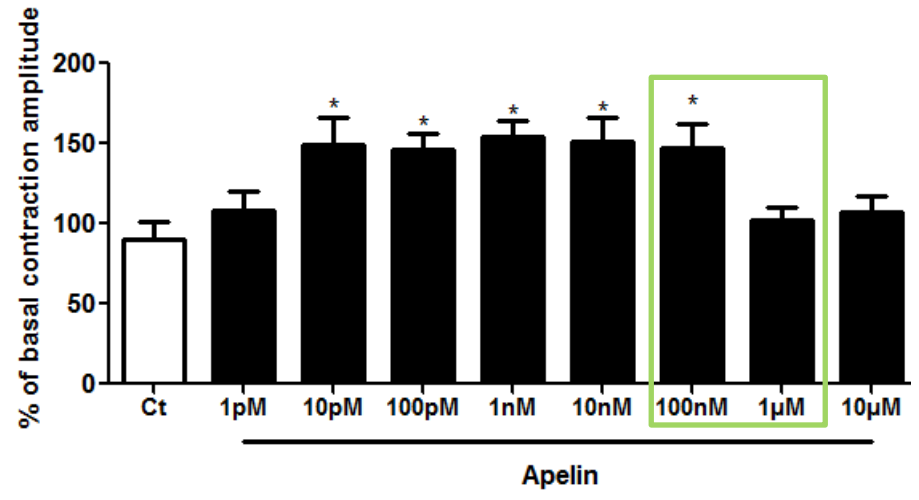
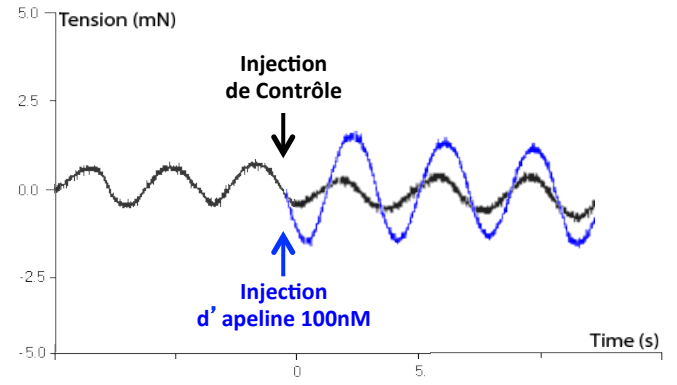
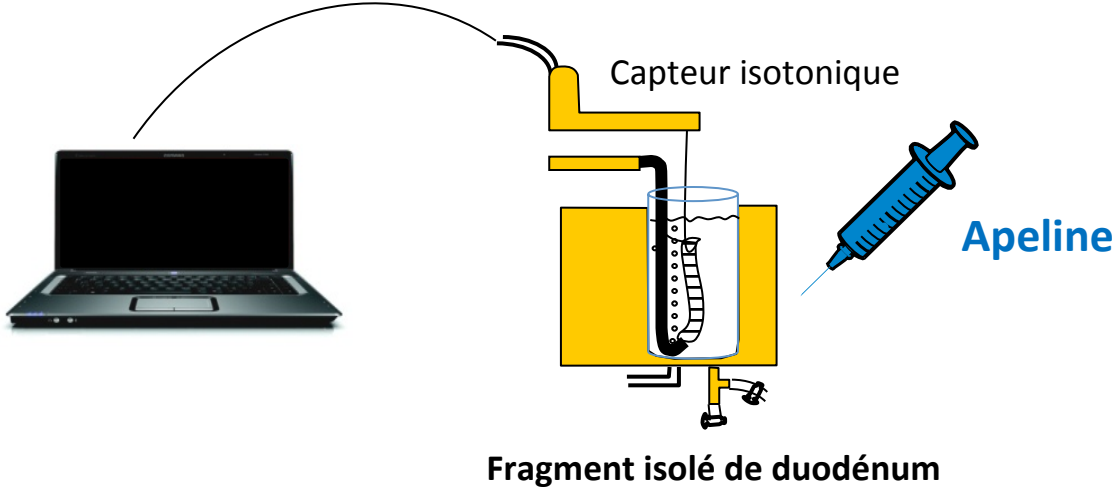
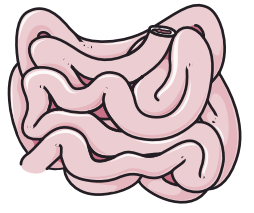
DUODENUM: CO-LOCALISATION APJ/ChAT ET APJ/nNOS



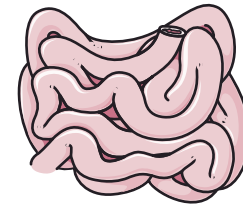
1- L' APELINE MODIFIE-T-ELLE L' ACTIVITE CONTRACTILE DU DUODENUM ?



