

# ALIMENTATION, IMMUNITÉ ET SANTÉ MENTALE : UN TRIO INSÉPARABLE

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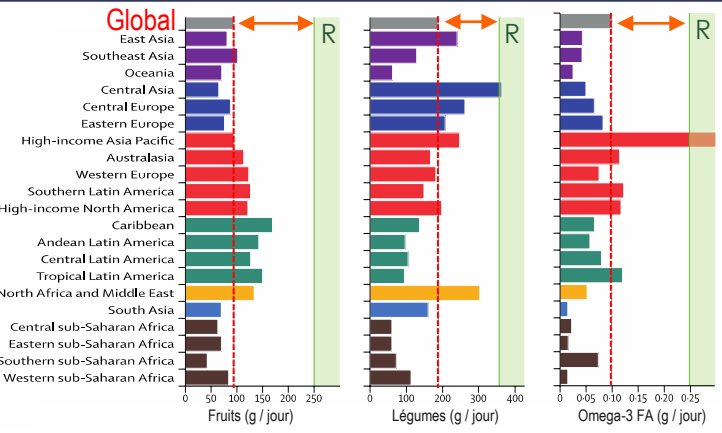
**lucile.capuron@inrae.fr**

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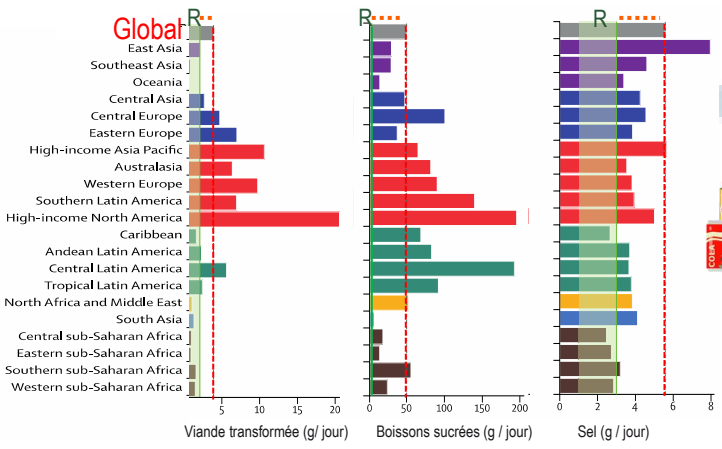


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# HABITUDES ALIMENTAIRES ET SANTÉ



Alimentation saine



Mauvaise alimentation

Santé métabolique

(Obésité)

Santé mentale

(Dépression  
Déclin cognitif)

