JFN 2014 - Bruxelles

Stress et régulation neuropeptidique de la prise alimentaire

Pierre Déchelotte
INSERM 1073 – IRIB- Service de Nutrition - CHU de Rouen

Instituts thématiques
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- **<u>Déclaration d'intérêts de Mme/M.</u>** : ……..

➢ **Activités de conseil, fonctions de gouvernance, rédaction de rapports**
Non *Société(s) : ……*

➢ **Essais cliniques, autres travaux, communications de promotion**
Non *Société(s) : ……*

➢ **Intérêts financiers (actions, obligations)**
Non *Société(s) : ……*

➢ **Liens avec des personnes ayant des intérêts financiers ou impliquées dans la gouvernance**
Non *Société(s) : ……*

➢ **Réception de dons sur une association dont je suis responsable**
Non *Société(s) : ……*

➢ **Perception de fonds d'une association dont je suis responsable et qui a reçu un don**
Non *Société(s) : ……*

➢ **Détention d'un brevet, rédaction d'un ouvrage utilisé par l'industrie**
Non *Société(s) : ……*

** Effacer l'option inadéquate*

Stress et prise alimentaire

- Stress : facteur de risque de TCA/obésité
- Régulation de la prise alimentaire : peptides, récepteurs, intégration, récompense
- Stress et régulation neuropeptidique
- Rôle de la barrière intestinale et de l’immunité
- Implications pratiques

Facteurs de risque de TCA/obésité

- **Stress :**
  - - violences (psychologiques, physiques, sexuelles)
  - - maladies, accidents, deuil
  - - stress affectif, scolaire, universitaire, professionnel...
  - - régimes restrictifs
  - - séparations parentales, conflits familiaux
- Antécédents familiaux : dépression, addictions, TCA,
- Périodes de vulnérabilité particulière:
  - adolescence, adulte jeune, grossesse et post-partum
- Facteurs génétiques

Prevalence and association of perceived stress, substance use and behavioral addictions: a cross-sectional study among university students in France, 2009–2011

Marie Pierre Tavolacci[1,2*], Joel Ladner[2,3], Sebastien Grigioni[2,4], Laure Richard[4], Herve Villet[5] and Pierre Dechelotte[2,4]

Table 4 Risk factors associated with perceived stress by quartile (logistic regression) (N = 1876)

	Q1 [0–09]	Q2 [10-15] AOR (95% CI)	p	Q3 [16-20] AOR (95% CI)	p	Q4 [>20] AOR (95% CI)	p
Male	1.00	0.58 [0.41-0.81]	0.0014	0.40 [0.28-0.57]	$<10^{-3}$	0.18 [0.11-0.26]	$<10^{-3}$
Curriculum							
Practice of sport	1.00	0.70 [0.51-0.97]	0.03	0.71 [0.51-1.00]	0.05	0.57 [0.39-0.80]	0.001
Regular smoker (≥1cigarette per day)	1.00	0.98 [0.67-1.43]	0.92	1.62 [1.11-2.36]	0.01	1.57 [1.04-2.37]	0.03
Regular alcohol user	1.00	0.87 [0.57-1.31]	0.49	0.64 [0.42-1.00]	0.05	0.63 [0.39-1.02]	0.06
Binge drinking	1.00	1.24 [0.76-2.05]	0.39	1.01 [0.60-1.71]	0.97	1.12 [0.62-2.03]	0.69
Alcohol abuse problems (Positive ADOSPA test)	1.00	1.32 [0.91-1.91]	0.14	1.65 [1.12-2.42]	0.01	2.22 [1.46-3.35]	0.0002
Drunkenness >10 per year	1.00	1.05 [0.65-1.68]	0.85	0.93 [0.57-1.54]	0.79	0.77 [0.43-1.36]	0.37
Eating disorders (positive Scoff)	1.00	1.61 [0.99-2.61]	0.05	2.72 [1.42-3.64]	0.0007	5.45 [3.42-8.69]	$<10^{-3}$
Risk of cyber addiction (Orman test)	1.00	1.58 [1.09-2.30]	0.01	2.02 [1.39-2.95]	0.0003	2.85 [1.90-4.28]	$<10^{-3}$

Stress et TCA chez les étudiants coréens

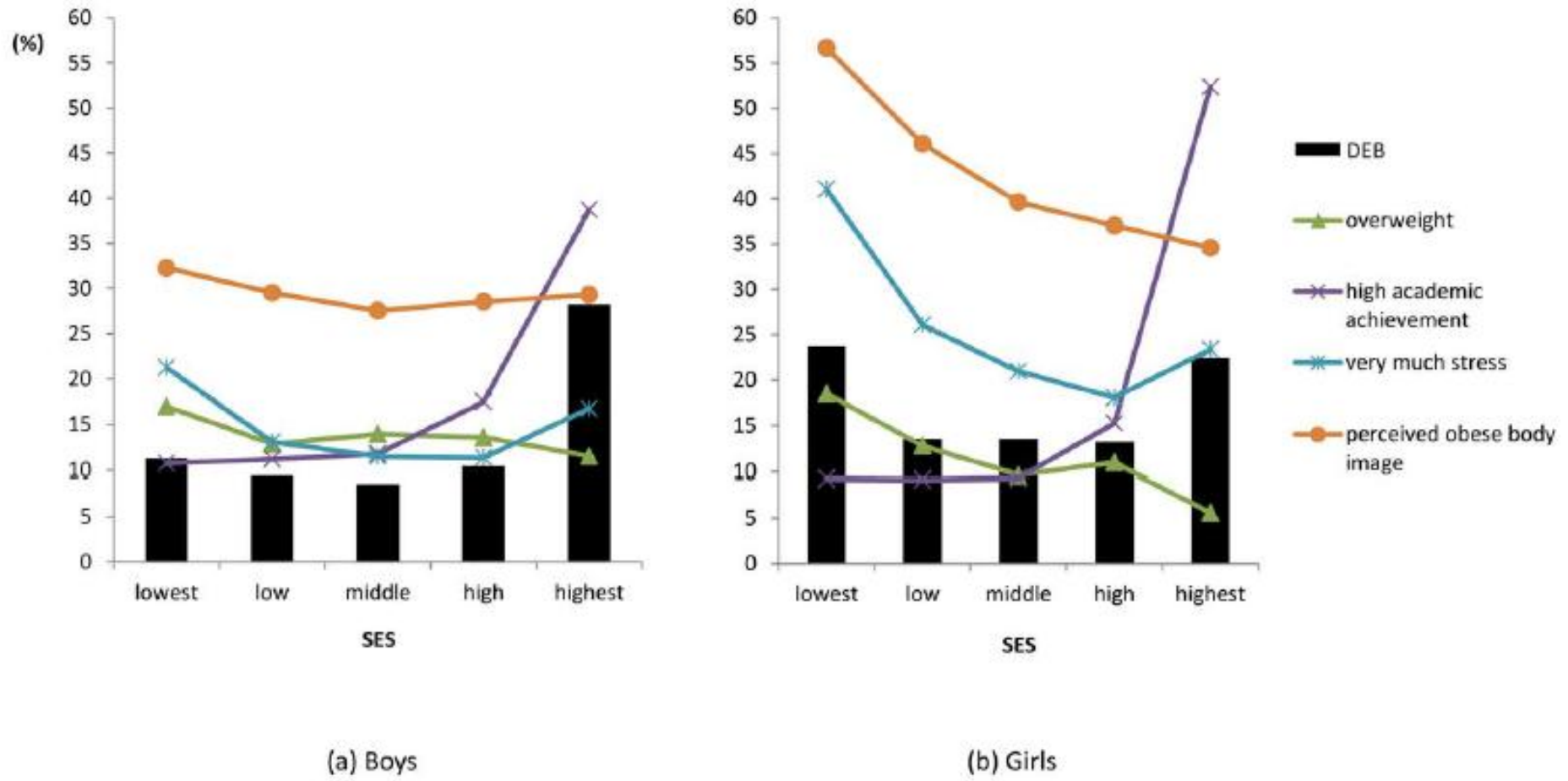

Figure 1. Distribution of Disturbed Eating Behavior (DEB) and related factors by Socioeconomic Status (SES) in boys and girls. We calculated the prevalence (%) and 95% Confidence Interval of DEB among those who were overweight, were very stressed, perceived themselves as fat, and had high academic achievement according to SES by gender.
doi:10.1371/journal.pone.0057880.g001

Lee Plos one 2013

Stress as a Common Risk Factor for Obesity and Addiction

Rajita Sinha and Ania M. Jastreboff

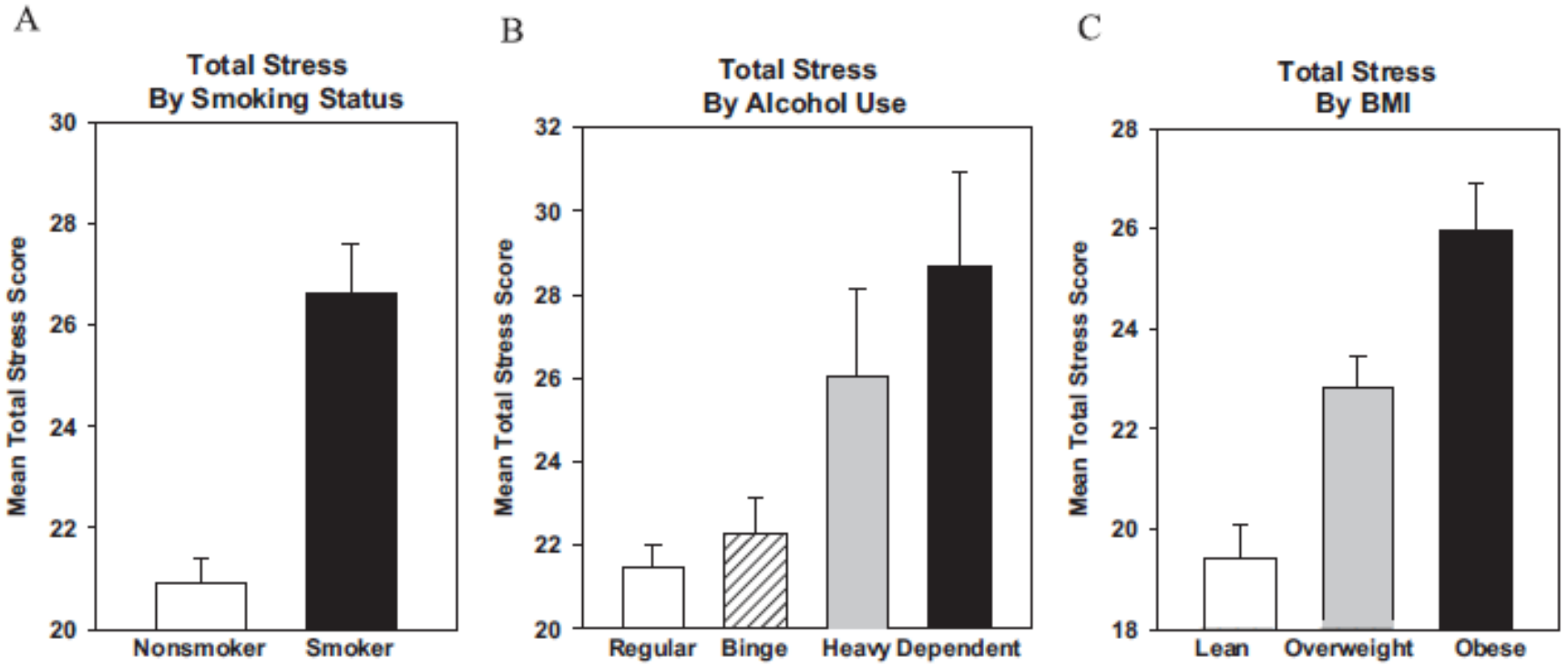

Figure 1. Total stress scores for cumulative adverse life events and chronic stress associated with **(A)** current smoking status [$\chi_1^2 = 31.66$, $p < .0001$; odds ratio (OR): 1.196 (95% confidence interval [CI]: 1.124–1.273)]; **(B)** current alcohol use as categorized by National Institute on Alcohol Abuse and Alcoholism criteria for regular, binge, and heavy levels of consumption and DSM-IV-R diagnosis for alcohol dependence [$\chi_1^2 = 15.37$, $p < .0001$; OR: 1.113 (95% CI: 1.055–1.173)]; and **(C)** current body mass index (BMI) groups for lean ($n = 206$), overweight ($n = 199$), and obese ($n = 183$) [$\chi_1^2 = 25.47$, $p < .0001$, OR: 1.146 (95% CI: 1.087–1.208)] assessed in a community sample of 588 participants.

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Neuropeptides hypothalamiques, récepteurs et appétit

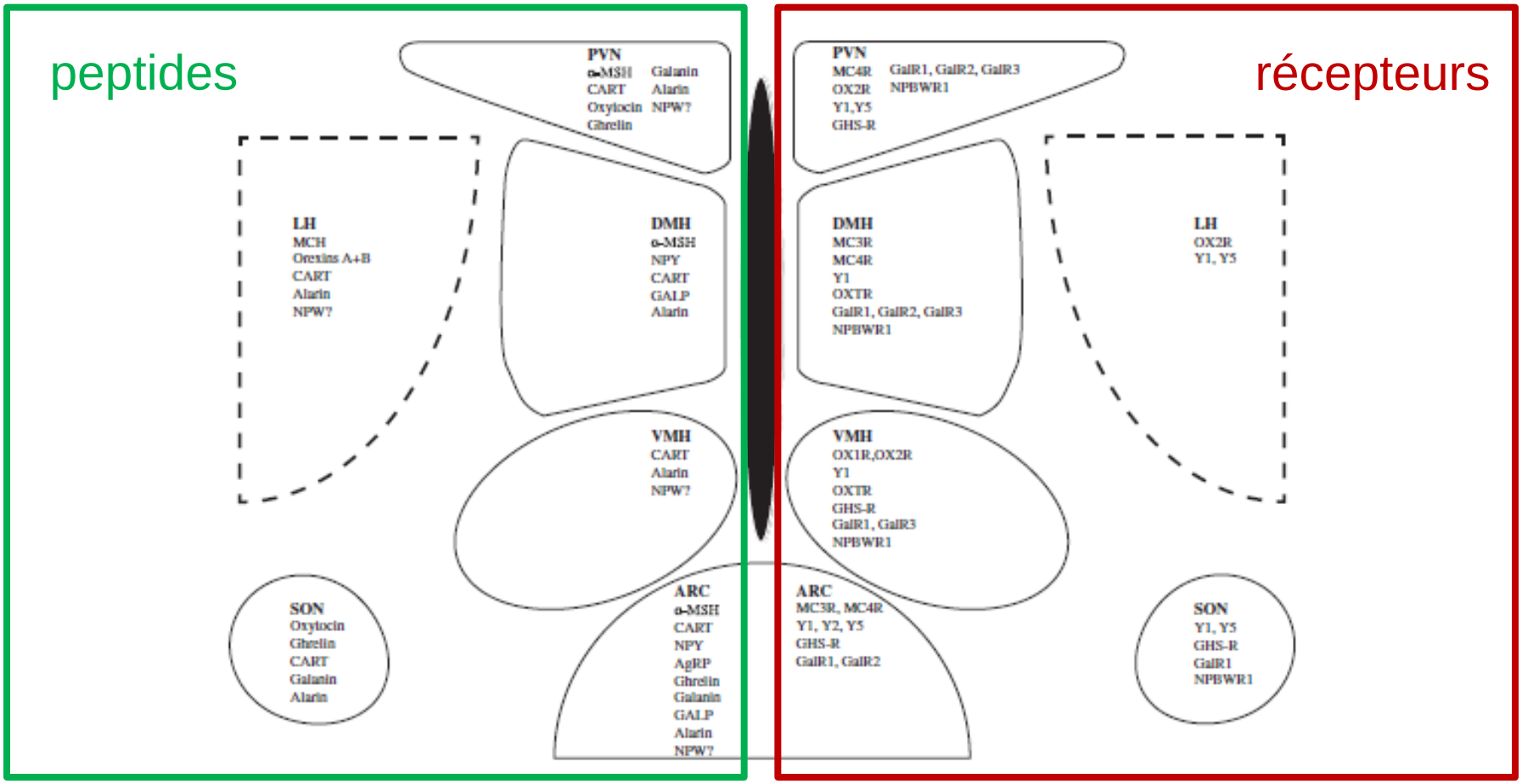
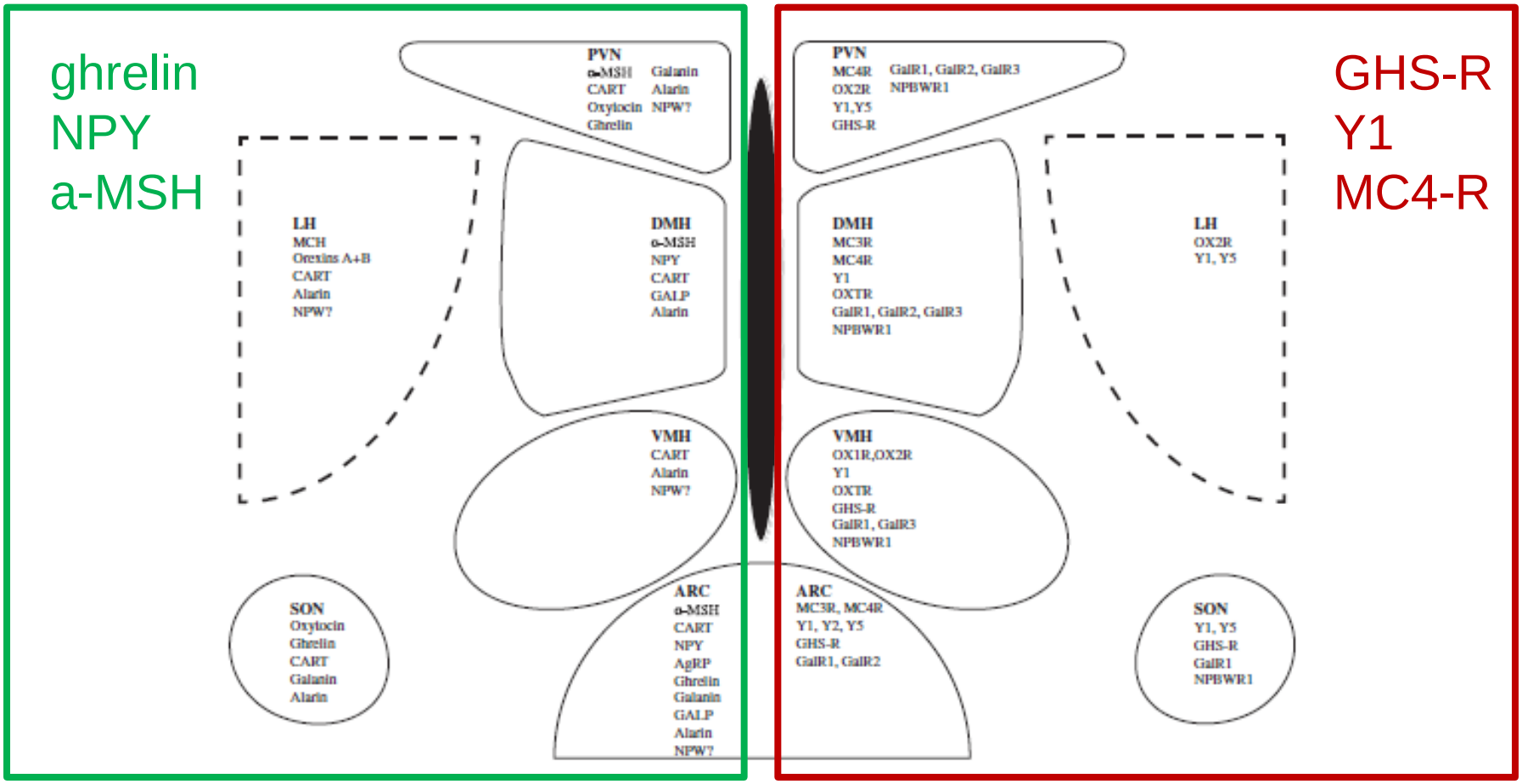


Fig. 1. Hypothalamic neuropeptides and their receptors within the hypothalamus. Left hand side shows where cell bodies of neuropeptide expressing neurons are located, right hand side shows where cells bodies of neuropeptide receptor expressing neurons are found. PVN paraventricular nucleus, LH lateral hypothalamus, DMH dorsomedial hypothalamus, VMH ventromedial hypothalamus, SON supraoptic nucleus, ARC arcuate nucleus, α-MSH α-melanocyte stimulating hormone, CART cocaine and amphetamine-related transcript, NPW neuropeptide W, MCH melanin-concentrating hormone, NPY neuropeptide Y, GALP galanin-like peptide, AgRP agouti-gene related protein, MC4R melanocortin 4 receptor, MC3R melanocortin 3 receptor, OX1R orexin 1 receptor, OX2R orexin 2 receptor, GHS-R growth hormone secretagogue receptor, GalR1 galanin receptor 1, GalR2 galanin receptor 2, GalR2 galanin receptor 2, NPBWR1 neuropeptide B/W receptor 1, OXTR oxytocin receptor.