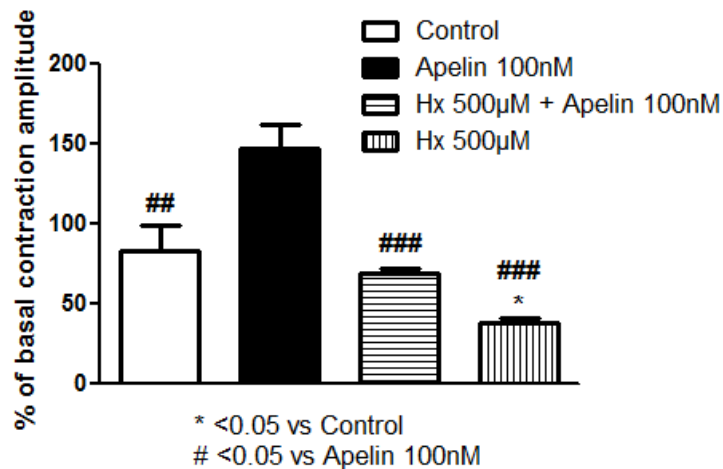
Activité mécanique *Ex vivo* avec un capteur isotonique



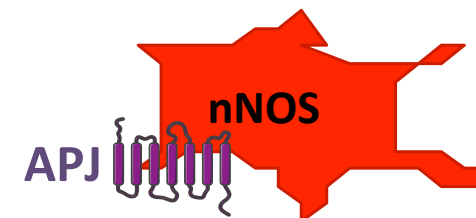
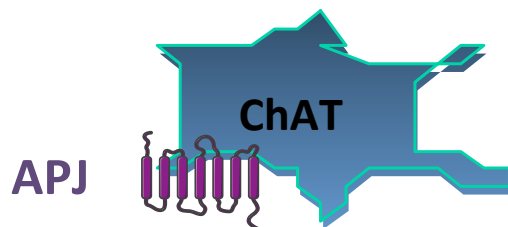
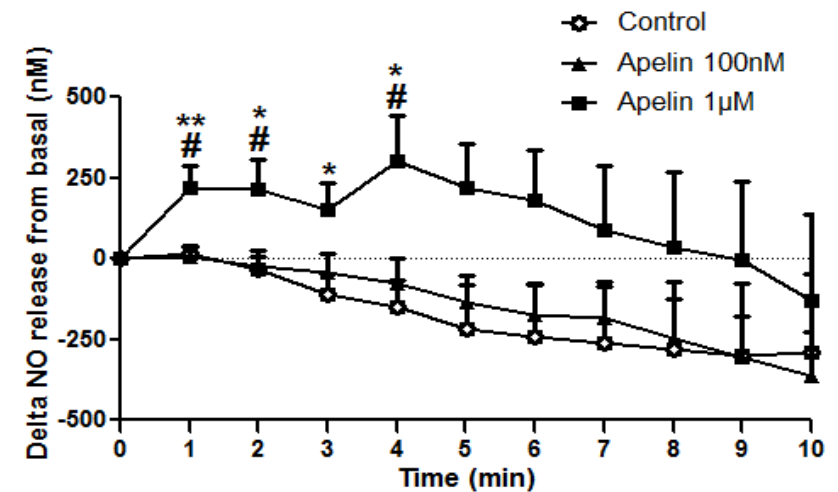
Acteurs moléculaires impliqués