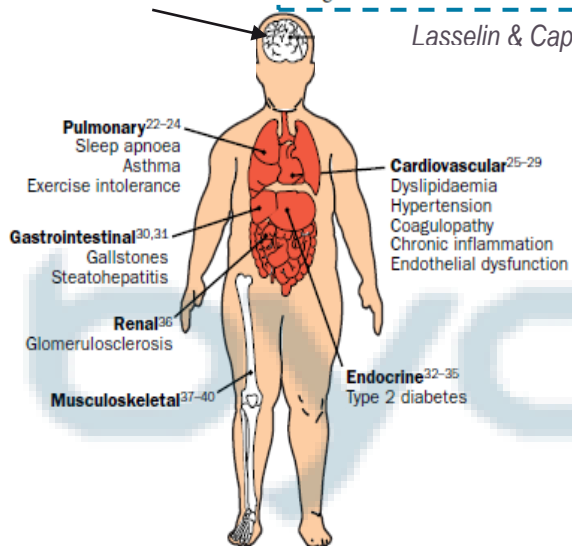
R = recommandations

# COMPLICATIONS MÉDICALES DE L'OBÉSITÉ

## Neuropsychiatric

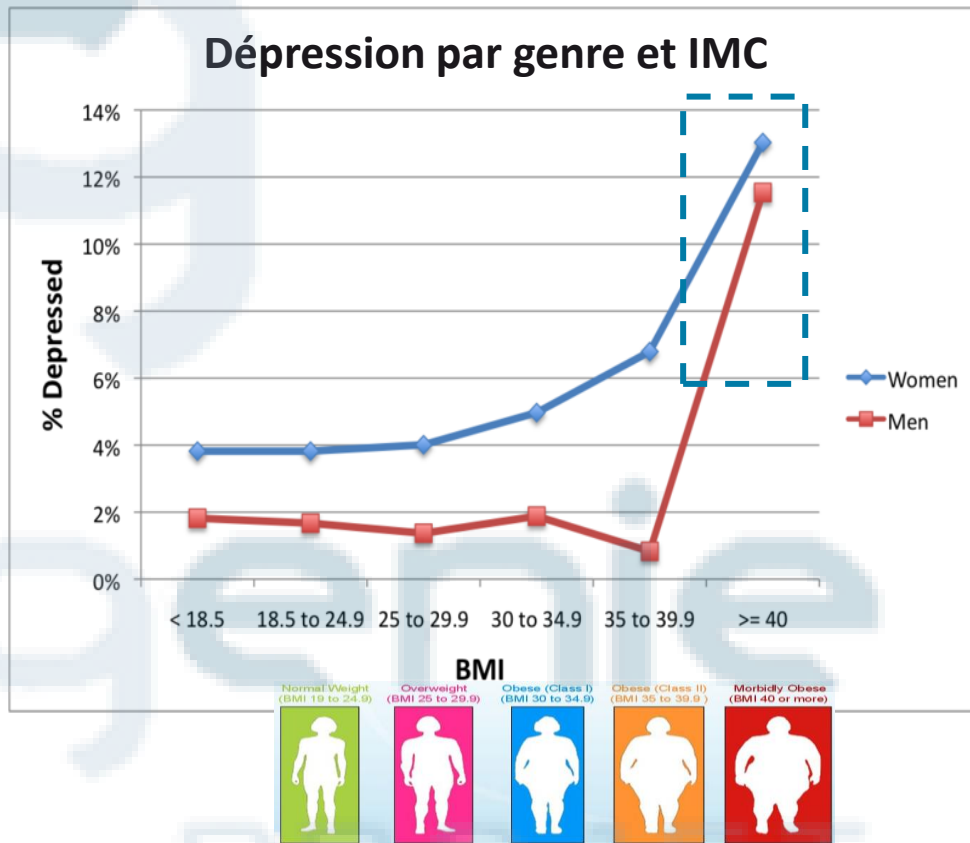
Behavioral symptoms	Prevalence rates
Depression	17.8–30%
Cognitive impairment	5.3–23%
Fatigue	59–60%