Parker & Bloom, Neuropharmacol 2012

Neuropeptides hypothalamiques, récepteurs et appétit



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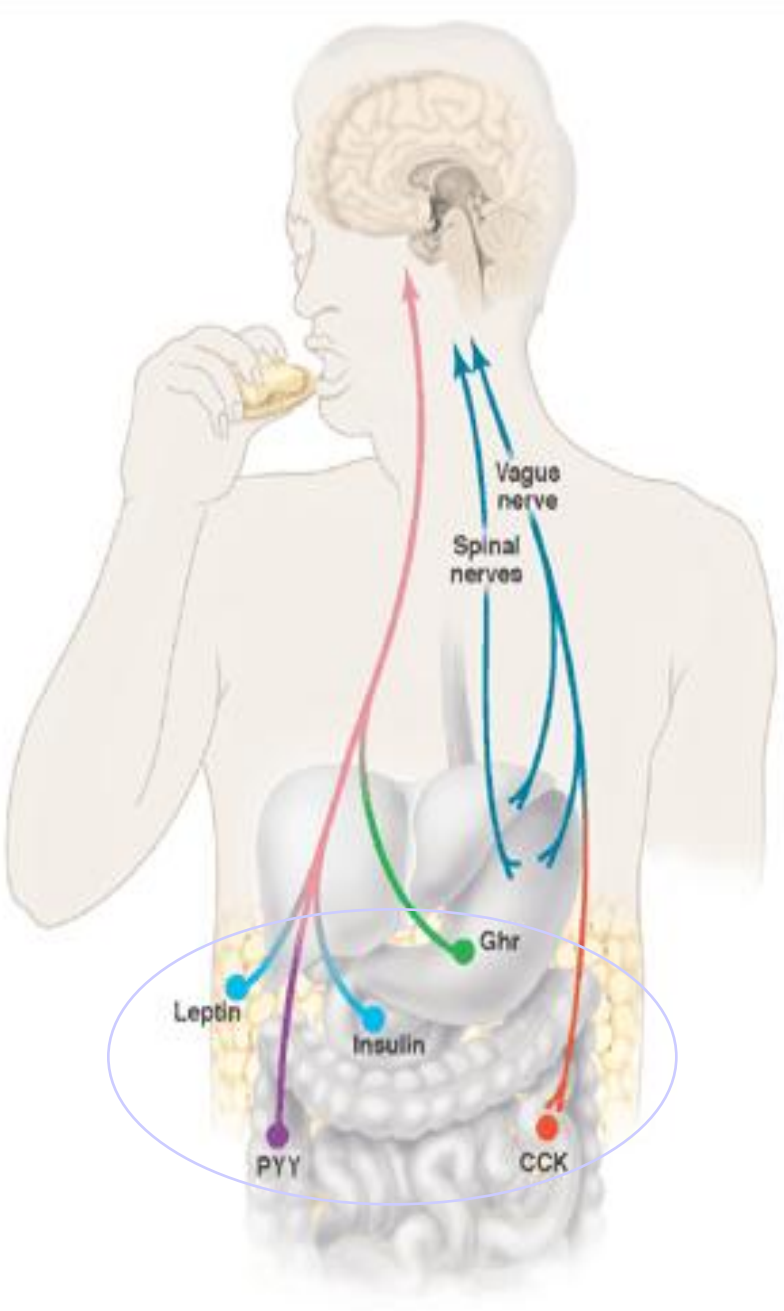
Parker & Bloom, Neuropharmacol 2012

Marx J., Science 299, 2003



Régulation hypothalamique de l'appétit

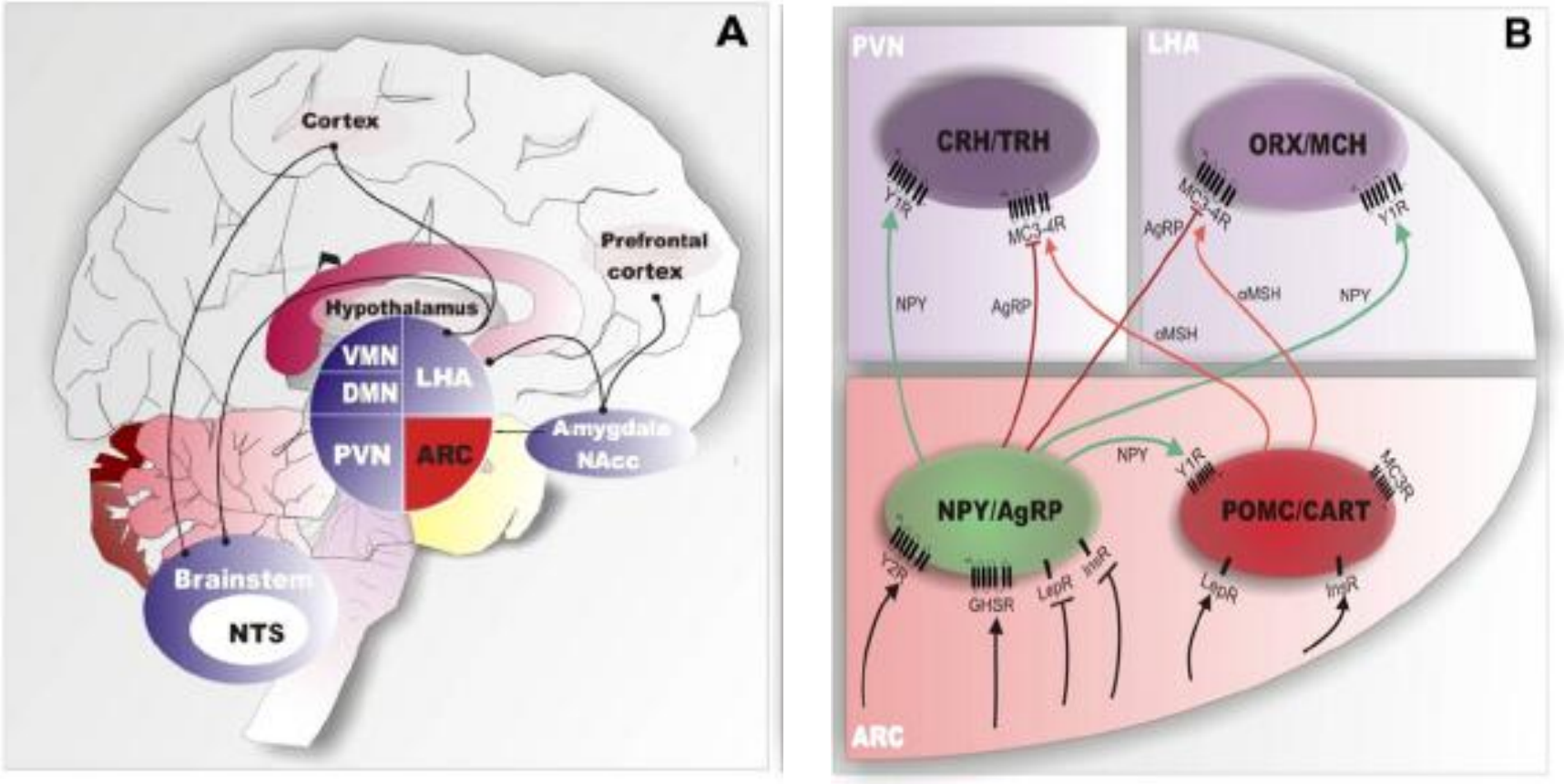
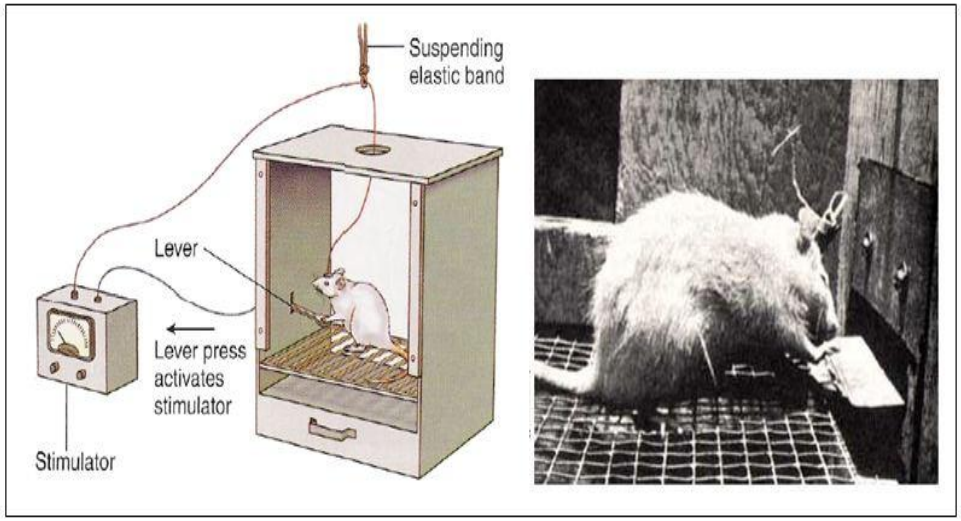
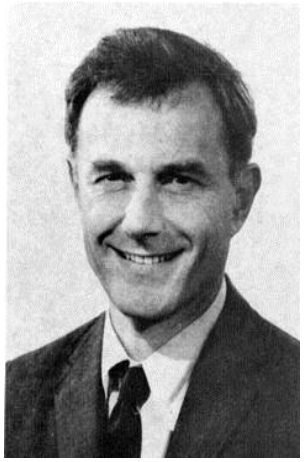


Fig. 2. Hypothalamic regulation of appetite. The ARC of the hypothalamus is the main area controlling appetite (**A**). Orexigenic neurons co-expressing NPY/AgRP and anorexigenic POMC/CART neurons are the major groups of neurons in the ARC modulating appetite control (**B**). Peripheral signals such as ghrelin, leptin and insulin directly modulate receptors expressed on these neurons leading to neuronal excitation and downstream signalling through MC_3 and MC_4 on neurons in other hypothalamic brain areas such as the PVN and LHA. Ghrelin stimulates NPY/AgRP neurons and increases food intake, whereas insulin and leptin inhibit NPY/AgRP neurons and stimulate POMC/CART neurons, suppressing food intake. POMC is processed into melanocortin peptides, including α-MSH following cleavage by prohormone convertases 1 and 2 (PC1 and PC2) and induce satiety by activation of the downstream MC_3 and MC_4. In contrast, NPY inhibit the POMC/CART neurons and AgRP antagonises α-MSH.

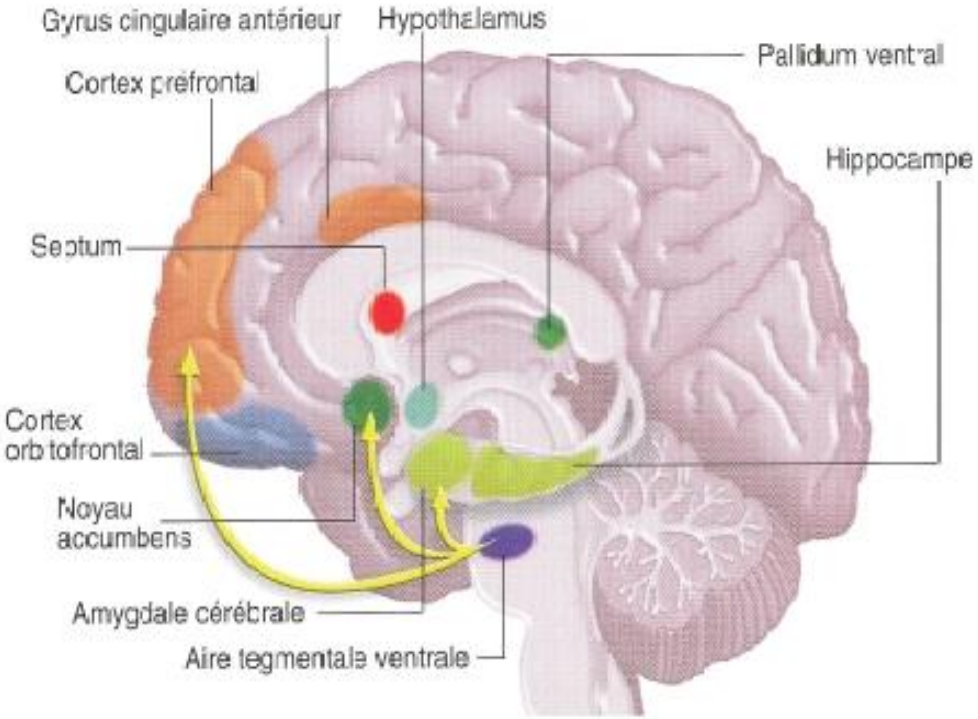
Schellekens, Pharm Therap 2012

Découverte du circuit de la récompense : Olds & Milner, 1954



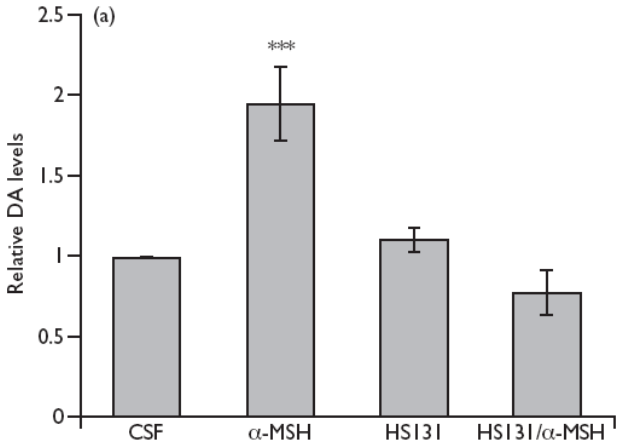


James Olds (1922 - 1976)

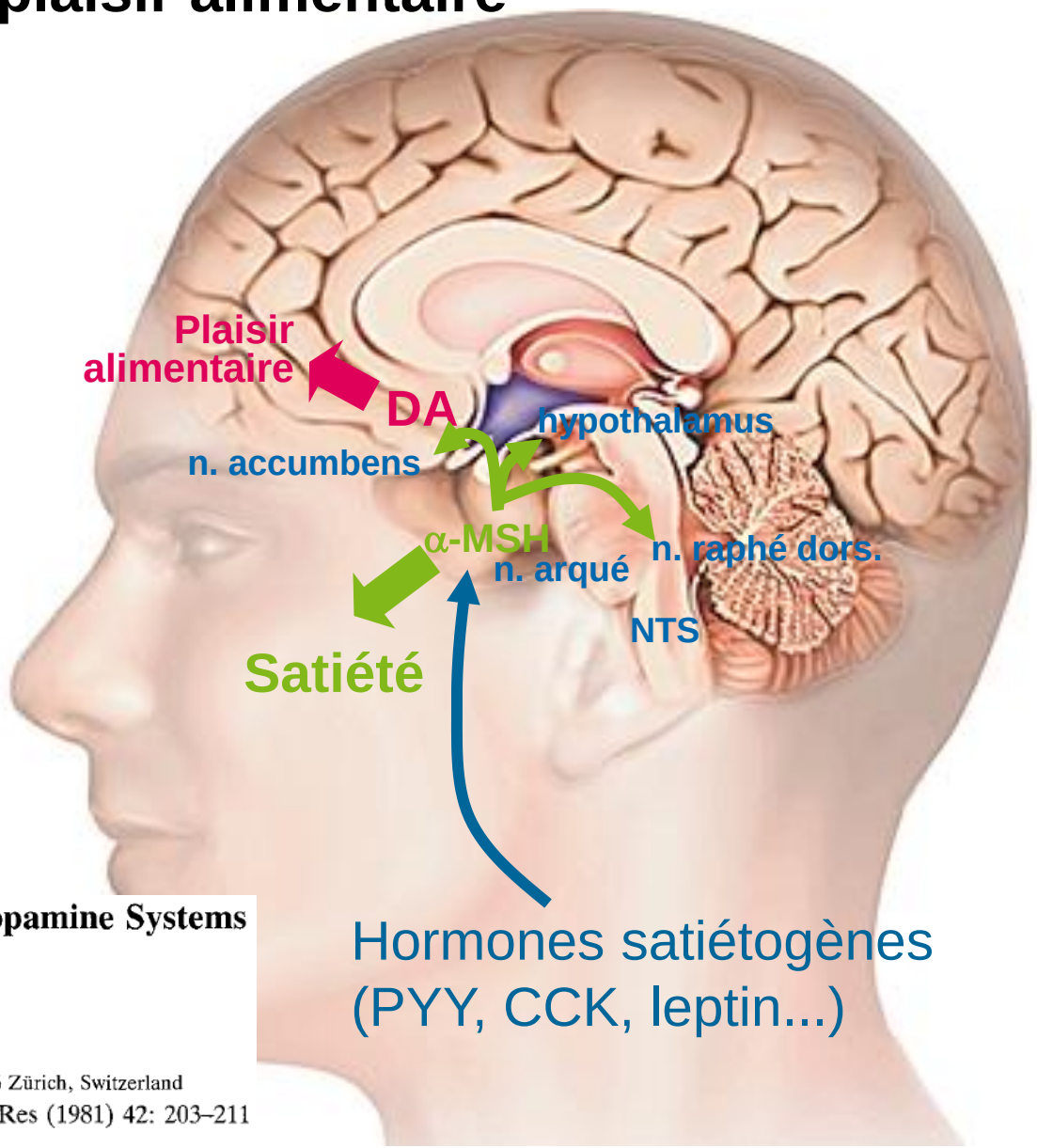


Interactions entre les voies centrales de la satiété et du plaisir alimentaire

Sécrétion de la dopamine dans le n. accumbens



(Lindblom et al Neuroreport 2001)