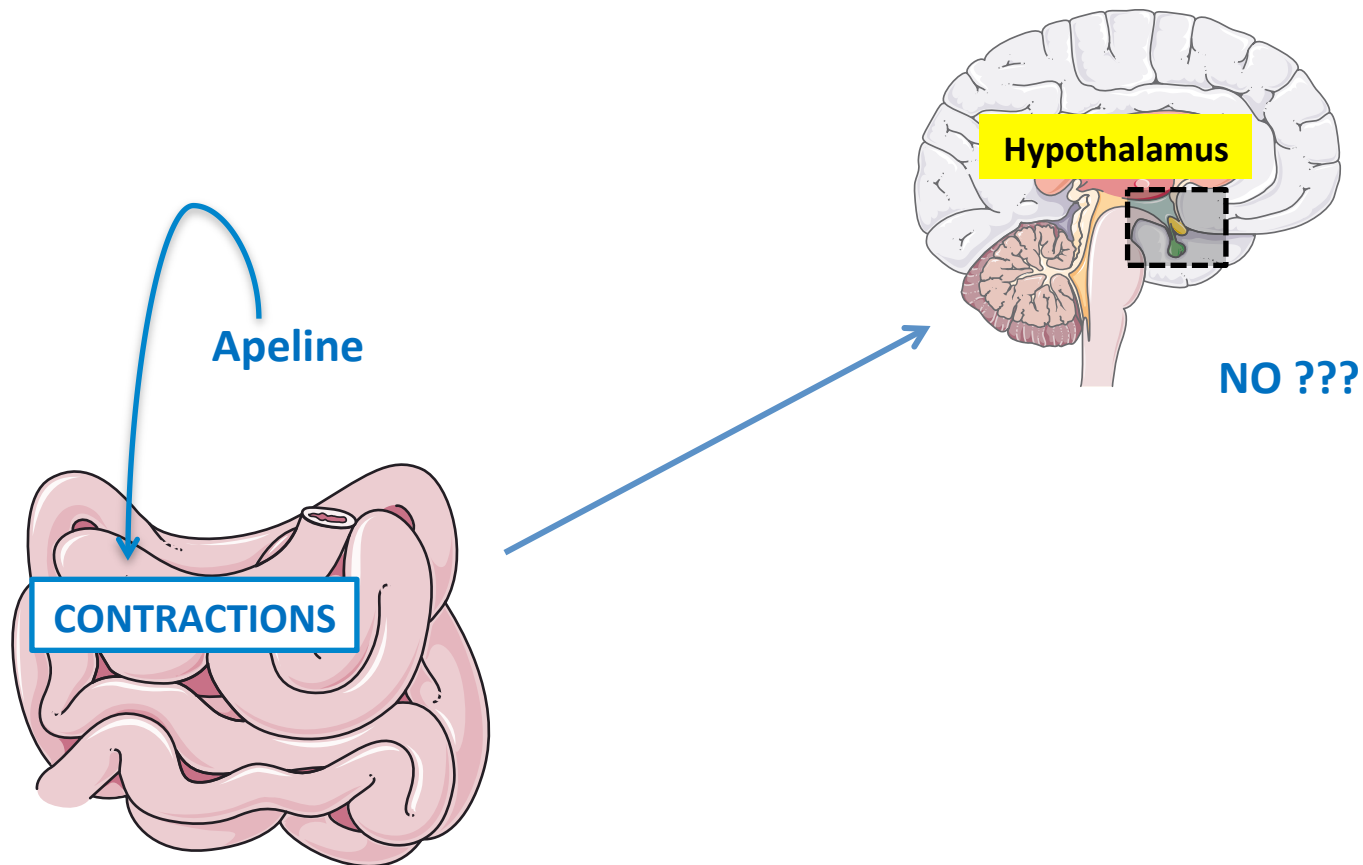
Acteur stimulateur (Neurones ChAT)

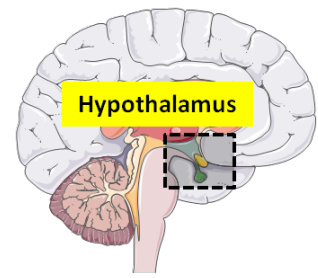


Acteur inhibiteur (Neurones nNOS)



2- L' APELINE MODIFIE-T-ELLE L' ACTIVITE NO HYPOTHALAMIQUE ?