Lasselin & Capuron, 2014



Adapté de Ebbeling et al., Lancet, 2002

## Dépression par genre et IMC

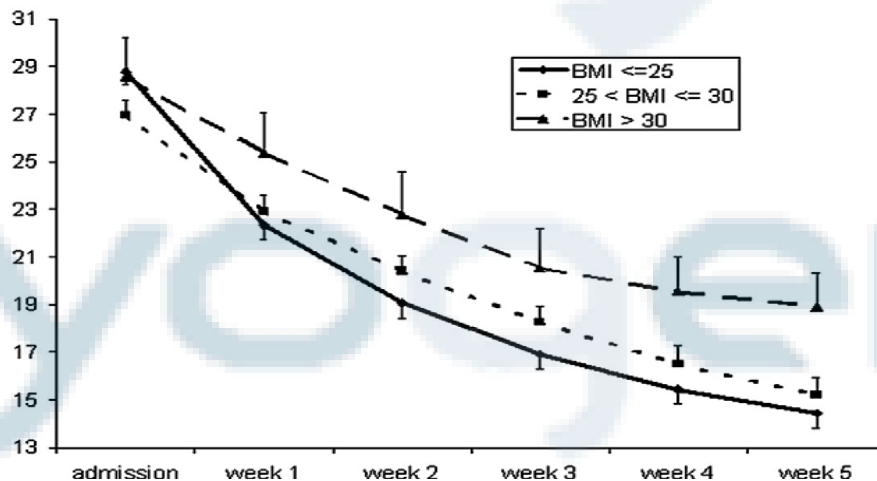


Onyique et al., Am J Epidemiol, 2003

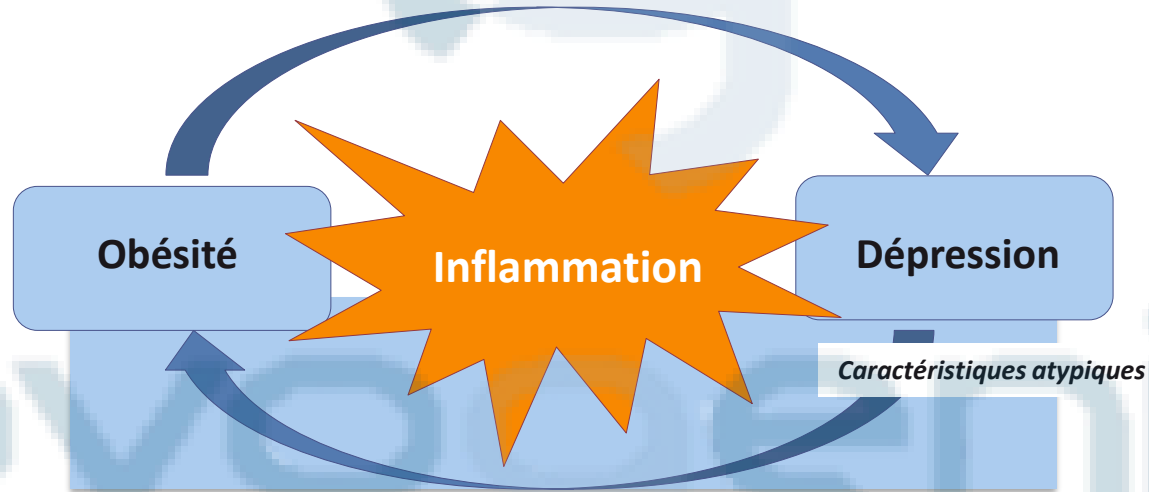
# L'OBÉSITÉ ET LE SURPOIDS SONT ASSOCIÉS À UN RISQUE AUGMENTÉ DE NON-RÉPONSE AUX ANTIDÉPRESSEURS

Diminution de la réponse au traitement chez les patients déprimés en surpoids ou obèses

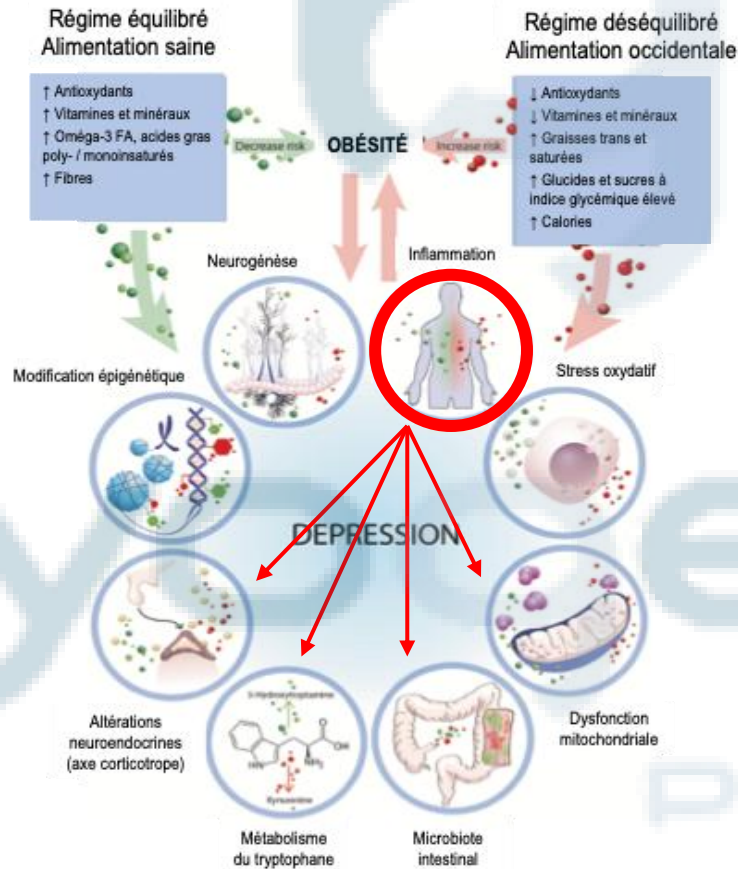
**Reponse to Antidepressants**



# OBÉSITÉ ET DÉPRESSION : UN CERCLE VICIEUX

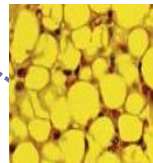


# INFLUENCE DE LA QUALITÉ DE L'ALIMENTATION SUR LES MÉCANISMES LIÉS À LA DÉPRESSION



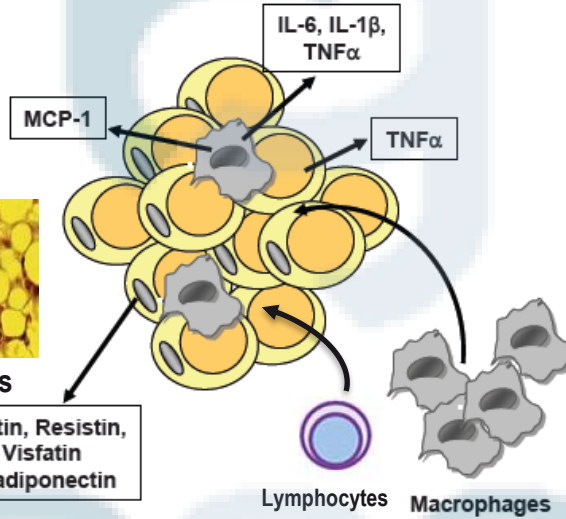
modulation bénéfique  
 modulation potentiellement néfaste