Endogenous α-Melanotropin and Central Dopamine Systems in Physical and Psychological Stress*

F. Monnet and W. Lichtensteiger

Department of Pharmacology, University of Zürich, Gloriastr. 32, CH–8006 Zürich, Switzerland

Exp Brain Res (1981) 42: 203–211

Ghrelin signalling and obesity: At the interface of stress, mood and food reward

Harriët Schellekens [a,e], Beate C. Finger [a,e], Timothy G. Dinan [a,b,c], John F. Cryan [a,b,d,*]

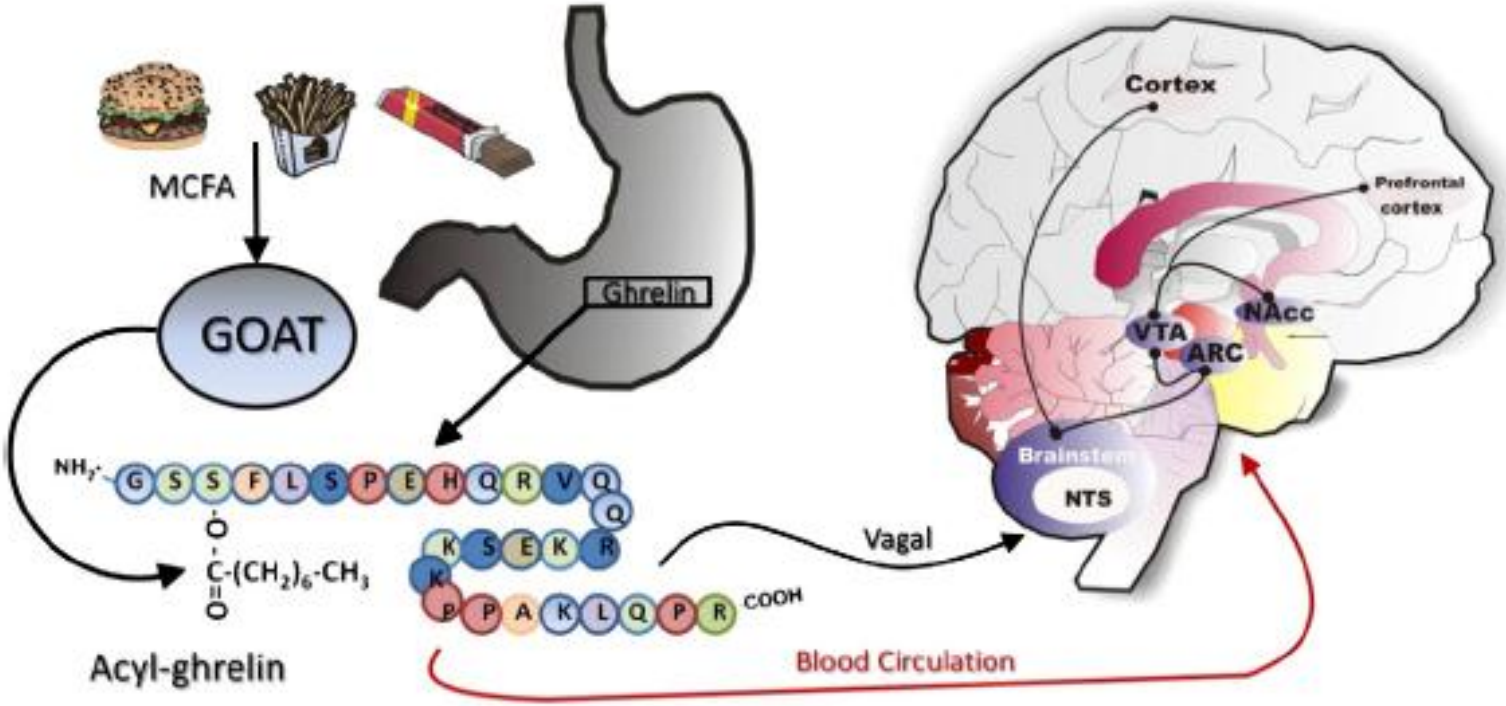


Fig. 1. Schematic of orexigenic ghrelin activation and signalling. Ghrelin is secreted from the stomach and in its activated form contains an eight-carbon fatty acid side chain at its serine 3 residue. Octanoylation of ghrelin is mediated by GOAT and is elevated depending on specific dietary lipids and medium chain fatty acids (MCFA) as acylation substrates. The activity of GOAT decreases during fasting but increases after ingesting MFCA. Peripheral acyl-ghrelin signals to the brain via GHS-R1a receptors expressed on afferent terminals of the vagus nerve and crosses the blood–brain barrier from the blood circulation, where ghrelin interacts with GHSRs expressed on neurons located in several brain areas, including (but not limited to) the NTS, ARC, VTA and NAcc.

Schellekens, Pharm Therap 2012

Stress et prise alimentaire

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Manian
Neuropharmacology 2012

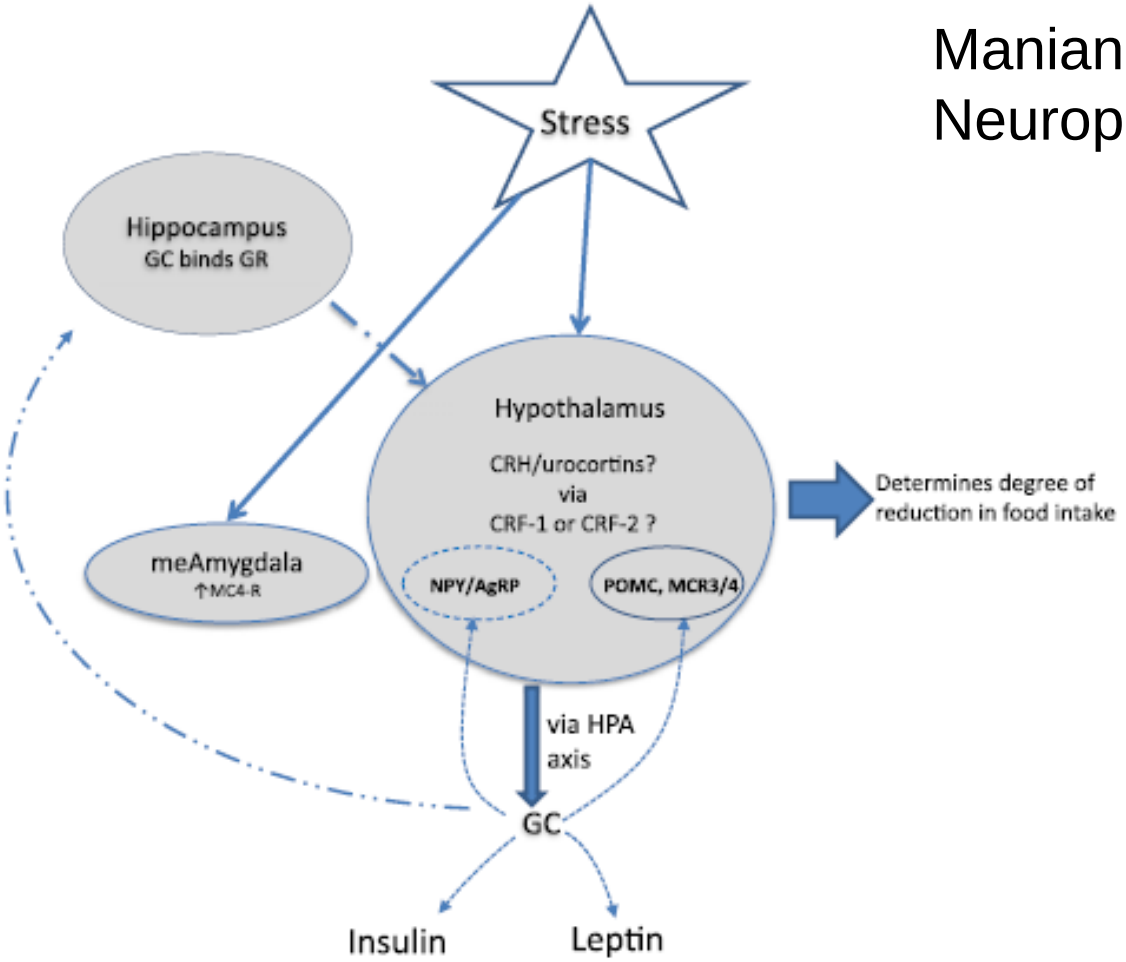
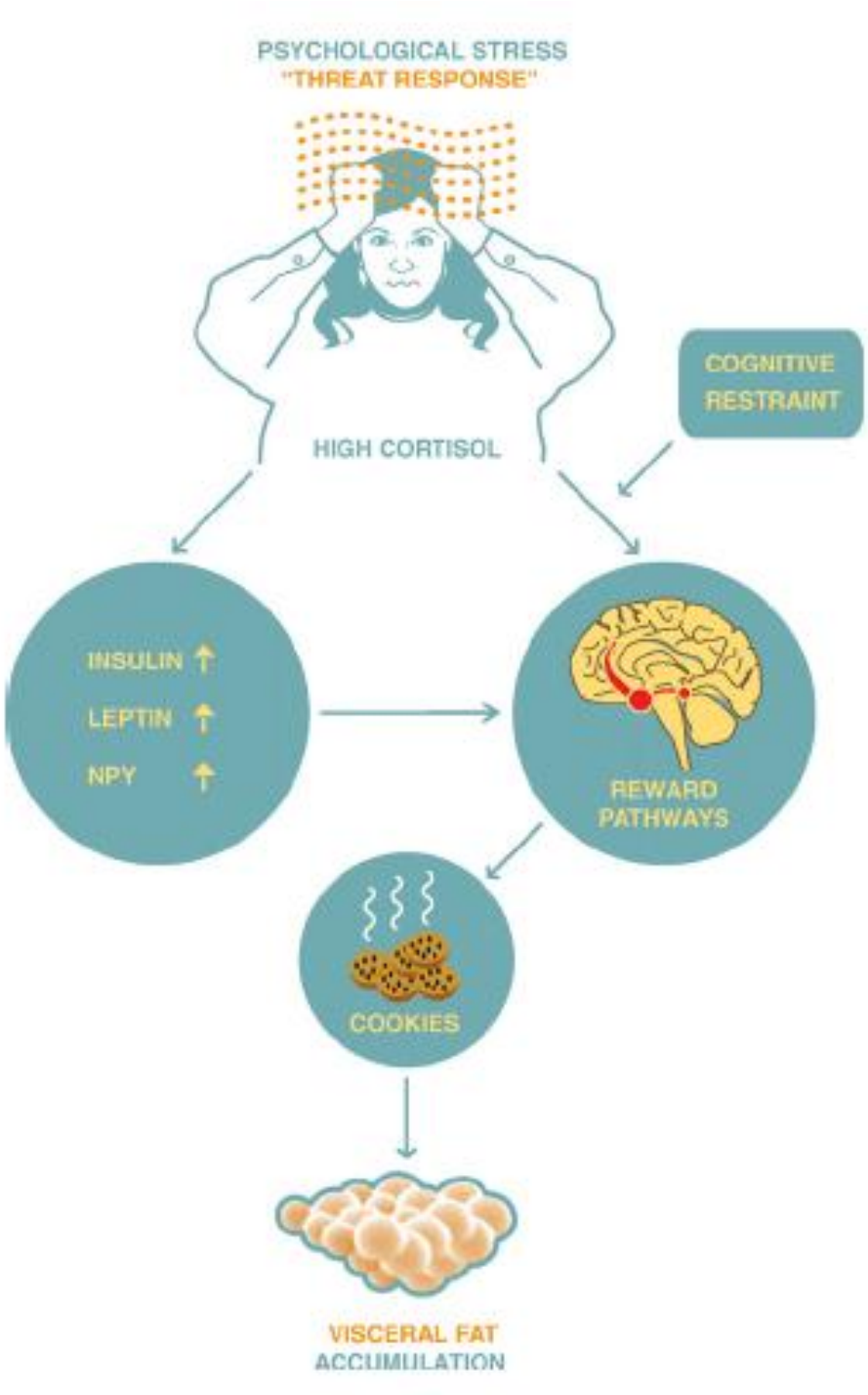


Fig. 1. Simplified schema of interactions between glucocorticoids (GC), hypothalamic appetite regulatory neuropeptides, and feeding hormones. Stress activates the HPA axis, stimulating CRH cells in the PVN as well as the medial amygdala (meAmygdala). Glucocorticoids released in response to stress bind GR in the hippocampus to reduce hypothalamic CRH/urocortin expression via CRH-1 or CRH-2 receptors (dotted line, negative feedback). The degree of activation or inhibition of appetite regulatory circuits depends on relative increases in CRH and urocortin, and the CRH receptor type activated. This determines the ultimate effect on food intake. Glucocorticods also affect insulin and leptin release, which can modulate feeding behaviour through hypothalamic appetite regulatory neuropeptides.



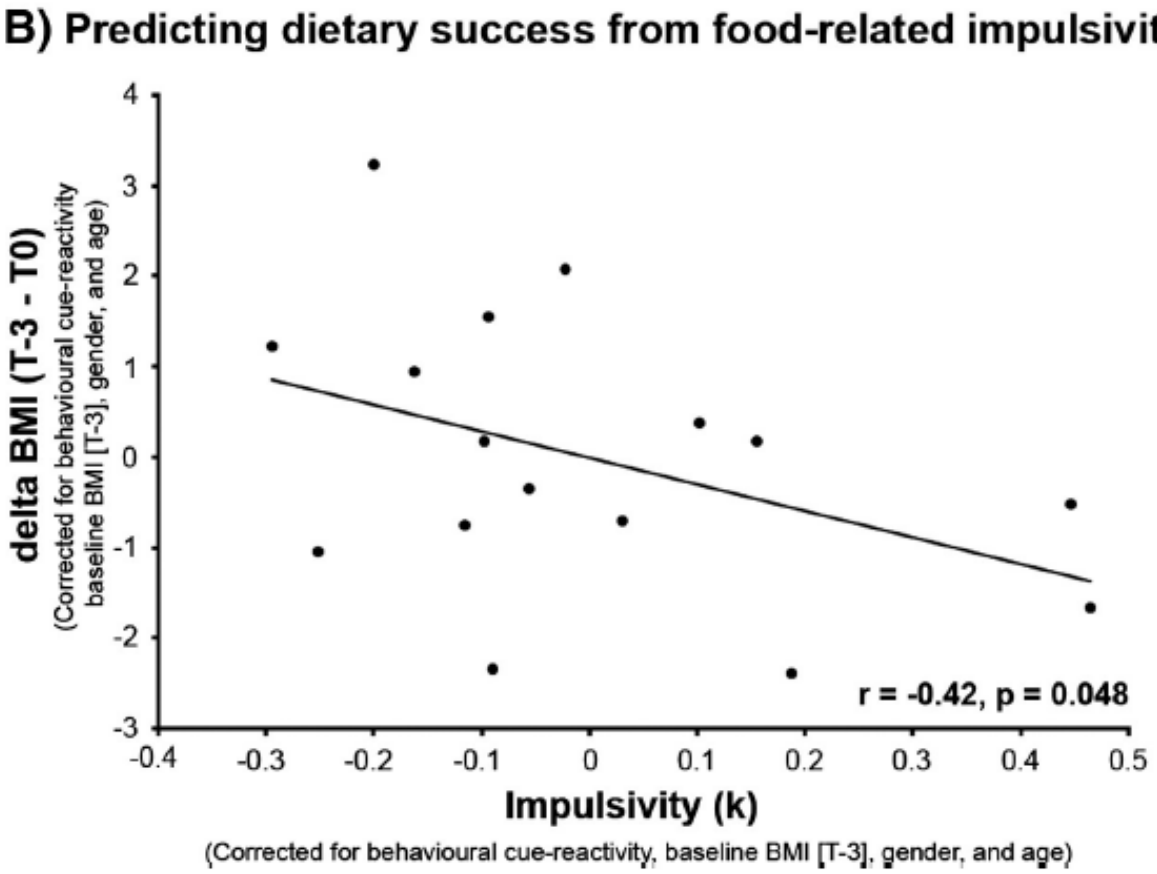
Stress aigu (physique)
→ Anorexie
→ Récupération adaptative

Stress chronique (métabolique, Psychologique)
→ Alimentation émotionnelle
→ Récompense > homéostasie
→ obésité

Adam Physiol Behav 2007

The role of neural impulse control mechanisms for dietary success in obesity

Martin Weygandt [a,b,c,*], Knut Mai [d], Esther Dommes [e], Verena Leupelt [d], Kerstin Hackmack [a,b,c], Thorsten Kahnt [a,f], Yvonne Rothemund [e], Joachim Spranger [d], John-Dylan Haynes [a,b,c,g]



NeuroImage 83 (2013) 669–678

Stress-related alterations of acyl and desacyl ghrelin circulating levels: Mechanisms and functional implications

Andreas Stengel[a,b], Lixin Wang[a], Yvette Taché[a,*]

- Impacts du stress variables selon stress :
  sécrétion,
  Acylation (ex. régime lipidique)
  liaison au récepteur

- Conséquences :
  prise alimentaire
  motricité gastro-intestinale
  immunité
  humeur et anxiété