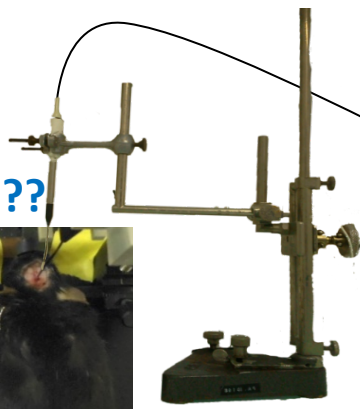
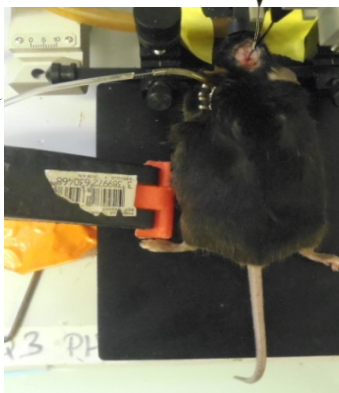




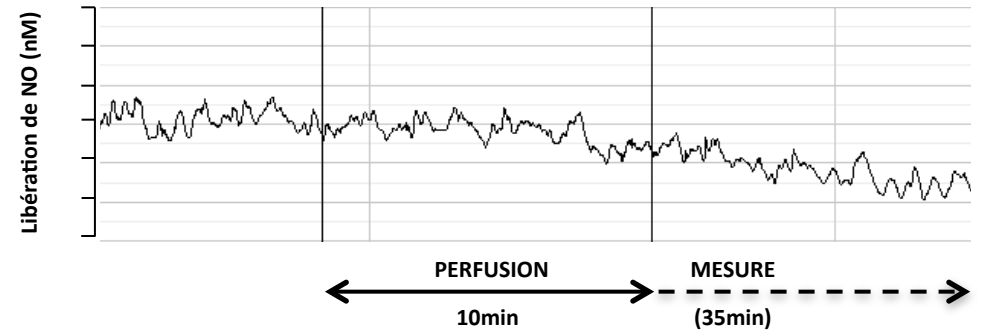
NO ???



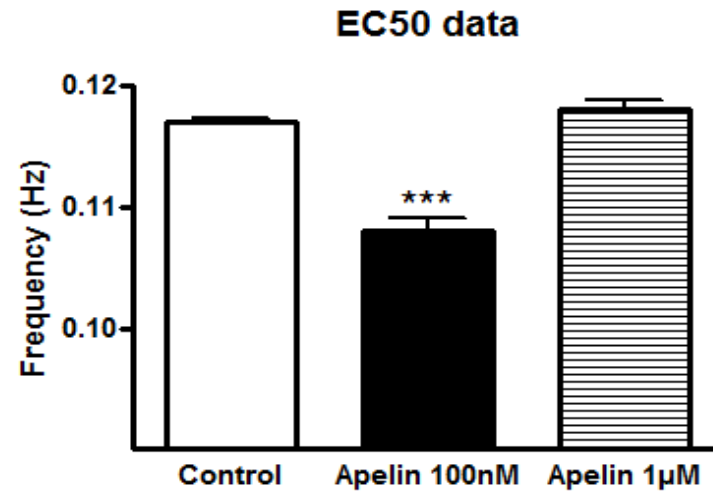
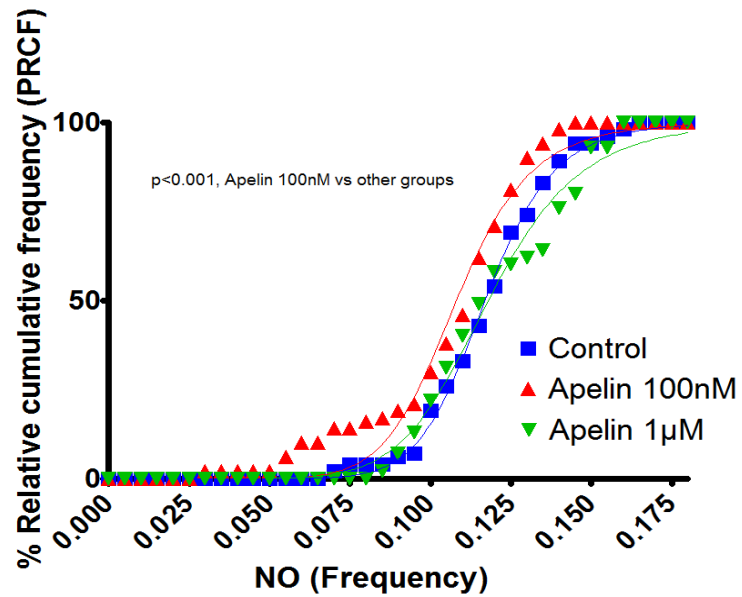
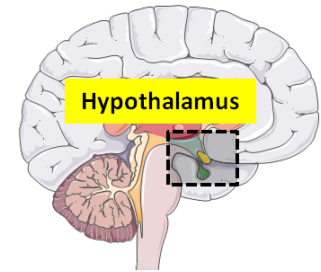
Apeline
(100nM ou 1µM)