# L'INFLAMMATION, UNE CARACTÉRISTIQUE MAJEURE DE L'OBÉSITÉ



Fat cells

Leptin, Resistin,  
Visfatin  
↓ adiponectin



## Comorbidités neuropsychiatriques



Inflammation

Lasselin et al., JCEM, 2014

Habitudes alimentaires  
obésogènes (sucres, gras, sel)

# L'AUGMENTATION DES MARQUEURS INFLAMMATOIRES EST ASSOCIÉE AUX COMORBIDITÉS NEUROPSYCHIATRIQUES DE L'OBÉSITÉ

Brain, Behavior, and Immunity 94 (2021) 104–110

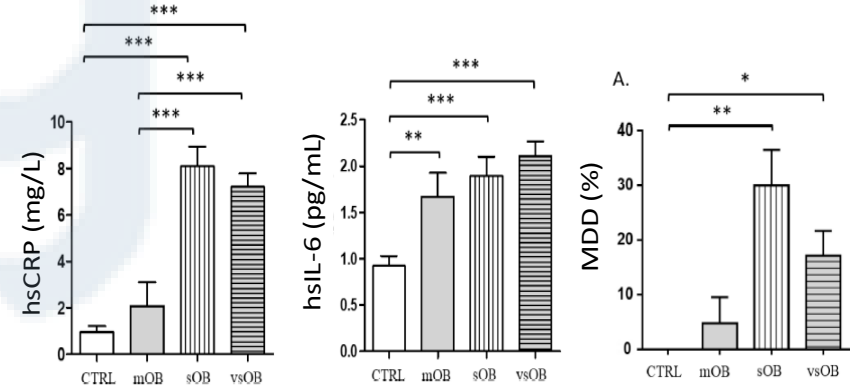
Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

**Brain Behavior and Immunity**

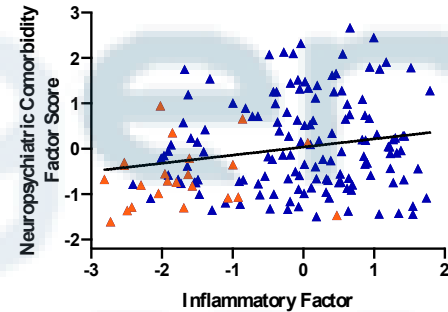
journal homepage: [www.elsevier.com/locate/ybrbi](https://www.elsevier.com/locate/ybrbi)

**Relationship between body mass index and neuropsychiatric symptoms: Evidence and inflammatory correlates**

Lison Huet<sup>a</sup>, Ines Delgado<sup>a</sup>, Sandra Dexpert<sup>a</sup>, Julie Sauvant<sup>a</sup>, Bruno Aouizerate<sup>a,b</sup>, Cédric Beau<sup>c,d</sup>, Damien Forestier<sup>c,d</sup>, Patrick Ledaguenel<sup>c,d</sup>, Eric Magne<sup>c,d</sup>, Lucile Capuron<sup>a,\*</sup>



	Lean controls BMI: <25	Mild-moderate obesity BMI: 25-34.9	Severe obesity BMI: 35-39.9	Very Severe obesity BMI: ≥40	
N	165	24	21	50	70
Mean BMI	21.6	30.0	37.7	44.0	
Weight (kg)	58.7	88.2	105.4	118.4	
Age	44.1	45.7	40.9	41.1	



	Neuropsychiatric Comorbidity		
	Negative n = 91	Positive n = 69	p
Log hs-CRP	0.41 (0.58)	0.64 (0.52)	< 0.01
Log hs-IL6	0.13 (0.31)	0.22 (0.22)	< 0.05

# LES COMPLICATIONS MÉTABOLIQUES DE L'OBÉSITÉ N'INFLUENCENT PAS LA RELATION ENTRE L'INFLAMMATION ET LA DÉPRESSION



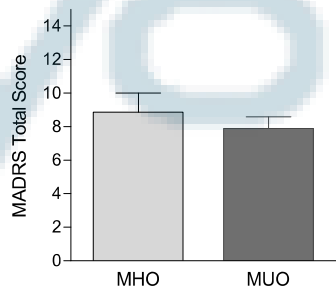
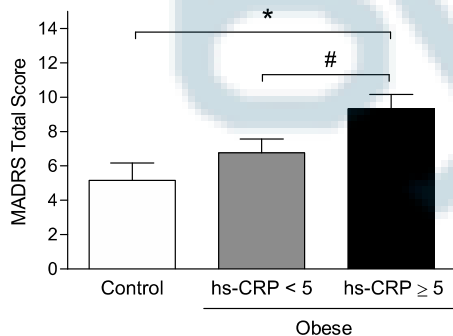
N= 99 (84% w; 39.2y)  
Mean BMI: 41.4 kg/m<sup>2</sup>