Stengel, Peptides 2011

Schellekens, Pharm Therap 2012

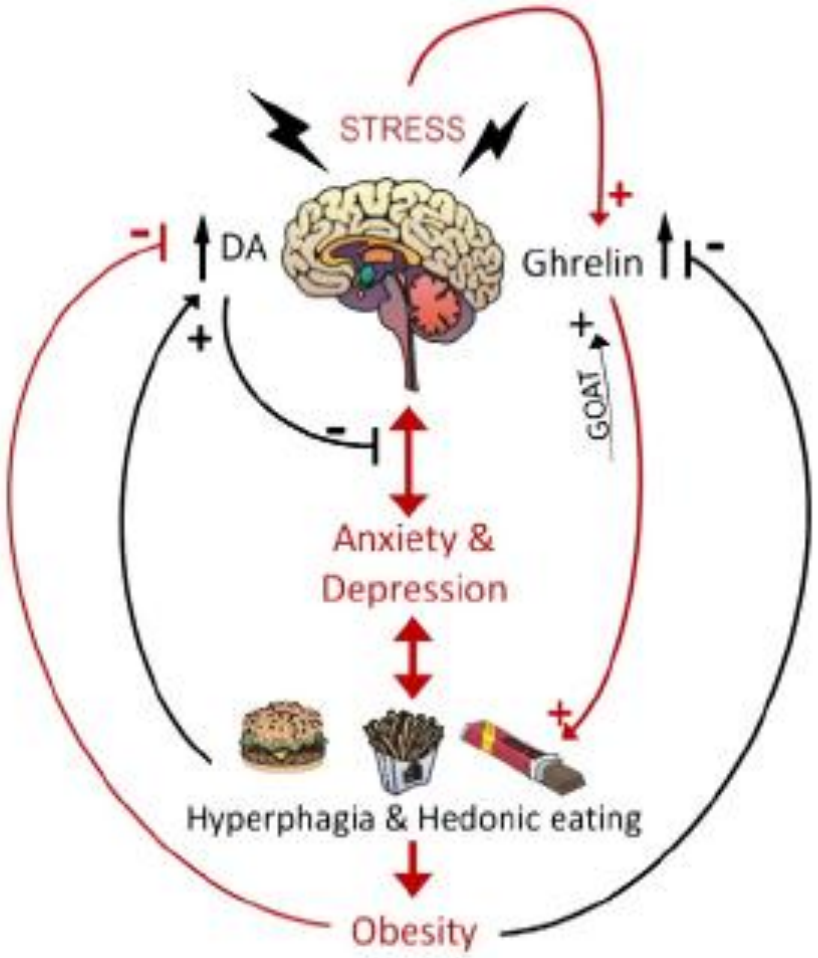


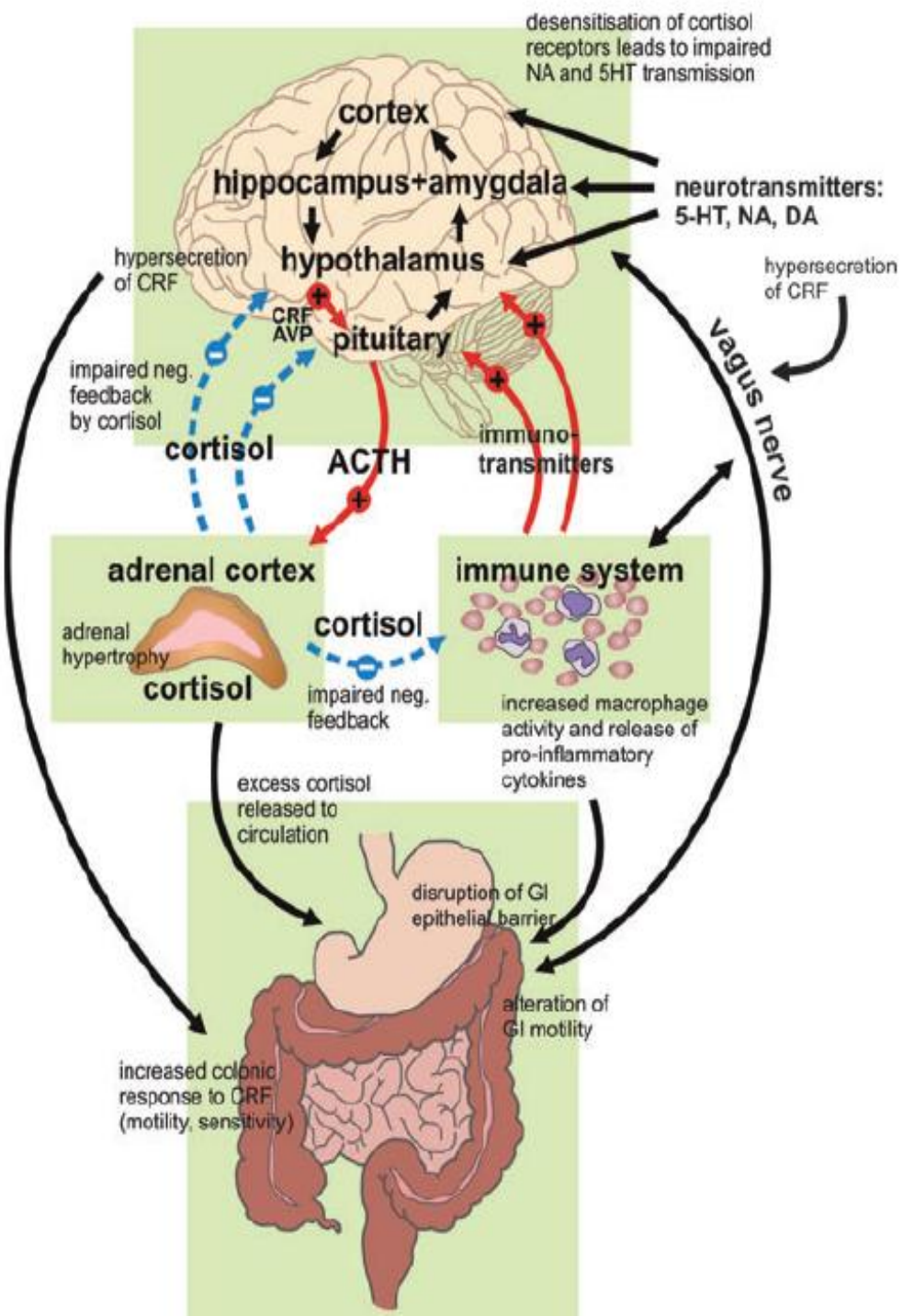
Fig 3. Model of the effect of stress on ghrelin-mediated eating behaviours in anxiety, depression and obesity. Prolonged stress increases the risk to develop psychological disorders of anxiety and depression. Increases in psychological stress elevate plasma ghrelin levels, which activates the hedonic signalling pathway and stimulates intake of caloric dense 'comfort' foods. Increased activity of the enzyme GOAT following fat digestion and lipid availability leads to enhance acylated-ghrelin levels further stimulating hyperphagia. Ghrelin-induced enhanced consumption of palatable foods elicits central reward pathways and increase dopamine signalling, which may act to reduce the deleterious effects of stress and minimises depression-like behaviours. However, this stress-induced food reward behaviour and hyperphagia of palatable caloric dense foods increases body weight, which in itself has been linked to major depressive disorders. While obesity generally decreases plasma ghrelin levels, the dopaminergic reward signalling is down-regulated, at the same time, following prolonged exposure to palatable foods leading to a desensitisation of reward signalling similar as observed in addiction behaviour. Thus, prolonged exposure to stress and 'comfort foods' may lead to worsening of the reward deficit, further fostering anxiety and depression and co-morbid obesity.

Ghrelin-derived peptides: a link between appetite/reward, GH axis, and psychiatric disorders?

*Alexandra Labarthe, Oriane Fiquet, Rim Hassouna, Philippe Zizzari, Laurence Lanfumey, Nicolas Ramoz, Dominique Grouselle, Jacques Epelbaum and Virginie Tolle **

FIGURE 2 | Plasma levels of preproghrelin-derived peptides in metabolic and psychiatric disorders. In anorexic patients, total ghrelin, acyl ghrelin, and obestatin are increased in the restrictive type and reduced in binge-purging. This may represent different abilities to adapt to starvation. In obesity syndromes, total ghrelin, acyl ghrelin and obestatin are either found reduced, unchanged, or increased. Discrepancies may be due to the variety of obesity syndromes (monogenic obesity, nutritionally induced obesity, presence of a metabolic syndrome, multifactorial disorders such as the Prader-Willi syndrome). In alcohol-dependent patients, ghrelin is found either reduced or increased compared to healthy subjects but there might be differences in gender, body mass index, nutritional/metabolic status and/or time after alcohol withdrawal from one study to another that can explain the contradictory results. In major depressive disorders, the majority of studies report no differences in plasma total or acyl ghrelin levels compared with healthy controls. Whether ghrelin can contribute to the degree of food craving, alcohol craving or depression is not clearly demonstrated as treatments and metabolic modifications can interfere with the results.

Labarthe, Frontiers Endoc 2014

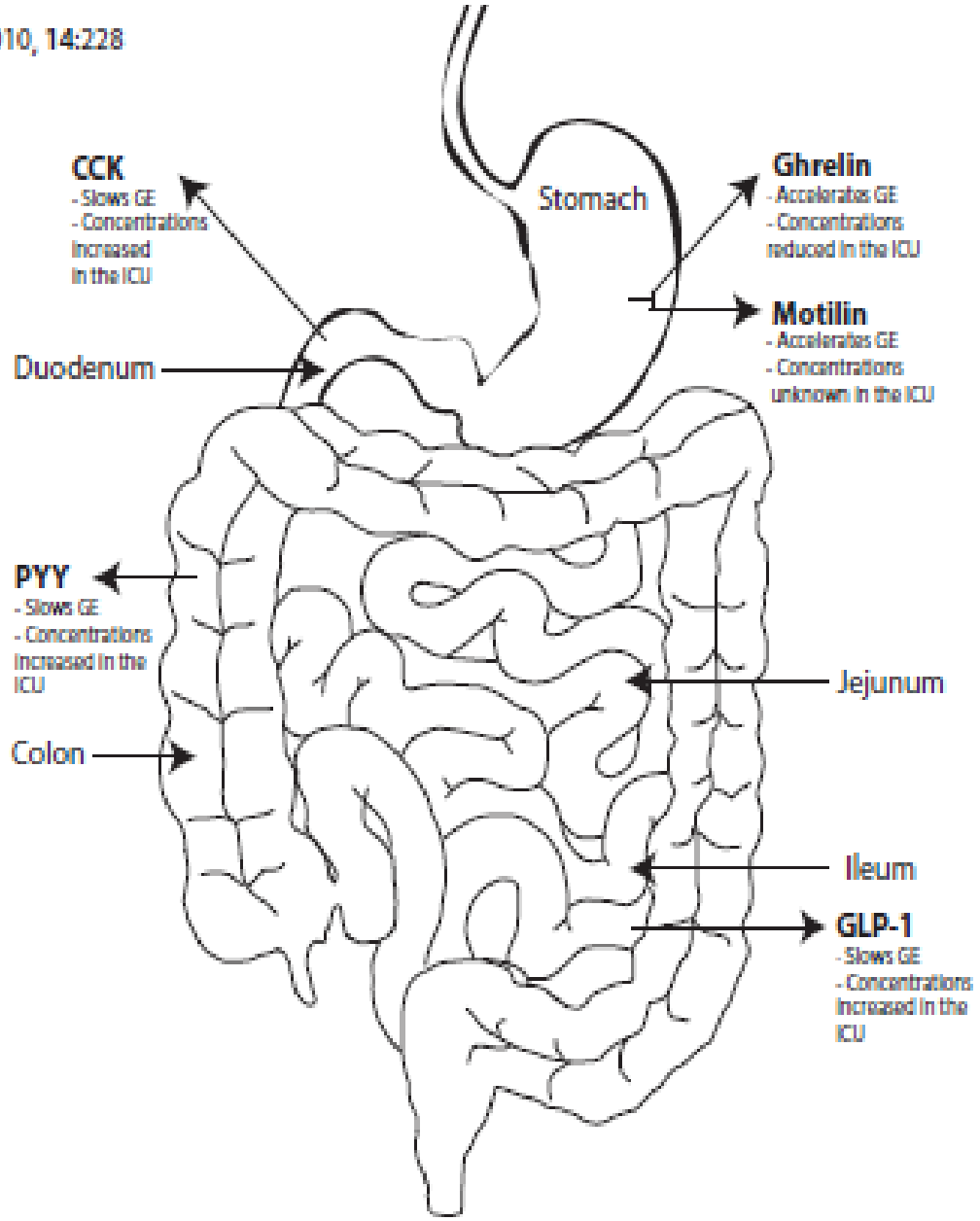


Stress chronique, dépression, obésité : implication de l'axe intestin-cerveau

Dinan & Cryan
Neurogastro 2013

Bench-to-bedside review: The gut as an endocrine organ in the critically ill

Deane *et al. Critical Care* 2010, 14:228



Annu. Rev. Physiol. 2009. 71:219–39

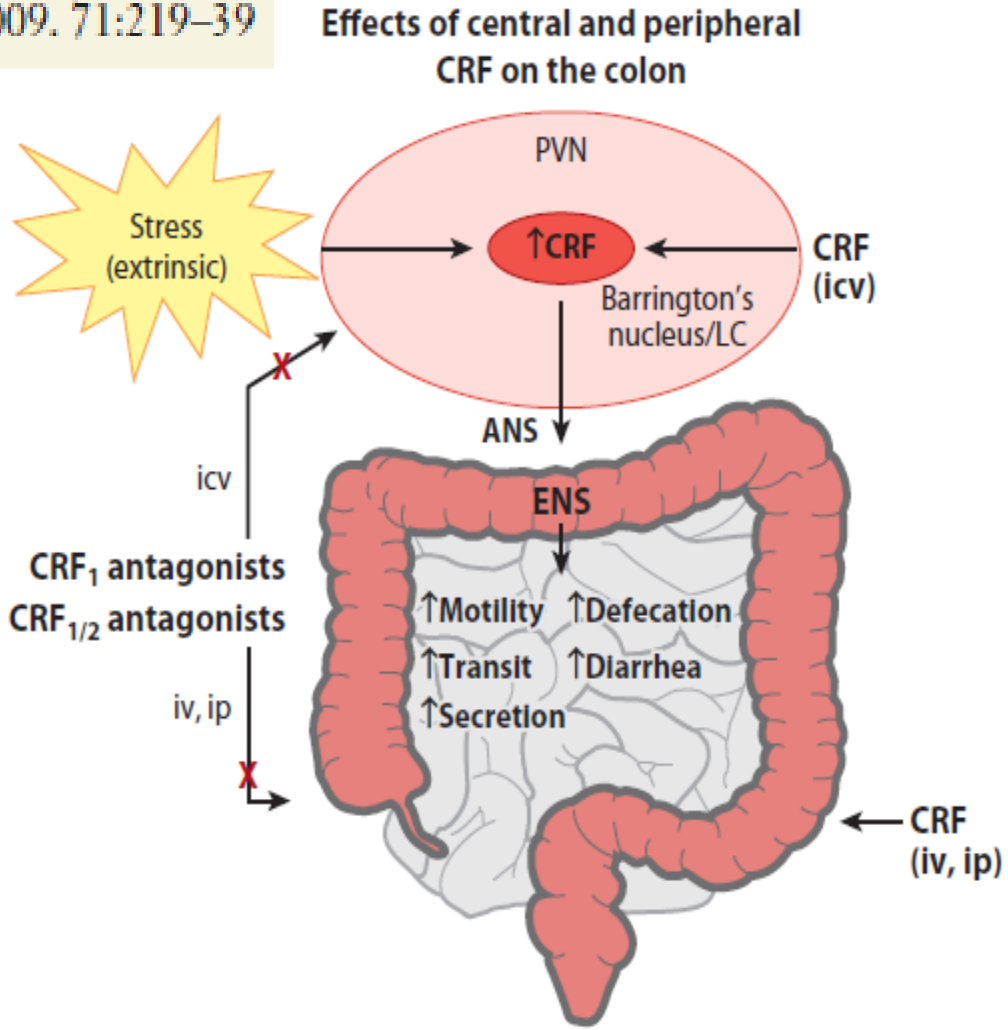


Figure 2

Summary of corticotropin-releasing factor (CRF) actions on colonic function. Central and peripheral CRF stimulates various colonic functions, which recapitulate the effects of stress and are blocked by nonselective and CRF_1-selective CRF receptor antagonists. Abbreviations: ANS, autonomic nervous system; ENS, enteric nervous system; icv, intracerebroventricularly injected; ip, intraperitoneally injected; iv, intravenously injected; LC, locus coeruleus; PVN, paraventricular nucleus of the hypothalamus.

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Corticotropin-releasing hormone (CRH) regulates macromolecular permeability via mast cells in normal human colonic biopsies *in vitro*

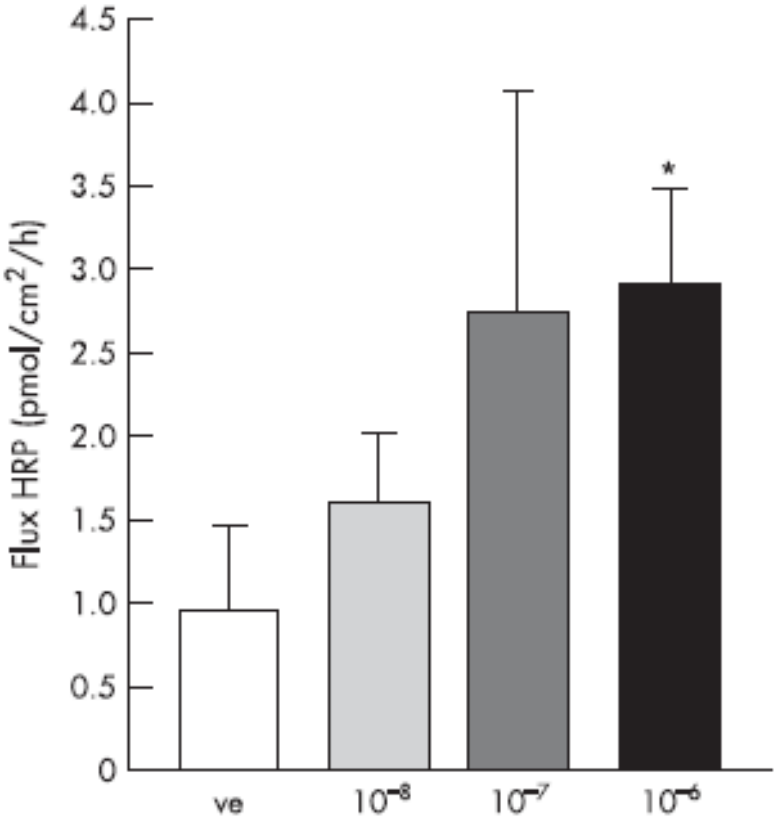


Figure 1 CRH exposure caused a dose-dependent increase in HRP permeation. There was a significant difference between CRH 10^{-6} mol/l (2.9 ± 0.5 pmol/cm²/h) compared to vehicle (ve) (1.0 ± 0.5); *ANOVA <0.05, $p = 0.0068$, Fischer PLSD. HRP uptake after exposure to CRH 10^{-8} mol/l (1.6 ± 0.4) or CRH 10^{-7} mol/l (2.7 ± 1.4) did not differ significantly from vehicle. Data are presented as mean $\pm$ SEM; $n = 6$ volunteers.