(Duparc et al, ARS, 2011b)

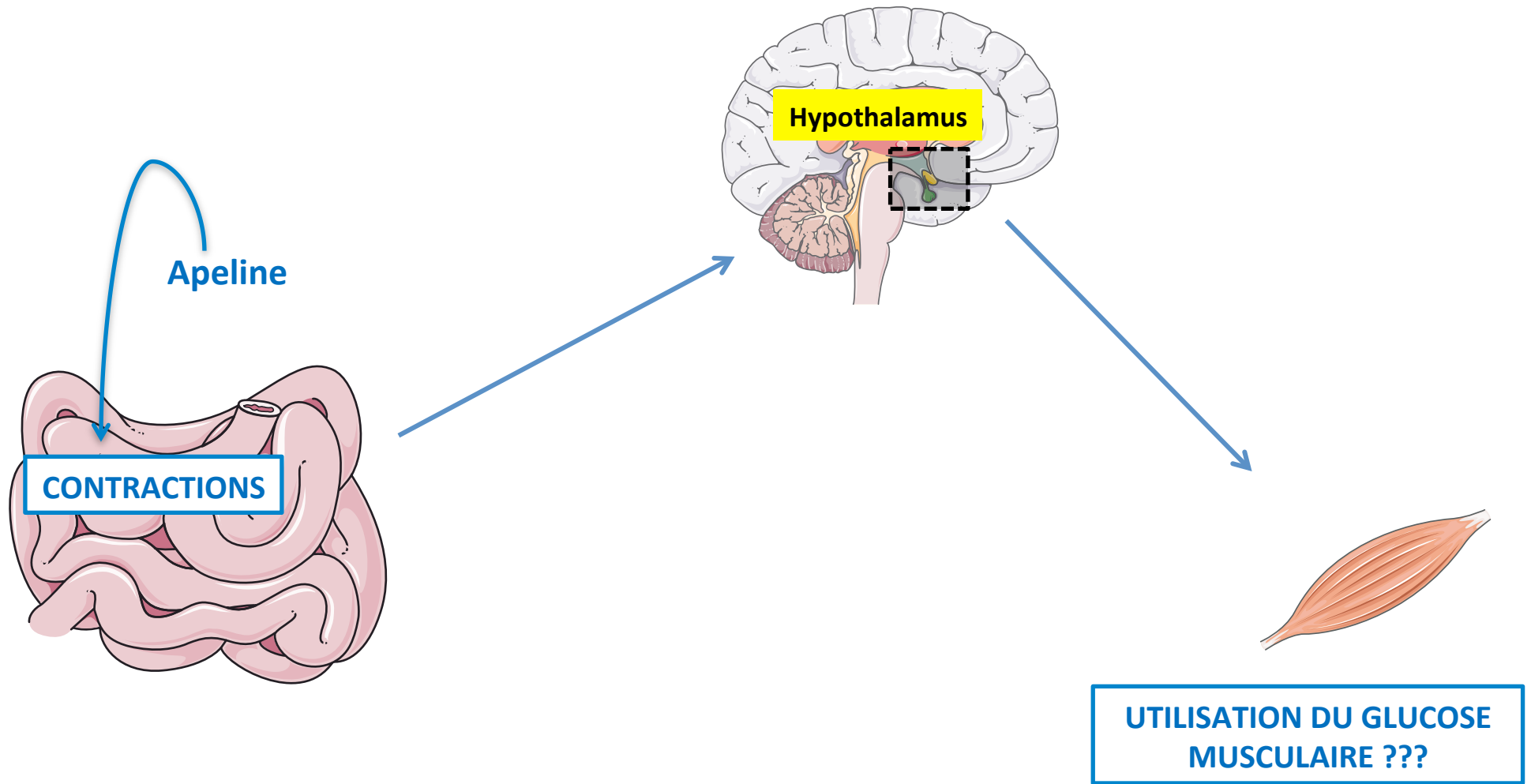


Acteur hypothalamique: le monoxyde d'azote (NO)



Quand les contractions duodénales augmentent, la libération de NO hypothalamique diminue

3- L' APELINE MODIFIE-T-ELLE L' UTILISATION DU GLUCOSE ?

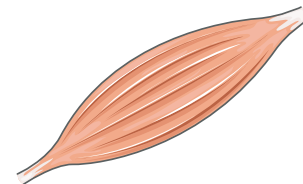


GAVAGE

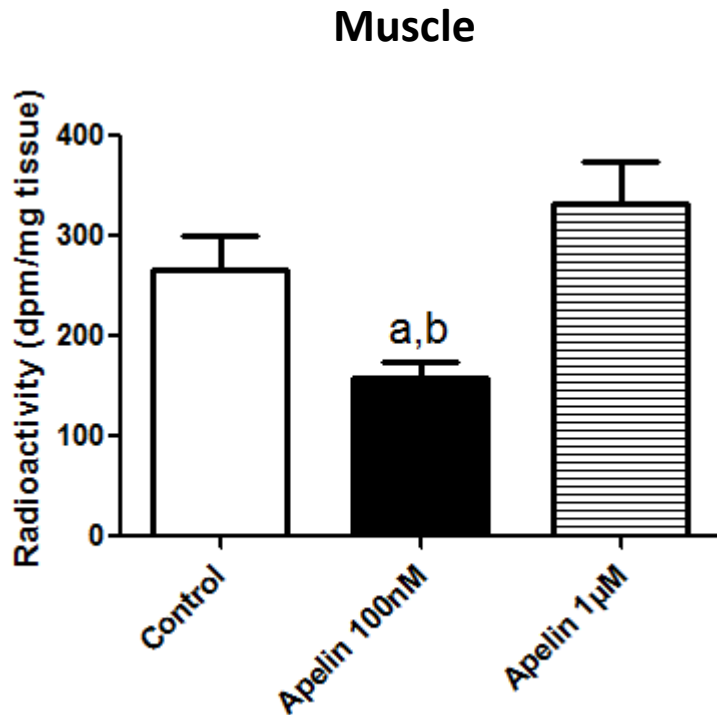
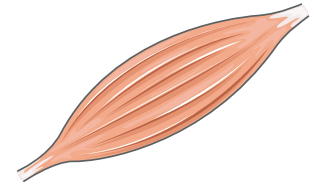
Apeline + 3H-Glucose



Mesure Glucose Radioactif (Tissus):
Entrée de Glucose ???



Utilisation du Glucose dans le Muscle



Quand les contractions duodénales augmentent, la libération de NO hypothalamique diminue ...et l'utilisation du glucose musculaire diminue

Concept ???



Prise Alimentaire

« Début »: Augmentation Faible Apeline
(sang, intestin...)

« Fin »: Augmentation Forte Apeline
(sang, intestin...)

**Favorise contraction, pour faciliter l'absorption,
mais pas utilisation (blocage NO hypothalamique)**

Arrêt contraction et favorise utilisation (pas de blocage NO hypothalamique)

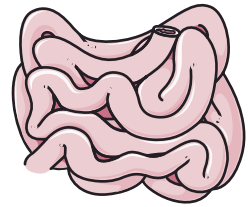
4- AXE PERTURBE SOUS REGIME HYPERLIPIDIQUE ?