Mean CRP 7.2 mg/L ; 57% CRP ≥ 5 mg/L

Low HDL-C = 62%; High Glucose Levels = 34%; High Triglycerides Levels = 39%; High Blood Pressure = 54% ; MUHO = 60%

	Metabolic abnormalities
HDL-C	< 0.40 (M); < 0.50 (W)
Fasting glucose	≥ 1 g/L
Triglycerides	≥ 1.5 g/L
Systolic and diastolic BP	≥ 140 mmHg/ ≥ 90 mmHg, or antihypertensive med
MHO (healthy): ≤ 1 abnormality; MUHO (unhealthy) ≥ 2	

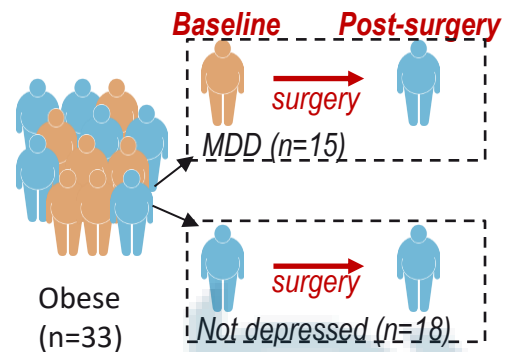
\*Jokela et al., 2014



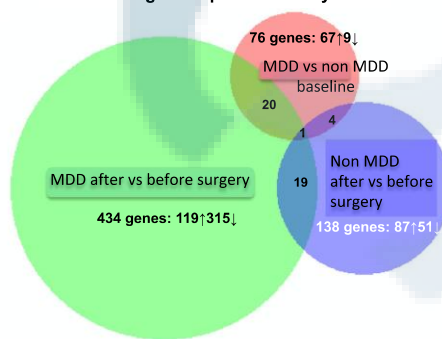
## MADRS Total Score

	β	p
<i>Model</i>		
CRP	2.89	<0.05
MUHO	0.17	0.89
CRP	2.88	<0.05

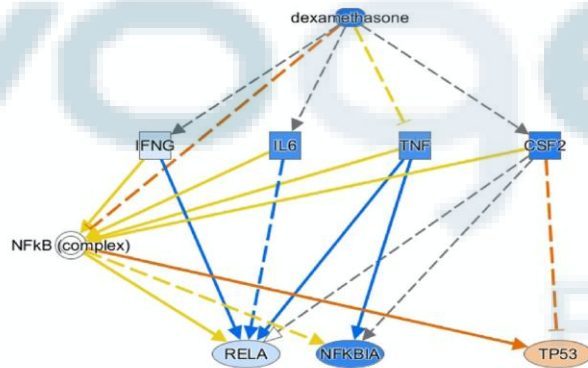
# LA VOIE DE SIGNALISATION DE L'INFLAMMATION (NFkB) PRÉDIT LES COMORBIDITÉS DÉPRESSIVES DE L'OBÉSITÉ ET LEUR REMISSION APRÈS CHIRURGIE BARIATRIQUE



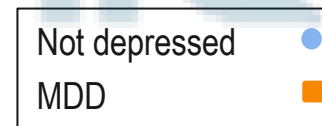
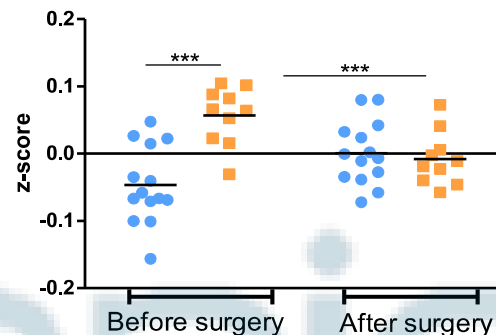
Differential gene expression analyses



Mechanistic network of upstream regulators (MDD after vs. before surgery analysis)