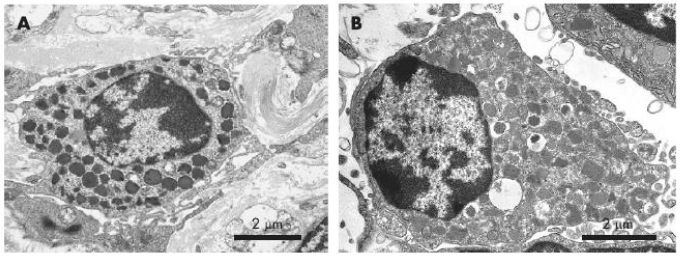
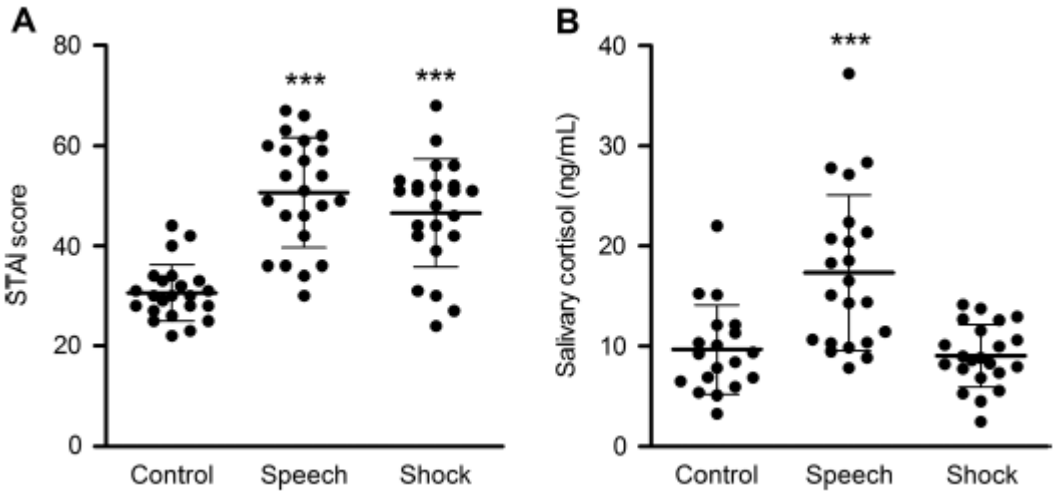


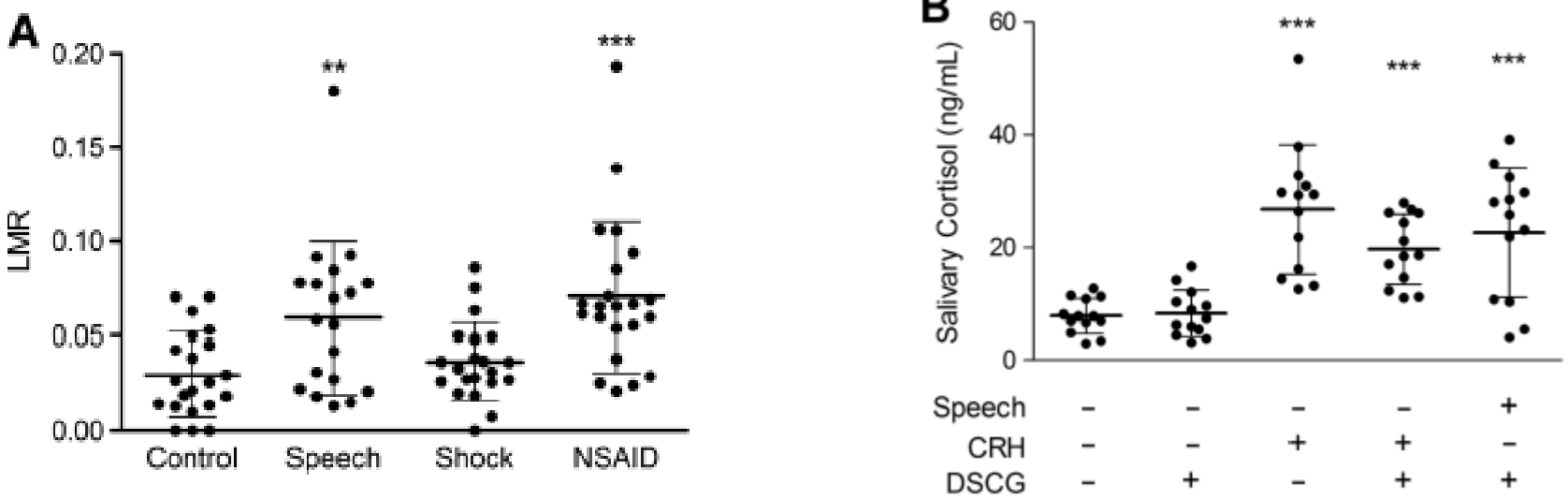
Figure 4 CRH exposure induced mast cell activation in human colon. Representative photomicrographs of sub-epithelial

Wallon Gut 2008

Psychological stress and corticotropin-releasing hormone increase intestinal permeability in humans by a mast cell-dependent mechanism

Vanuytsel Gut 2014





brain

↑

brain stem
spinal cord

↑

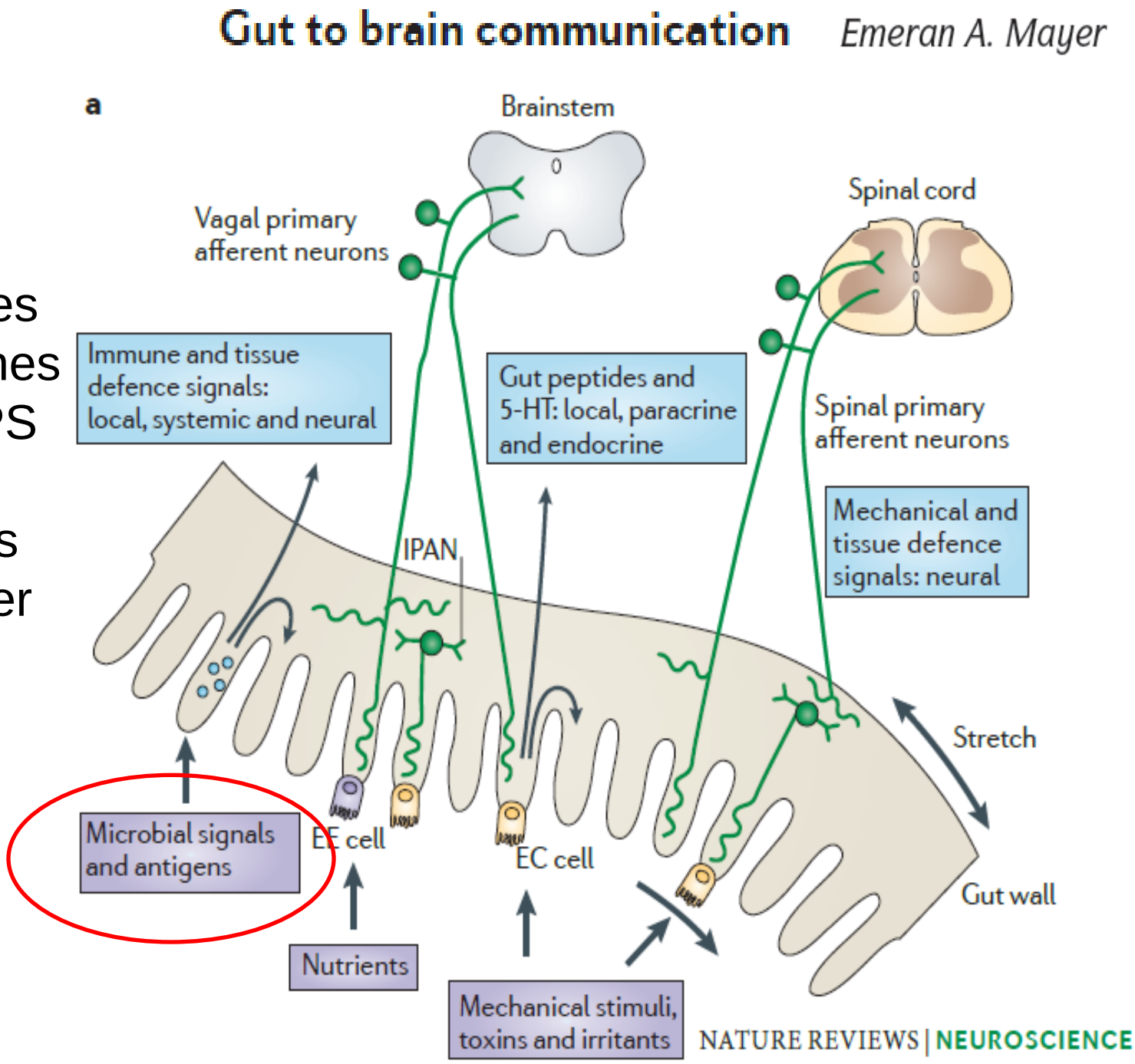
afferent nerves
peptides, amines
cytokines, LPS

↑

immune cells
epithelial layer
mucus

↑

nutrients,
microbiota,
toxins

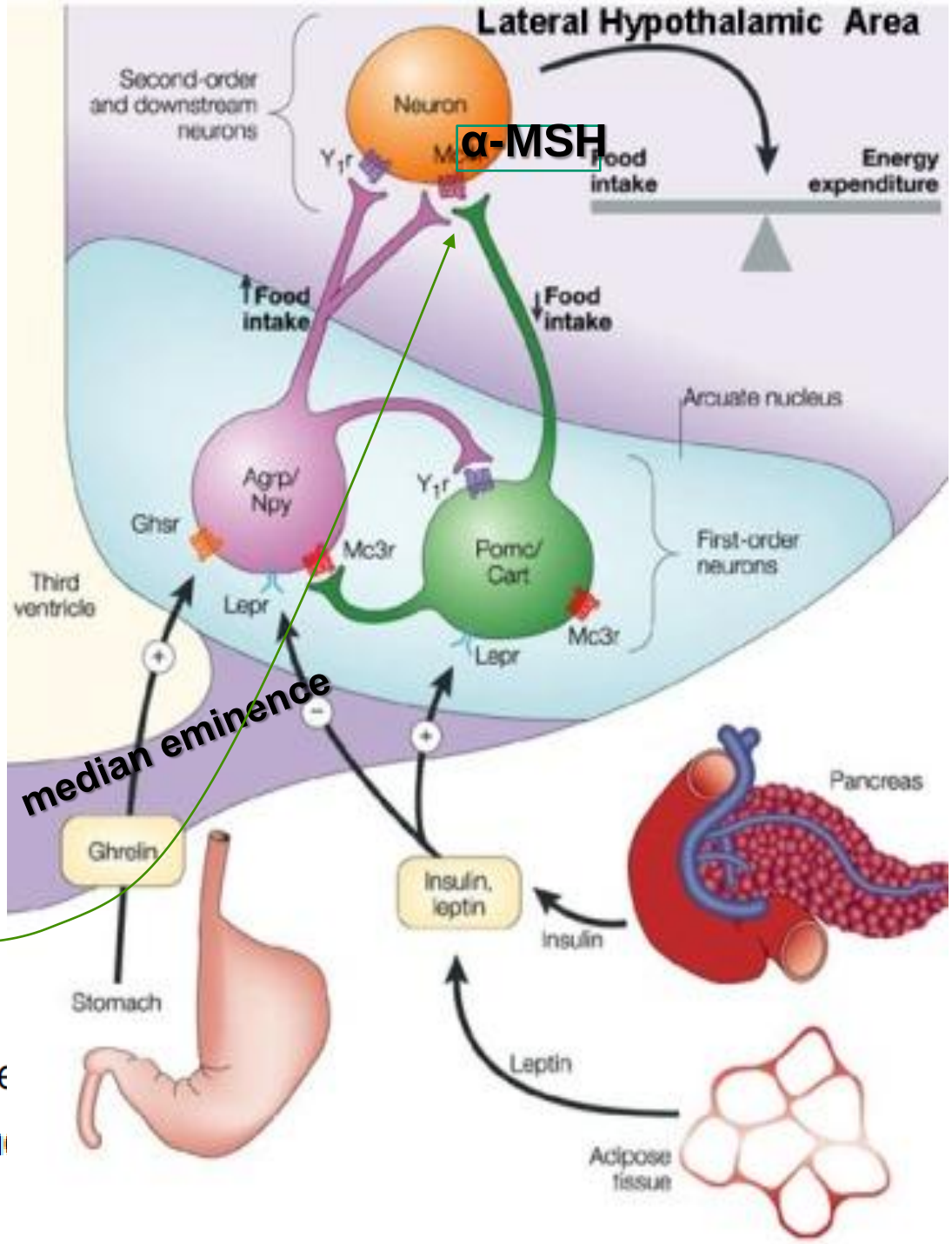


Immunoglobulins recognizing neuropeptides

↓

modulation of signal

α-MSH Ig



Sergueï O. Fetissov and Pierre Déchelotte

Current Opinion in Clinical Nutrition an
Metabolic Care 2008, 11:428–434

Psychoneuroendocrinology (2009) 34, 140–149

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Regulation of feeding and anxiety by α-MSH reactive autoantibodies

Maria Hamze Sinno [a], Jean Claude Do Rego [b], Moïse Coëffier [a], Christine Bole-Feysot [a], Philippe Ducrotté [a], Danièle Gilbert [c], François Tron [c], Jean Costentin [b], Tomas Hökfelt [d], Pierre Déchelotte [a], Sergueï O. Fetissov [a,*]

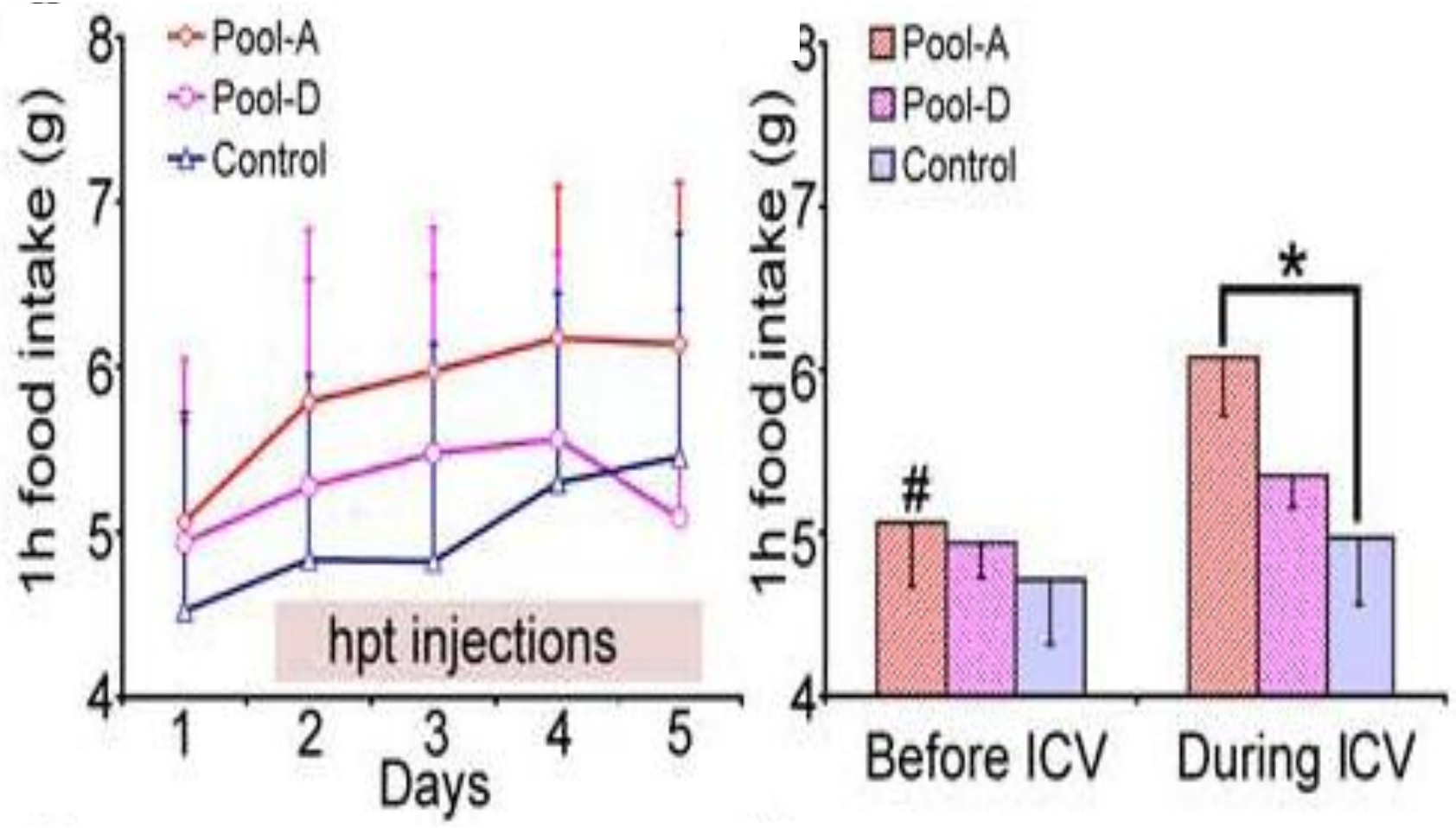
[a] *Digestive System & Nutrition Laboratory (ADEN EA4311), Institute of Biomedical Research, Rouen University & Hospital, IFR23, 76183 Rouen, France*

[b] *Experimental Neuropsychopharmacology Laboratory (CNRS FRE 2735), Institute of Biomedical Research, Rouen University & Hospital, IFR23, 76183 Rouen, France*

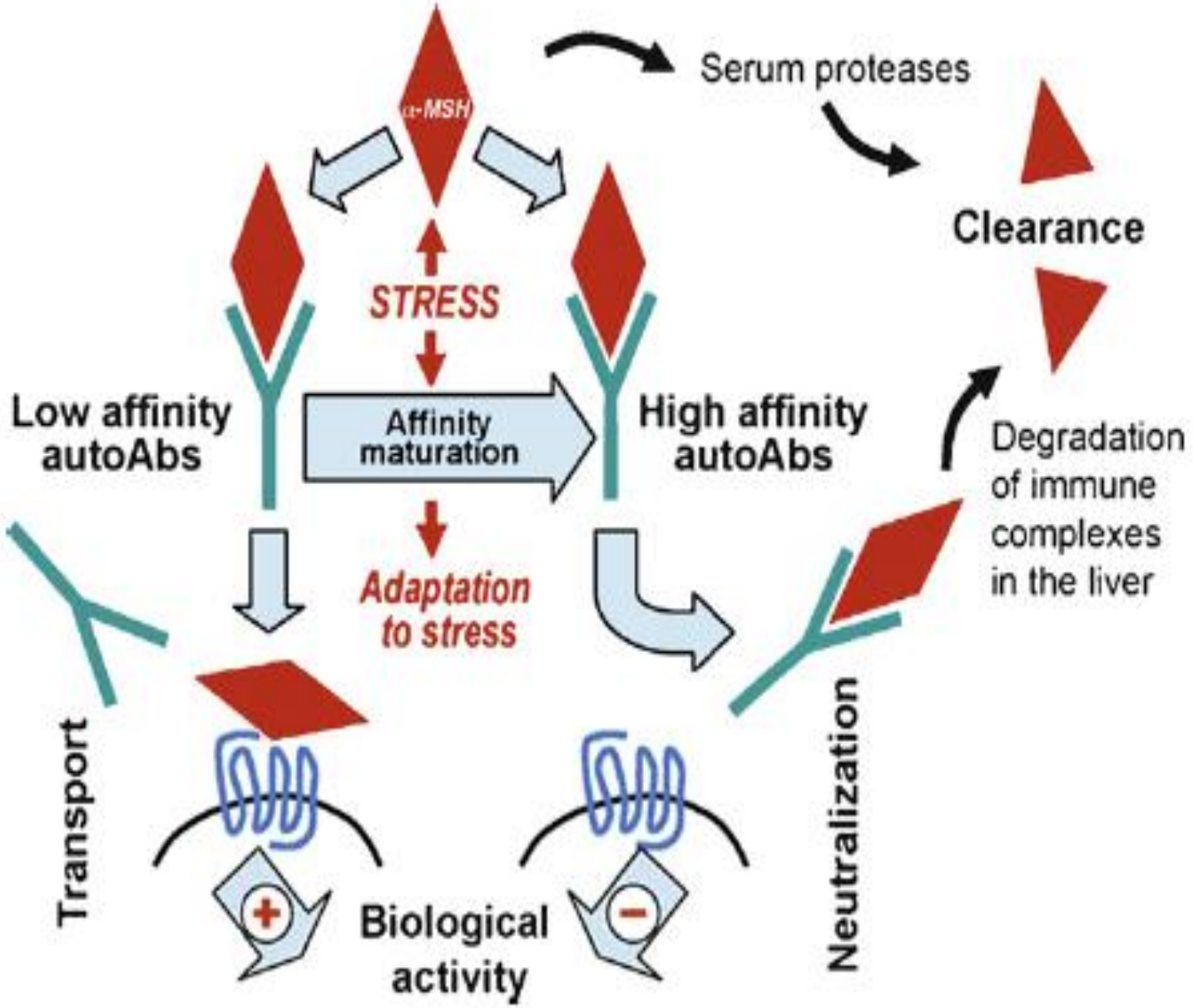
[c] *Immunopathology Laboratory (Inserm U519), Institute of Biomedical Research, Rouen University & Hospital, IFR23, 76183 Rouen, France*