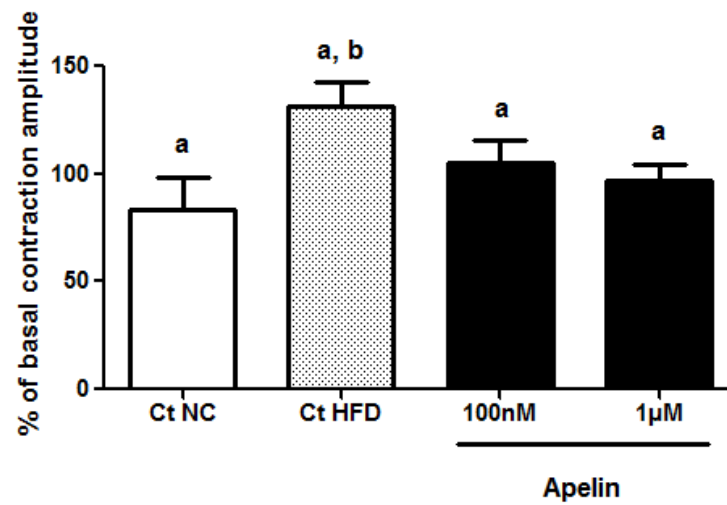
REGIME HYPERLIPIDIQUE (3 mois)



**Souris obèses/diabétiques
(SNE altéré...)**



CONTRACTIONS INTESTINALES (*ex vivo*)



NO HYPOTHALAMIQUE

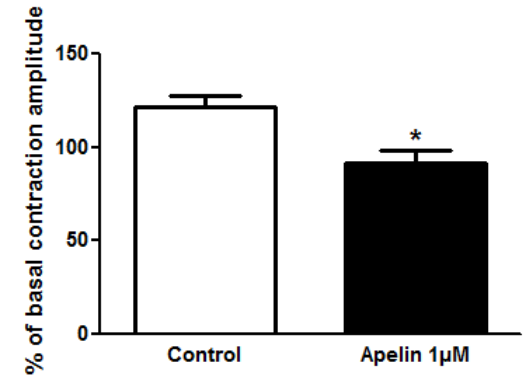
En cours...

4- GAVAGE CHRONIQUE A L' APELINE AMELIORE-T-IL LA TOLERANCE AU GLUCOSE DES SOURIS OBESES/DIABETIQUES SOUS REGIME HFD ?

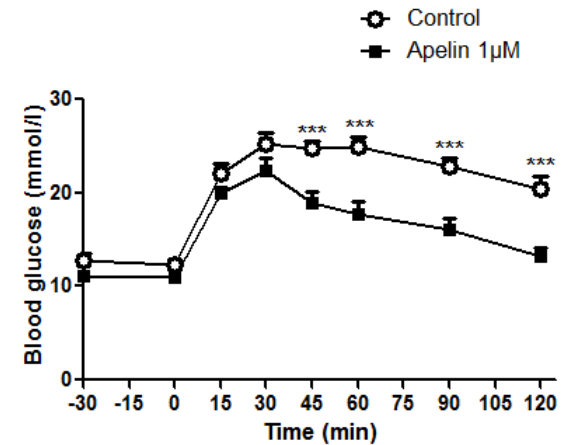
GAVAGE APELINE (1 μ M)
(1 SEMAINE)