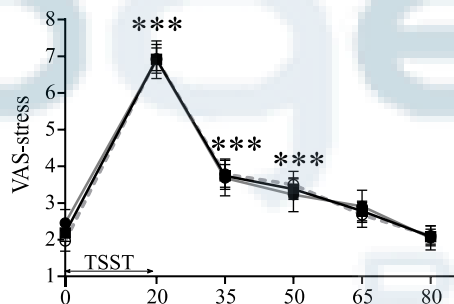
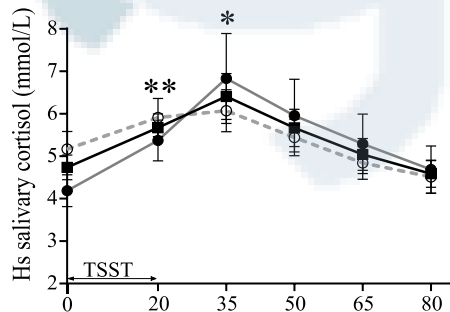
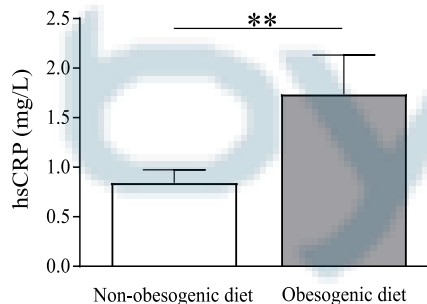


RELA target genes (NFkB)

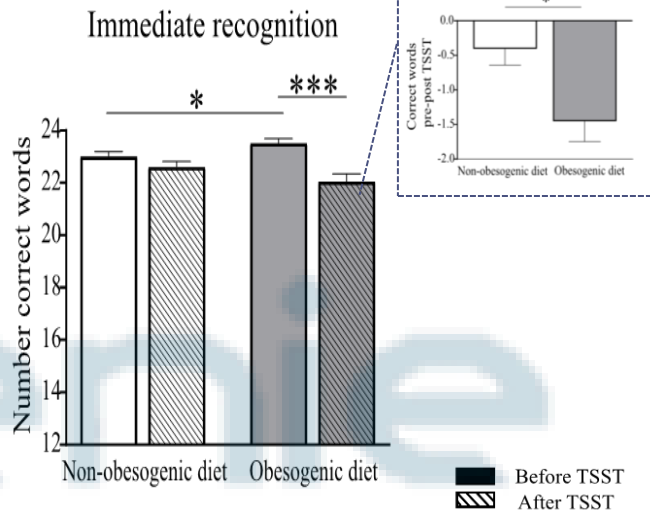


# LES RÉGIMES ALIMENTAIRES DÉSÉQUILIBRÉS (OBÉSOGÈNES) AUGMENTENT L'INFLAMMATION SYSTÉMIQUE DE BAS-GRADE ET LA VULNÉRABILITÉ AU STRESS

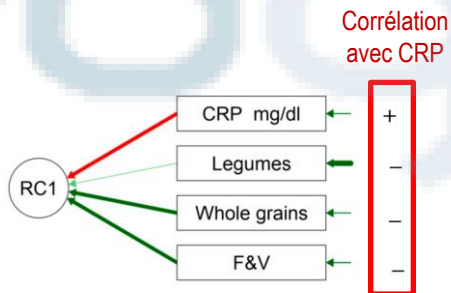
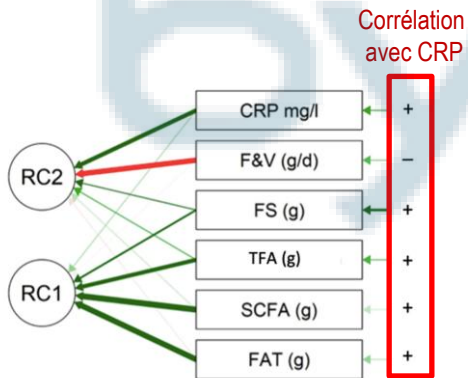
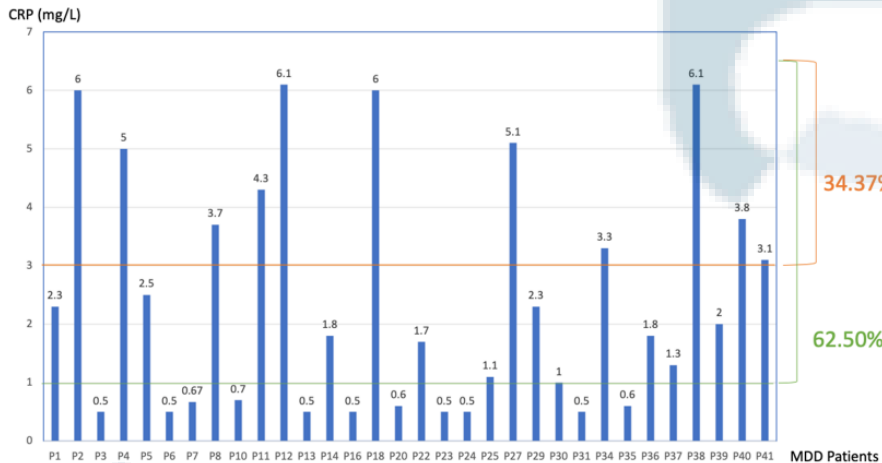
	Non-obesogenic diet group	Obesogenic diet group	p
Sample size, n (%)	28 (56)	22 (44)	
High consumers of sugar, n (%)	11 (42.3)	15 (57.7)	0.04
High consumers of salt, n (%)	4 (14.3)	15 (68.2)	<0.001
High consumers of fat, n (%)	3 (10.7)	20 (90.9)	<0.001
Age, years (SD)	38.8 (7.3)	36.3 (8.5)	0.27
Females, n (%)	26 (92.9)	17 (77.3)	0.22
BMI, kg/m <sup>2</sup> (SD)	23.8 (3.3)	24.99 (5.0)	0.32
Metabolic and endocrine alterations, n yes(%)	2 (7.4)	3 (13.6)	0.64