[d] *Department of Neuroscience, Karolinska Institutet, 17177 Stockholm, Sweden*

• Most stressed rats (group A) displayed increased food intake and high affinity α-MSH Igs
• ICV injection of these Igs in naïve rats acutely increased food intake = reduced the satieting effect of a-MSH and reduced anxiety (T-maze)



Psychoneuroendocrinology (2009) 34, 140–149



Psychoneuroendocrinology (2009) 34, 140–149

nature COMMUNICATIONS

ARTICLE

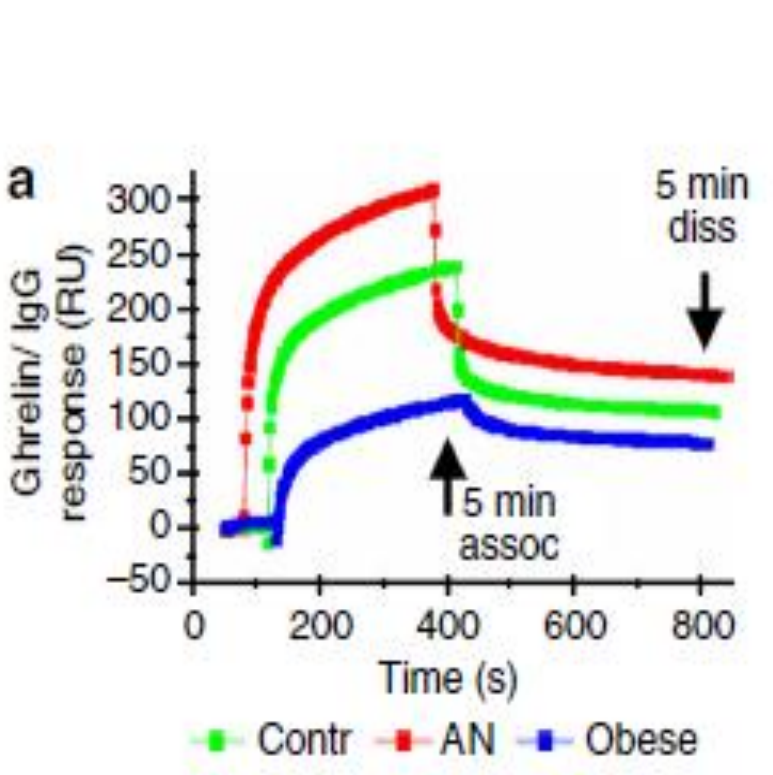
Received 8 Aug 2013 | Accepted 30 Sep 2013 | Published 25 Oct 2013

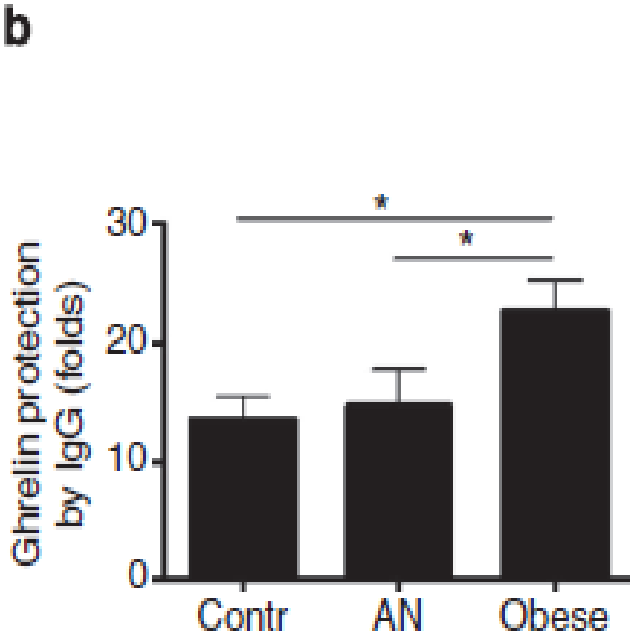
DOI: 10.1038/ncomms3685 OPEN

Anti-ghrelin immunoglobulins modulate ghrelin stability and its orexigenic effect in obese mice and humans

Kuniko Takagi[1,2,3,*], Romain Legrand[1,2,*], Akihiro Asakawa[3], Haruka Amitani[3], Marie François[1,2], Naouel Tennoune[1,2], Moïse Coëffier[1,2,4], Sophie Claeyssens[1,2,4], Jean-Claude do Rego[2,5], Pierre Déchelotte[1,2,4], Akio Inui[3] & Sergueï O. Fetissov[1,2]

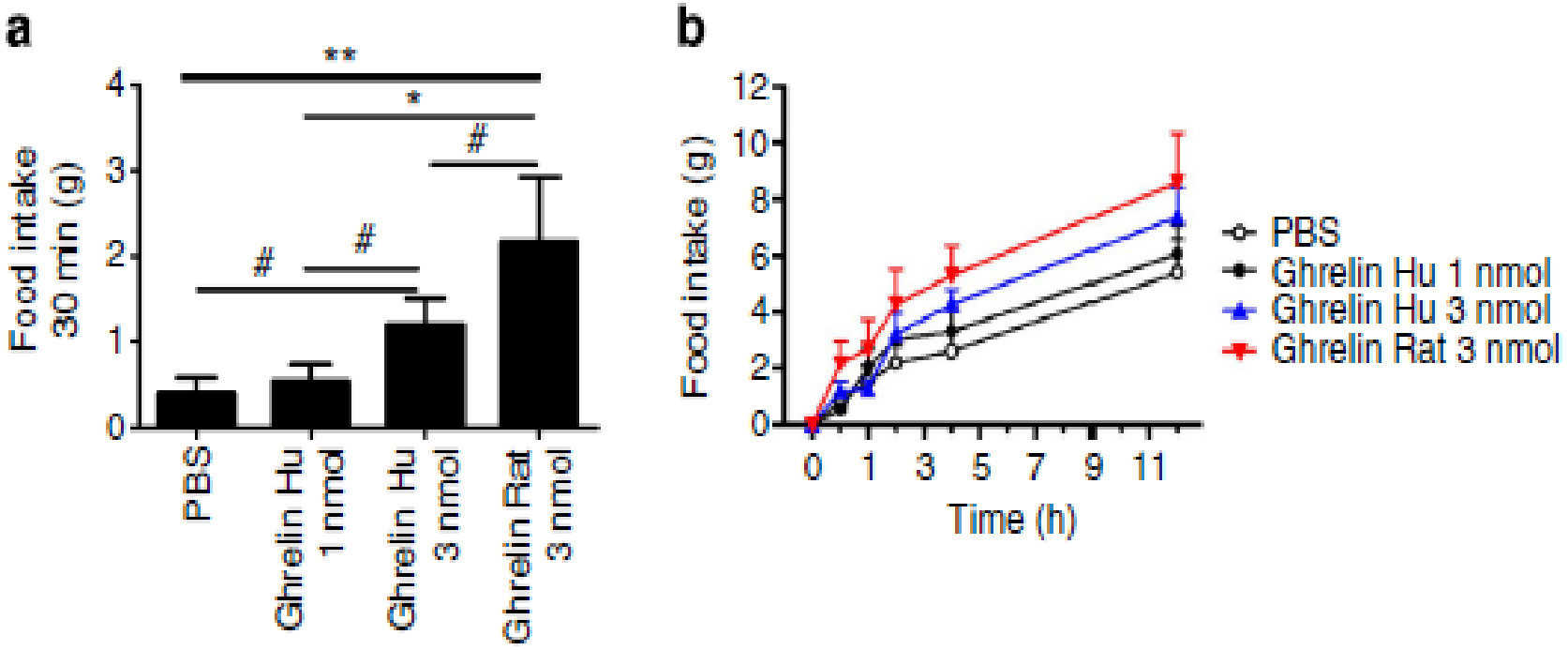
Ghrelin antibodies from obese patients reduce ghrelin degr





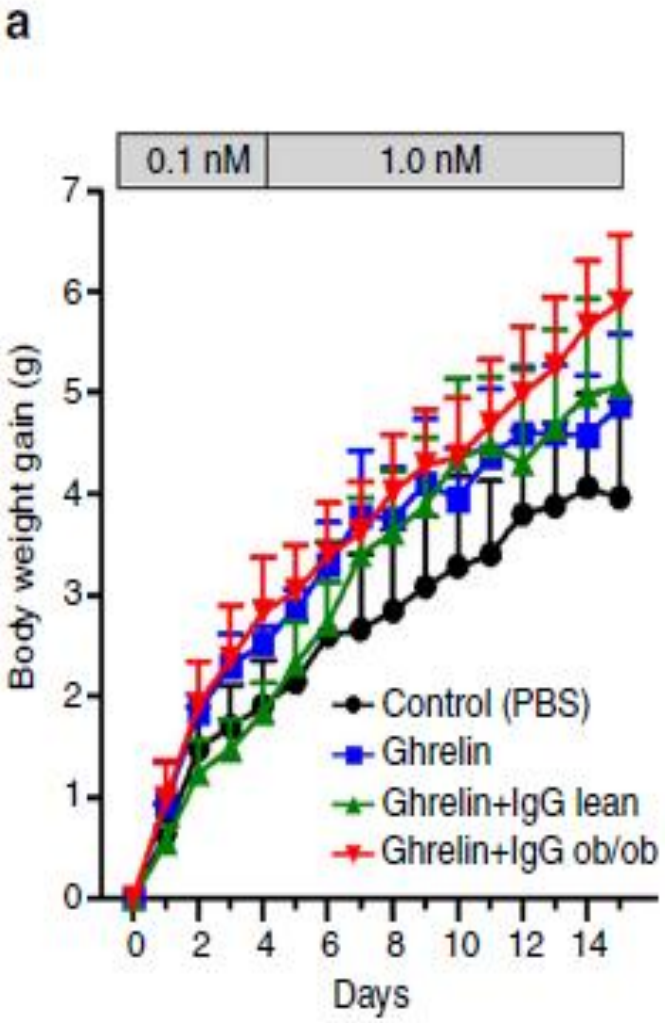
Takagi et al, Nat Comm 2013

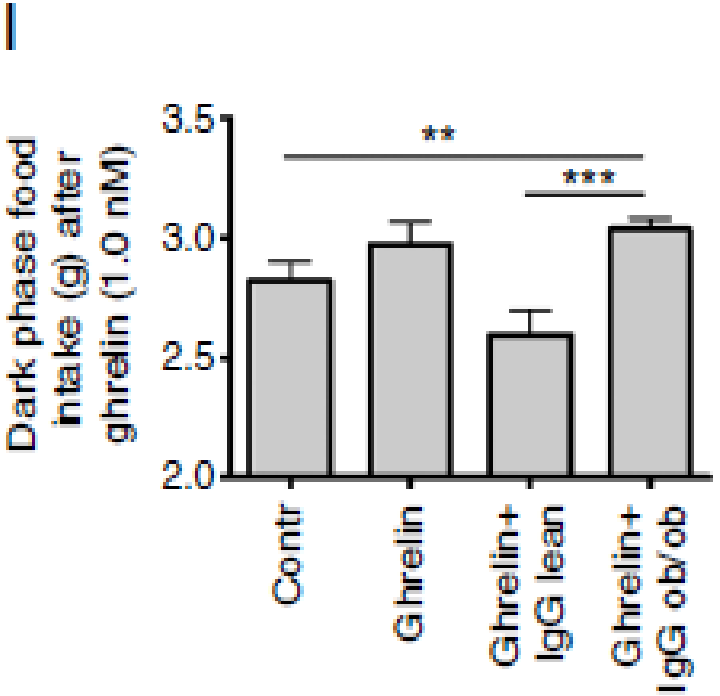
Transfer of Ghrelin antibodies from obese patients to mice increases food intake



Takagi et al, Nat Comm 2013

Transfer of ghrelin antibodies from ob/ob to naive mice increases food intake





Takagi et al, Nat Comm 2013

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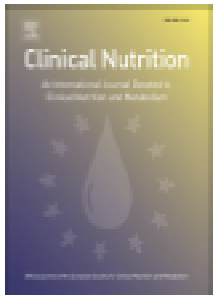
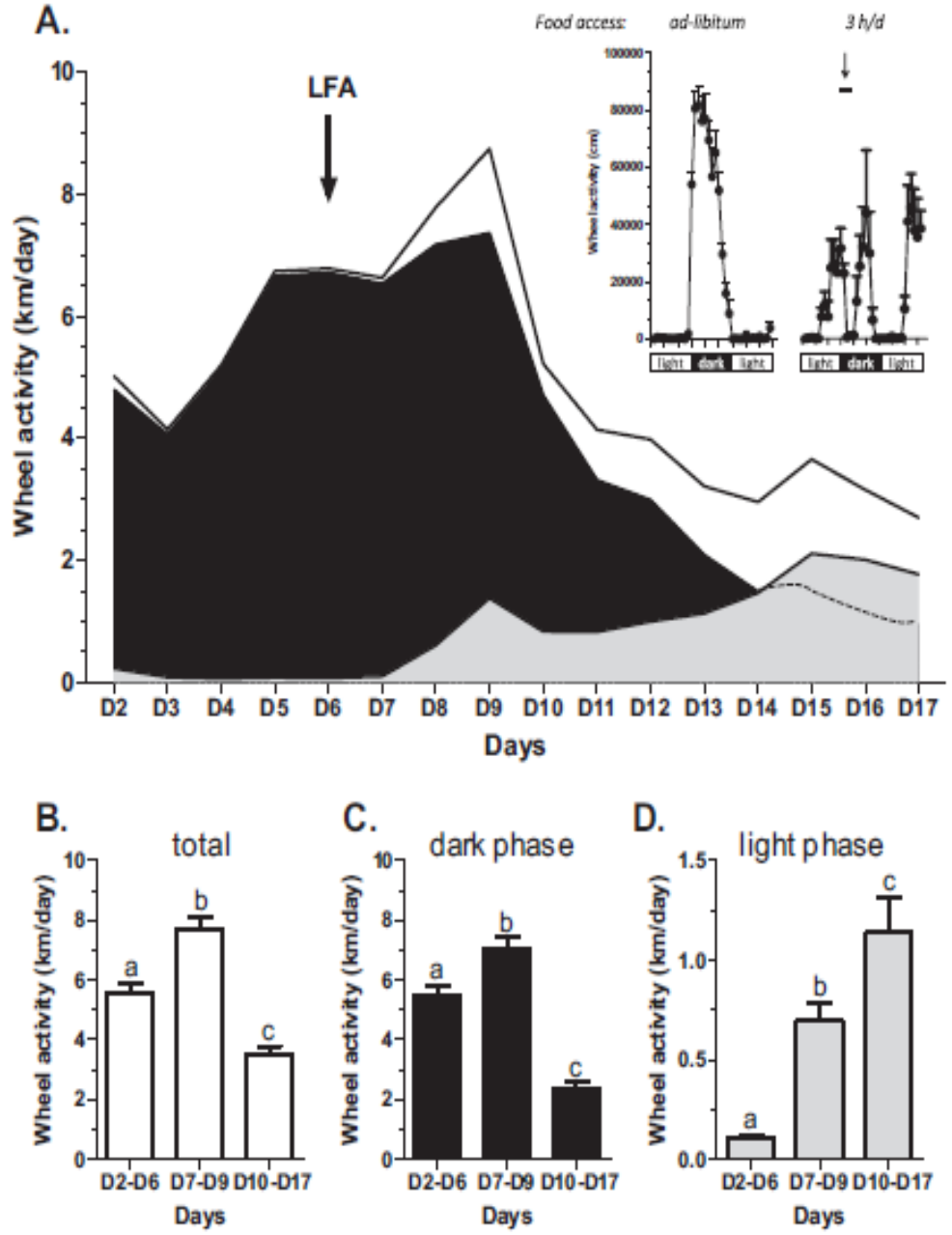


Original article

Alteration of intestinal barrier function during activity-based anorexia in mice

Pierre Jésus [a,b,c], Wassila Ouelaa [a,b], Marie François [a,b], Lina Riachy [a,b], Charlène Guérin [a,b], Moutaz Aziz [d], Jean-Claude Do Rego [b,e,f], Pierre Déchelotte [a,b,c], Sergueï O. Fetissov [a,b], Moïse Coëffier [a,b,c,*]

Jésus et al Clin Nutr 2013

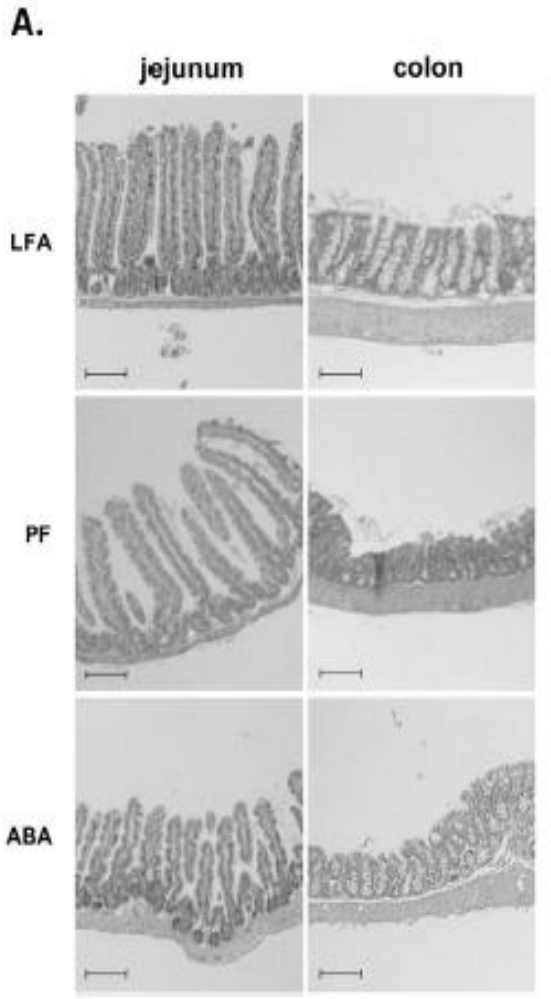


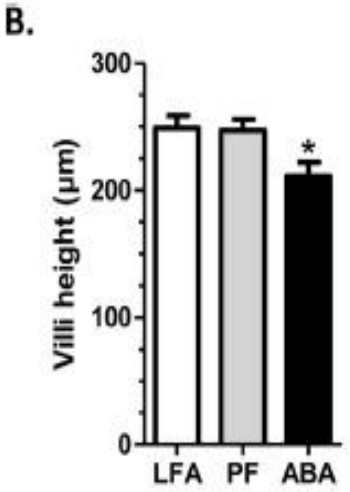
altered quantitative and qualitate pattern of food intake