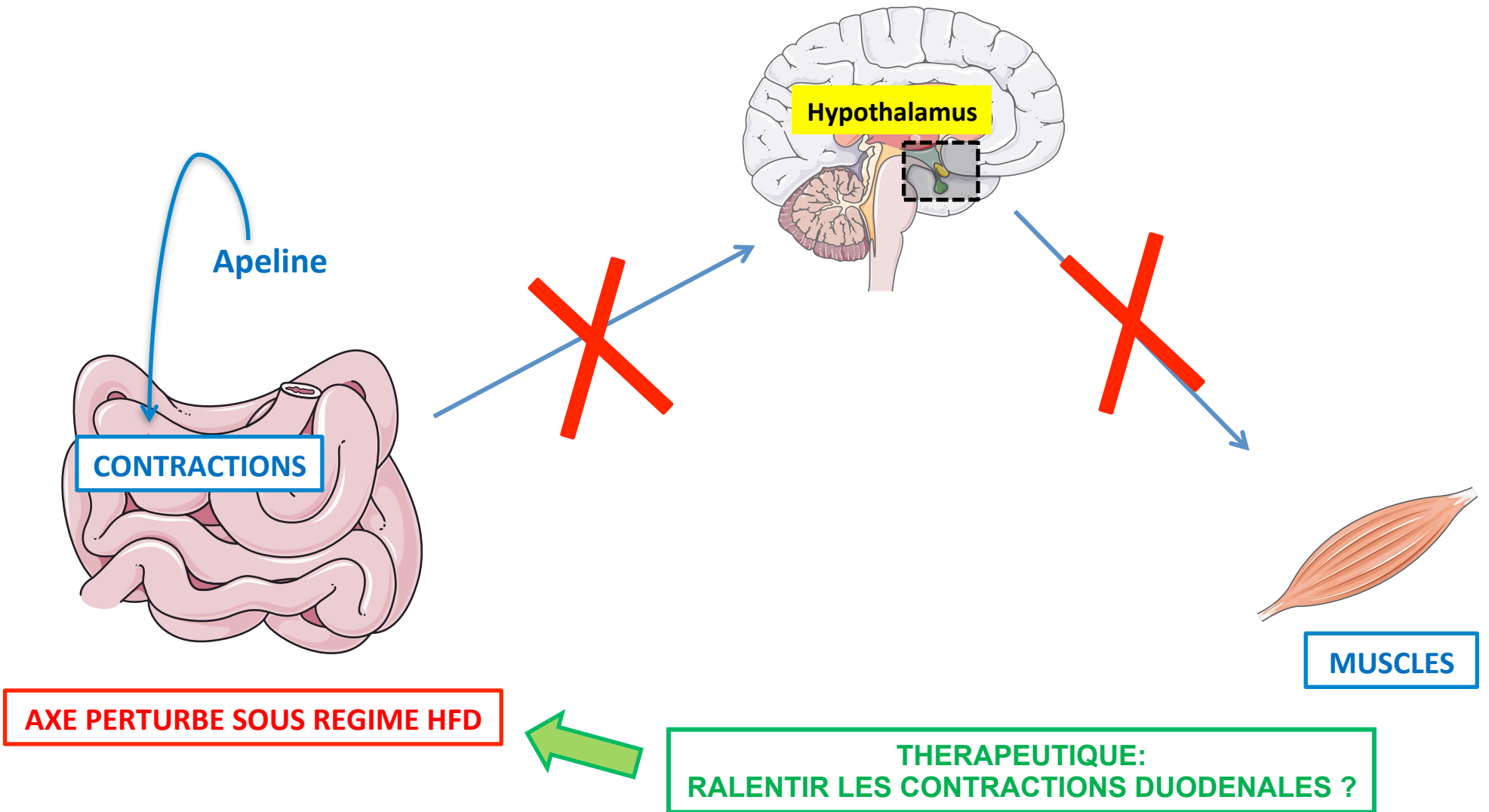
CONTRACTION INTESTINALE
BASALE



TEST TOLERANCE ORAL
AU GLUCOSE (OGTT)



CONCLUSIONS



PUBLICATIONS ASSOCIEES AU PROJET

1) Hypothalamic Apelin/Reactive Oxygen Species Signaling Controls Hepatic Glucose Metabolism in the Onset of Diabetes.

Drougard A, Duparc T, Brenachot X, Carneiro L, Gouazé A, Fournel A, Geurts L, Cadoudal T, Prats AC, Pénicaud L, Vieau D, Lesage J, Leloup C, Benani A, Cani PD, Valet P, Knauf C.

***Antioxidant and Redox Signaling*, 2013 in press (IF2012=7.2)**

2) Hypothalamic Actions of Apelin on Energy Metabolism: New Insight on Glucose Homeostasis and Metabolic Disorders.

Knauf C, Drougard A, Fournel A, Duparc T, Valet P.

***Hormones and Metabolic Research*, 2013 (revue, IF2012=2.1)**

3) Mechanical intestinal contractions control muscle glucose utilization via the hypothalamus: Impact of apelin on enteric nervous system

Fournel A, Drougard A, Duparc T, Brierley S, Page A, Colom A, Le-Gonidec S, Cenac N, Vergnolle N, Valet P, Cani PD, Knauf C.

A soumettre en 2014



REMERCIEMENTS



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« NeuroMicrobiota »**