## Reconnaissance verbale CANTAB



# L'AUGMENTATION DES NIVEAUX DE CRP EST ASSOCIÉE À DES HABITUDES ALIMENTAIRES DE TYPE OCCIDENTAL CHEZ LES PATIENTS DÉPRIMÉS



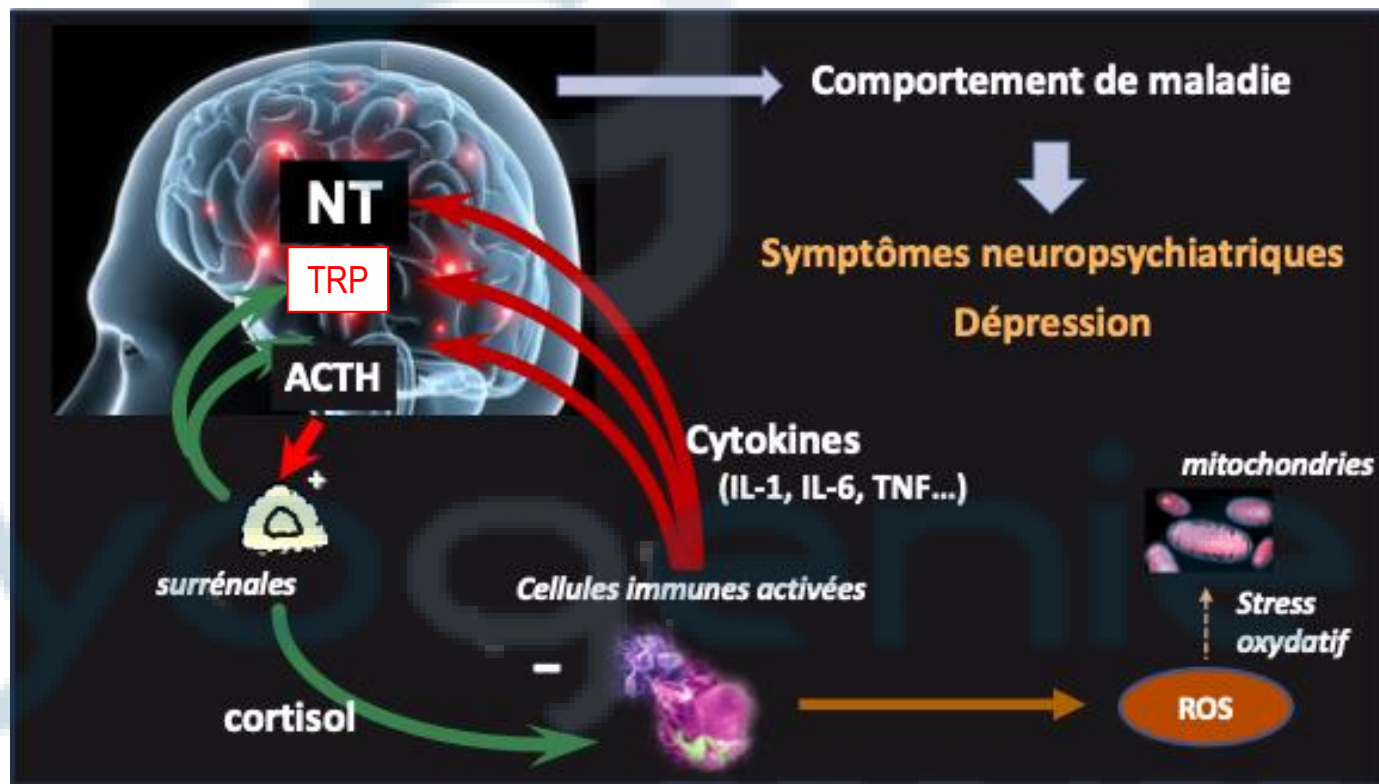
Food Categories/ NR	Patient		CTRL	p-Value
	Mean + SD	Mean + SD	Mean + SD	
Fruits & vegetables (F&V) 550 g/day	226 ± 182	451 ± 199	451 ± 199	<0.001 <sup>a</sup>
Whole grains NR:125 g/day	65.4 ± 63.8	68.0 ± 46.3	68.0 ± 46.3	0.502 <sup>a</sup>
Legumes g/week NR:100 g/day	32.8 ± 72.2	166 ± 207	166 ± 207	<0.001 <sup>a</sup>