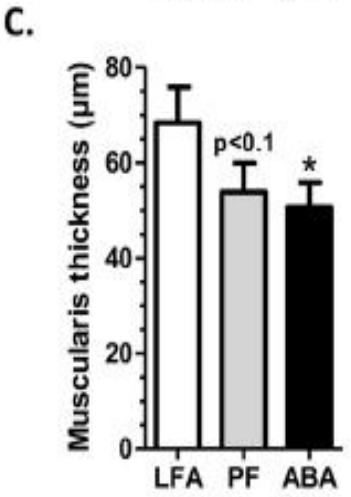
Jésus et al Clin Nutr 2013

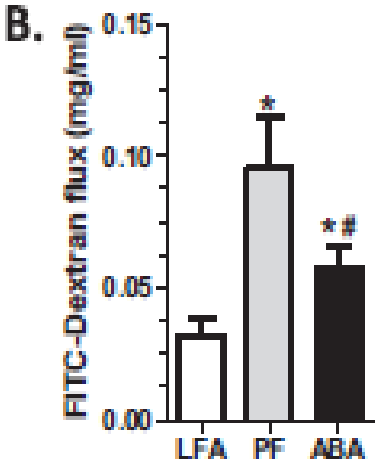
Impaired gut barrier integrity

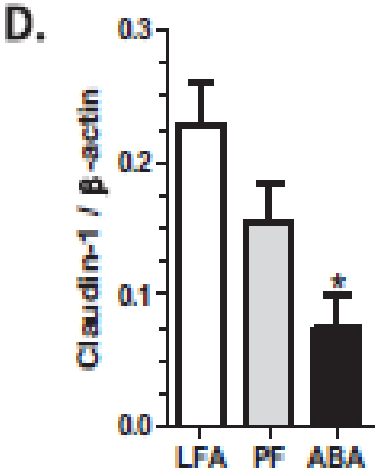
enhanced colonic permeability







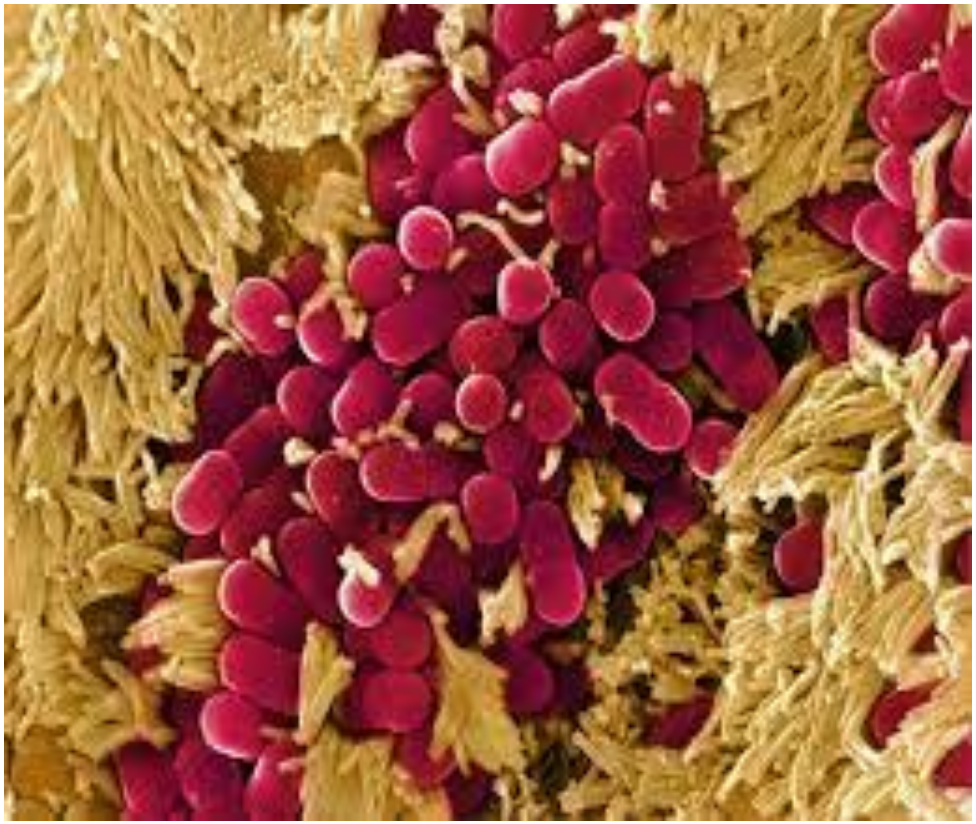




Jésus et al Clin Nutr 2013

→ Effets inflammatoires et sur TLR-4 : Liliana Belmonte, CO, 16:00

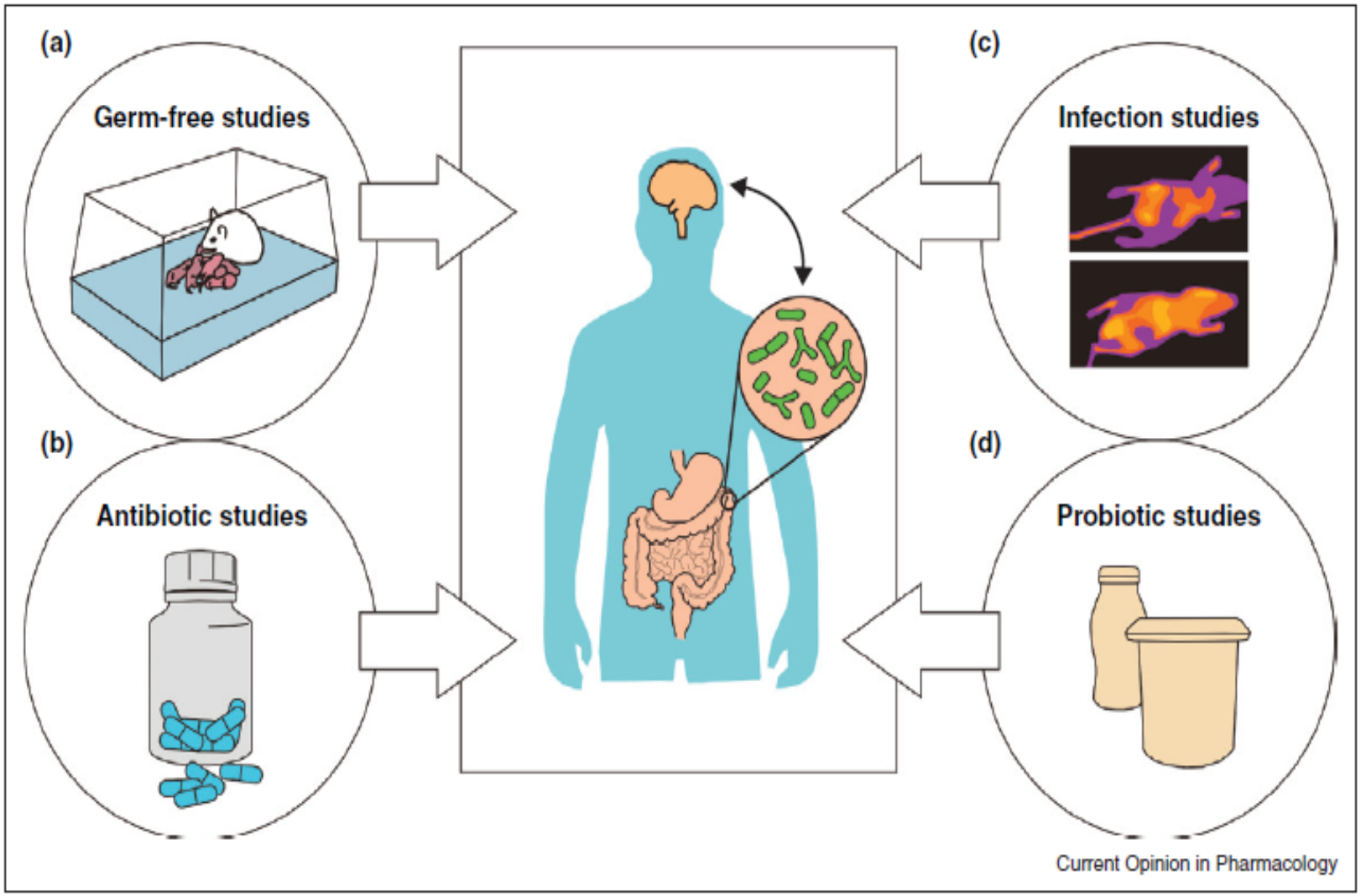
Stress et comportement alimentaire: rôle du microbiote



Communication between gastrointestinal bacteria and the nervous system

Current Opinion in Pharmacology 2012, 12:667–672

Javier A Bravo[1], Marcela Julio-Pieper[1], Paul Forsythe[2,3], Wolfgang Kunze[4], Timothy G Dinan[6,8], John Bienenstock[2,5] and John F Cryan[7,8]



Current Opinion in Clinical Nutrition and Metabolic Care 2008, 11:428–434

Table 1 Molecular mimicry of appetite-regulating peptide hormones and microbial proteins

α-MSH	*Bifidobacterium longum* (5 a. a.), *Bacteroides* (5 a. a.), *Bacillus cereus* (6 a. a.), *Escherichia coli* enteropathogenic and commensal strains (5 a. a.), Enterobacteria phage (5 a. a.), *Yarrowia lipolytica* (5 a. a.), *Candida albicans* (5 a. a.), *Cryptococcus neoformans* (5 a. a.). *Aspergillus fumigatus* (5 a. a.).
Ghrelin (24–51)	*Enterococcus faecalis* (7 a. a.), *Clostridium perfringens* (6 a. a.), *Lactobacillus casei* bacteriophage (5 a. a.), Mycobacteriophage (6 a. a.), *Saccharomyces cerevisiae* (5 a. a.), *Yarrowia lipolytica* (6 a. a.), *Candida albicans* (6 a. a.), *Cryptococcus neoformans* (7 a. a.).
Leptin (22–56)	*Lactococcus lactis* (7 a. a.), *Helicobacter pylori* (5 a. a.), *Campylobacter* (5 a. a.), *Lactobacillus* bacteriophage (5 a. a.), *Candida albicans* (7 a. a.), *Yarrowia lipolytica* (5 a. a.), *Aspergillus fumigatus* (6 a. a.).

OPEN

Citation: Transl Psychiatry (2014) **4**, e458; doi:10.1038/tp.2014.98

www.nature.com/tp

ORIGINAL ARTICLE

Bacterial ClpB heat-shock protein, an antigen-mimetic of the anorexigenic peptide α-MSH, at the origin of eating disorders

N Tennoune[1,2], P Chan[2,3], J Breton[1,2], R Legrand[1,2], YN Chabane[2,4], K Akkermann[5], A Järv[6], W Ouelaa[1,2], K Takagi[1,2], I Ghouzali[1,2], M Francois[1,2], N Lucas[1,2], C Bole-Feysot[1,2], M Pestel-Caron[2,7,8], J-C do Rego[2,9], D Vaudry[2,3], J Harro[5], E Dé[2,4], P Déchelotte[1,2,8] and SO Fetissov[1,2]

Tennoune et al Transl Psych 2014

Proteomics + immunoblotting of E. Coli proteins : identification of ClpB as α-MSH mimetic

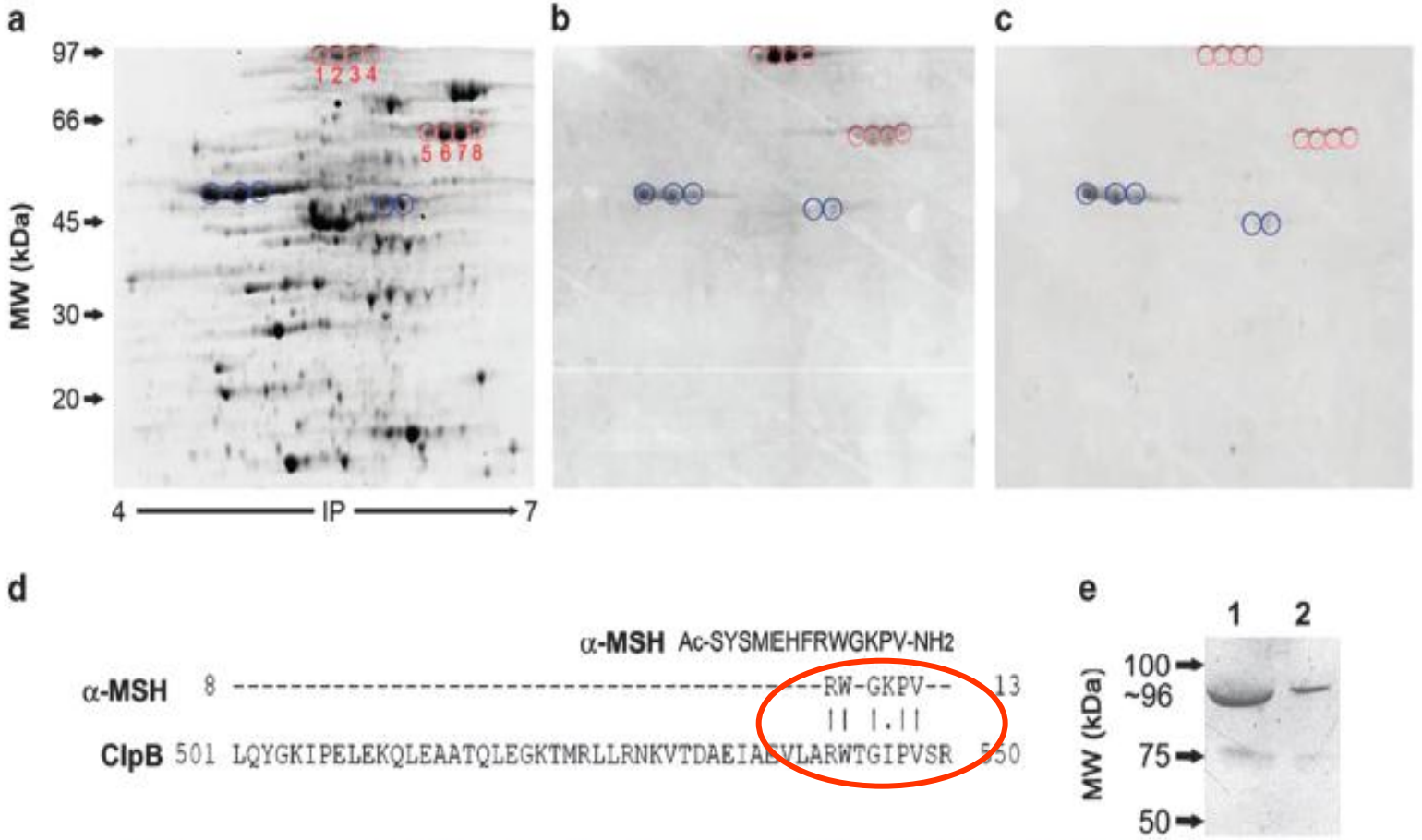
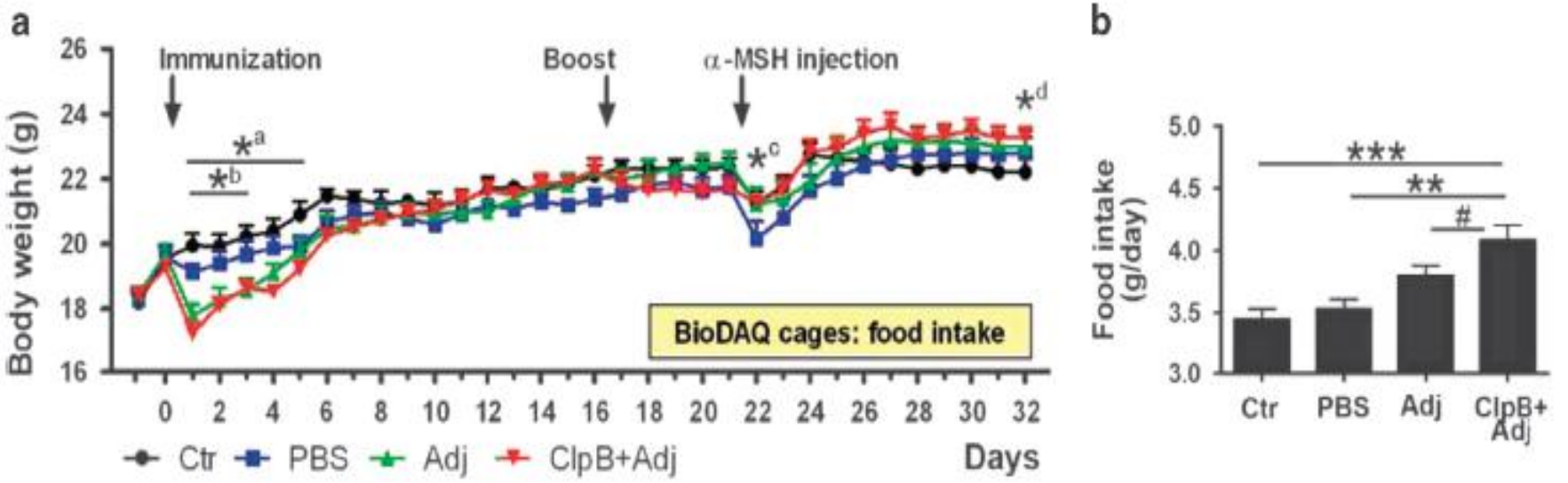
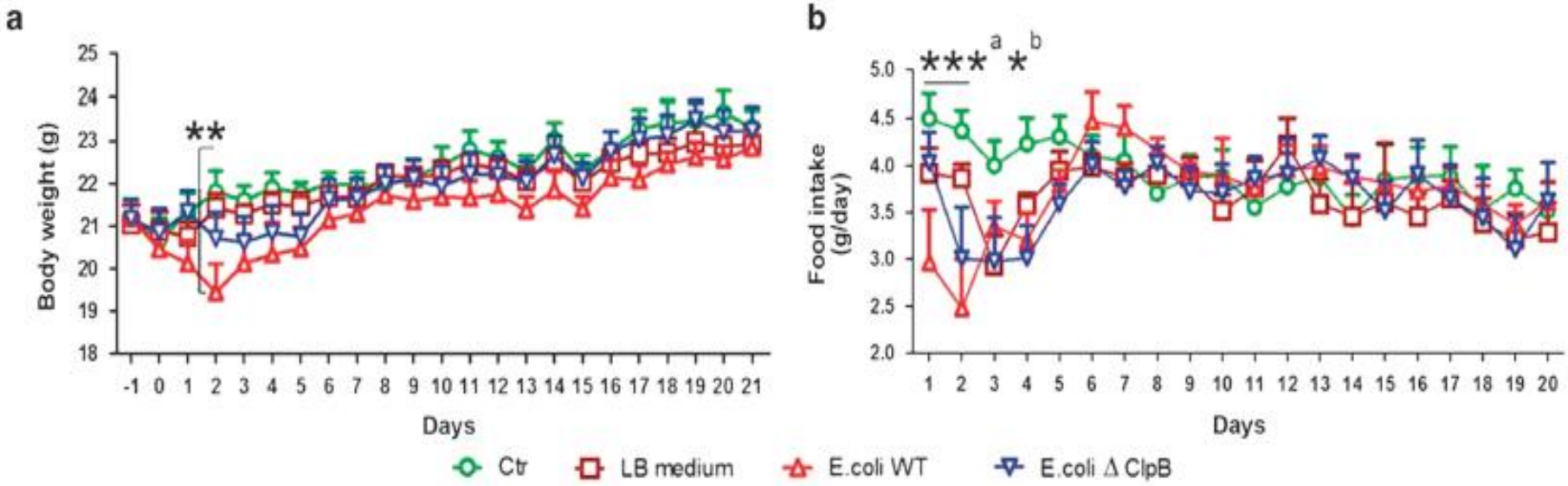


Figure 1. Proteomic identification of molecular mimicry between *E. coli* K12 proteins and α-MSH. (**a**) 2D GE of *E. coli* cytoplasmic proteins. (**b**, **c**) Immunoblots of *E. coli* proteins detected with rabbit anti-α-MSH IgG, preadsorbed (**c**) or not (**b**) with α-MSH. Circles in red surround the spots specifically recognized by α-MSH IgG which were used for protein identification. Circles in blue indicate nonspecific spots. Proteins identified in the spots 1–4 are isoforms of ClpB. (**d**) α-MSH and ClpB amino-acid sequence alignments using the Stretcher program. (**e**) Western blot of the recombinant ClpB, revealed with anti-α-MSH IgG. Lanes 1 and 2, 20 and 10 μg of ClpB, respectively. IP, isoelectric point.

Tennoune et al Transl Psych 2014

ClpB interferes with food intake directly and via auto-antibodies





Tennoune et al Transl Psych 2014

ClpB antibodies are present in ED patients, with different profiles, and correlate with behavioral traits

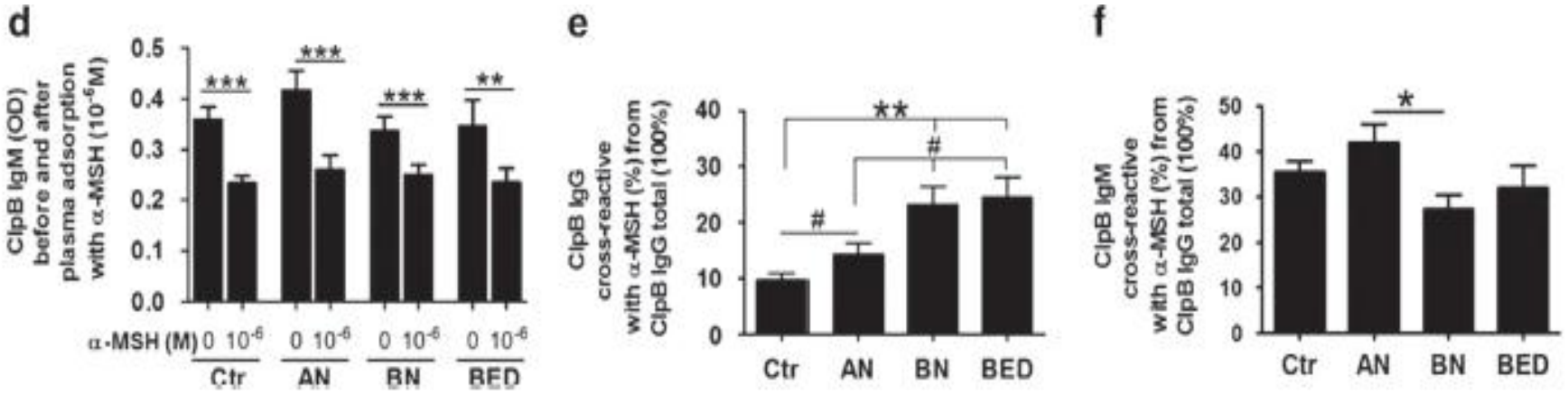


Table 1. Significant correlations between plasma levels of anti-ClpB IgG or IgM and behavioral traits in eating disorder patients and Ctr. assayed by the Eating Disorder Inventory-2

ClpB IgG (Ctr.)	Maturity fears, $r=-0.31^{*}$	Impulse regulation, $r=-0.26^{*}$	Social insecurity, $r=-0.26^{*}$
ClpB IgG (AN)	Body dissatisfaction, $r=0.4^{*}$	Drive for thinness, $r=0.35^{*}$	Perfectionism, $r=0.38^{*}$
ClpB IgM (AN)	Ineffectiveness, $r=-0.42^{*}$	Interpersonal distrust, $r=-0.58^{**}$	Social insecurity, anhedonia, $r=-0.52^{**}$, $r=-0.35^{*}$
ClpB IgM (BED)	Bulimia, $r=0.53^{*}$	Perfectionism, $r=0.6^{*}$	Age, $r=-0.74^{**}$

Abbreviations: AN, anorexia nervosa; Ctr., controls; BED, binge-eating disorder; Ig, immunoglobulin. All Spearman's r $^{*}P<0.05$, $^{**}P<0.01$, except Pearson's r$^{*}P<0.05$ for perfectionism. ($n=65$, Ctr.; $n=27$, AN; and $n=14$, BED).

Tennoune et al Transl Psych 2014

→ Protéome bactérien et prise alimentaire : Jonathan Breton, CO, 16:00

The Melanocortin-4 Receptor Is Expressed in Enteroendocrine L Cells and Regulates the Release of Peptide YY and Glucagon-like Peptide 1 In Vivo

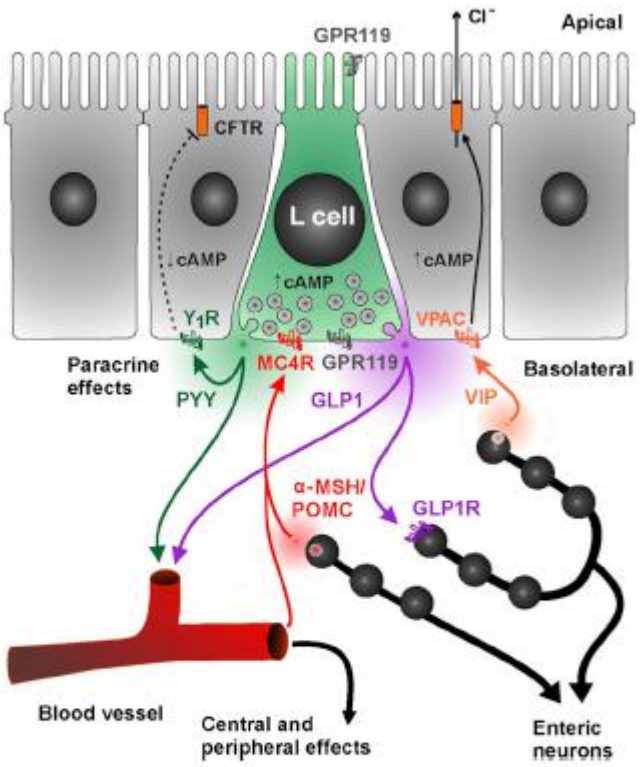


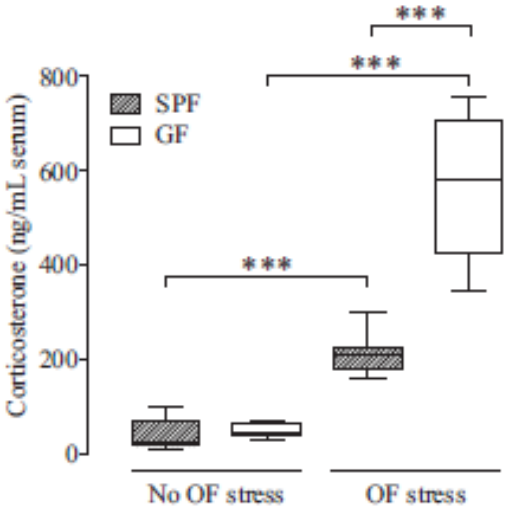
Figure 7. Regulation of GI Epithelial Function by MC4R Activation

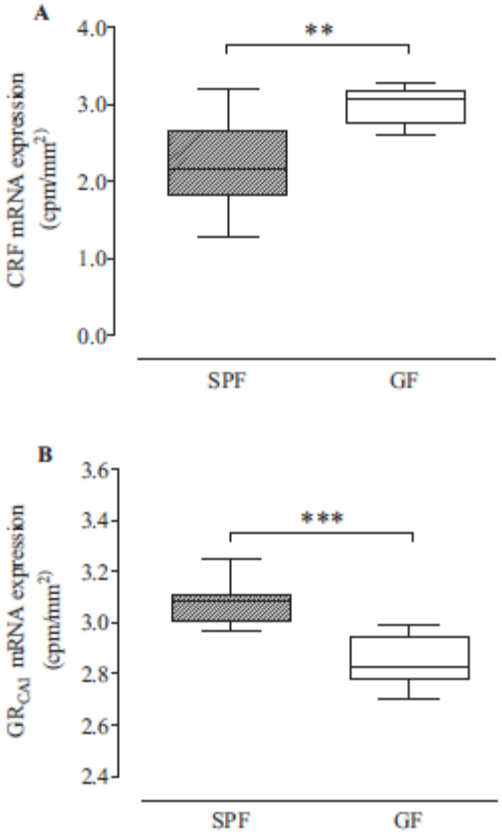
L cells receive basolateral regulatory input from enteric neurons, circulatory factors, and paracrine agents. MC4R, targeted primarily to the basolateral surface of L cells (as opposed to GPR119 which appears present on both domains), is capable of inducing release of PYY and GLP-1 in response to melanocortin peptides. The PYY release, up to two to four times above basal levels in vivo, is sufficient to decrease local intestinal epithelial Cl^- secretion, shown here, and inhibit motility (an example of another peripheral effect). The physiological source of ligand remains to be determined but could be α-MSH or another POMC melanocortin derivative.

Panaro et al
Cell Metabolism 2014

Absence of the gut microbiota enhances anxiety-like behavior and neuroendocrine response to acute stress in rats

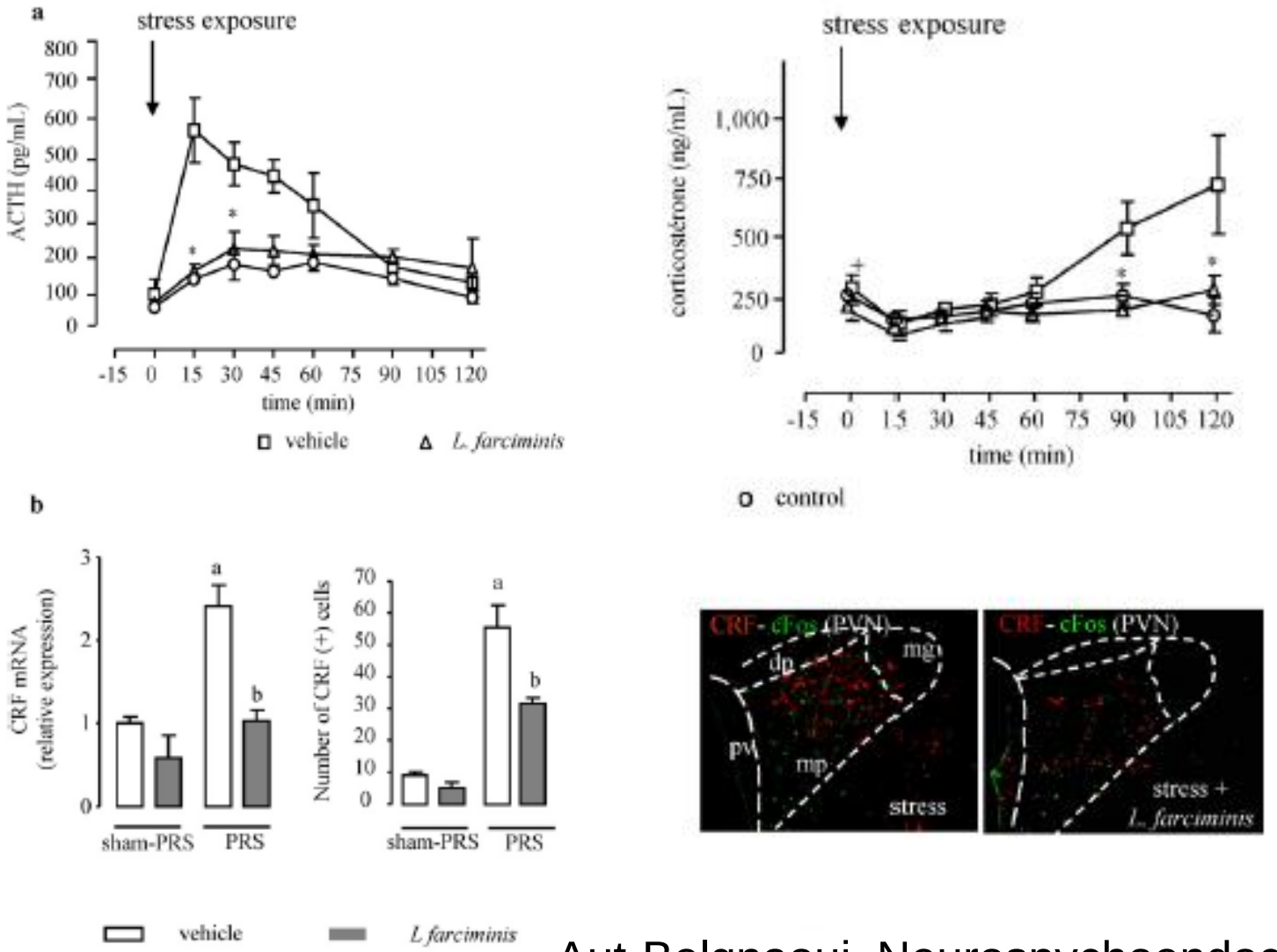
Michèle Crumeyrolle-Arias [a,b,c,1], Mathilde Jaglin [d,e,1], Aurélia Bruneau [d,e], Sylvie Vancassel [f], Ana Cardona [g,†], Valérie Daugé [a,b,c,h], Laurent Naudon [a,b,c,h], Sylvie Rabot [d,e,*]





Psychoneuroendocrinology (2014) 42, 207–217

Prevention of gut leakiness by a probiotic treatment leads to attenuated HPA response to an acute psychological stress in rats



Aut-Belgnaoui, Neurospychoendoc 2012

Stress et prise alimentaire

- Stress : facteur de risque de TCA/obésité
- Régulation de la prise alimentaire : peptides, récepteurs, intégration, récompense
- Stress et régulation neuropeptidique
- Rôle de la barrière intestinale et de l’immunité
- Implications pratiques

Stress et prise alimentaire: quelles implications pratiques?

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- réduction des stress évitables
- Thépapies cognitivo-comportementales
- Ciblage intestinal (nutriments, pré- ou pro-biotiques)
- Approches complémentaires: sophrologie, méditation, musicothérapie, activité physique adaptée….
- Accompagnement social, familial, associatif

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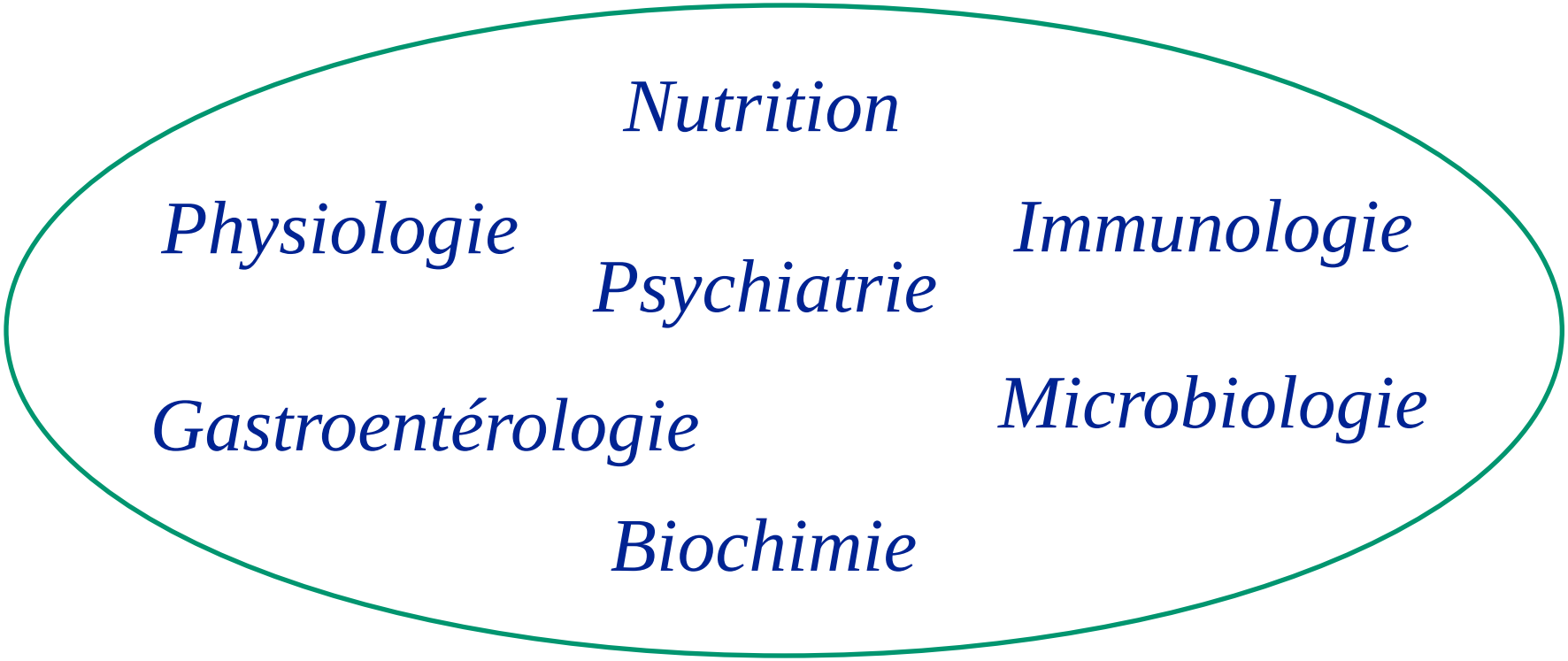
approche globale et multidisciplinaire



UMR 1073 – Nutrition et dysfonction de l'axe intestin-cerveau

L’axe intestin-cerveau en action!

Moïse Coëffier
Super-**Gut**man

Sergueï Fetissov
Super-**Brain**man