Macronutrients/ NR	Patient		CTRL	p-Value
	Mean + SD	Mean + SD	Mean + SD	
%FAT/ <35%	37.6 ± 4.83	41.2 ± 5.77	41.2 ± 5.77	0.009 <sup>b</sup>
%SCFA/ <10%	14.262 ± 3.845	14.830 ± 3.455	14.830 ± 3.455	0.283 <sup>a</sup>
%TFA/ 0%	0.709 ± 2.048	0.342 ± 0.182	0.342 ± 0.182	0.989 <sup>a</sup>
%n-6 PUFA/ 4-8%	2.127 ± 1.098	2.484 ± 1.343	2.484 ± 1.343	0.360 <sup>a</sup>
%n-3 PUFA/ 1-2%	0.330 ± 0.181	0.519 ± 0.338	0.519 ± 0.338	0.017 <sup>a</sup>
PUFA n-6/n-3 ratio	7.441 ± 3.970	5.932 ± 4.035	5.932 ± 4.035	0.051 <sup>a</sup>
%MUFA/ >10%	8.756 ± 3.087	12.144 ± 5.677	12.144 ± 5.677	0.006 <sup>a</sup>
%Free Sugar (FS) <20%	22.650 ± 13.314	14.428 ± 4.760	14.428 ± 4.760	<0.001 <sup>a</sup>
Fibres/ 25 g/day	16.891 ± 7.102	22.988 ± 6.397	22.988 ± 6.397	0.001 <sup>b</sup>

# MÉCANISMES INFLAMMATOIRES A L'ORIGINE DES COMORBIDITÉS NEUROPSYCHIATRIQUES DE L'OBÉSITÉ



Habitudes alimentaires obésogènes



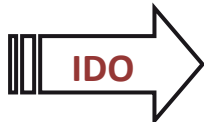
PROJET

# ALTÉRATIONS DU MÉTABOLISME DU TRYPTOPHANE DANS L'OBÉSITÉ



**Inflammation**

IDO: indoléamine 2,3 dioxygénase

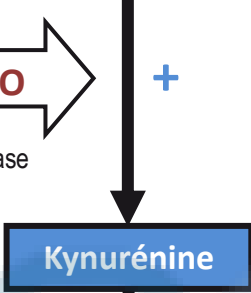


**Tryptophane**

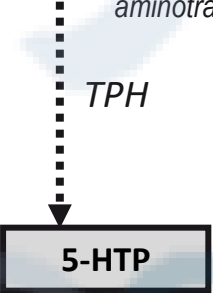


**Indolepyruvate**

*Clostridium sporogenes*  
*Lactobacillus spp.*  
*Bifidobacterium spp.*



**Kynurénine**

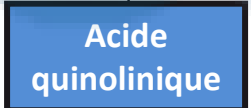


**5-HTP**

**Acide Indole-3-lactique**

e.g.: *Clostridium sporogenes*;  
*Peptostreptococcus russellii*

**NMDA R  
Glutamate**



**Acide quinolinique**



**Sérotonine**

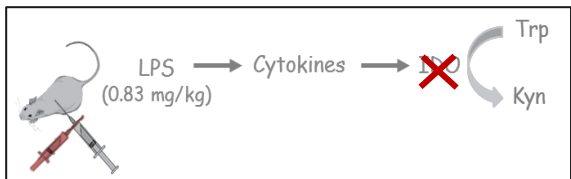
**Acide Indole-3-propionique**



**Symptômes neuropsychiatriques**

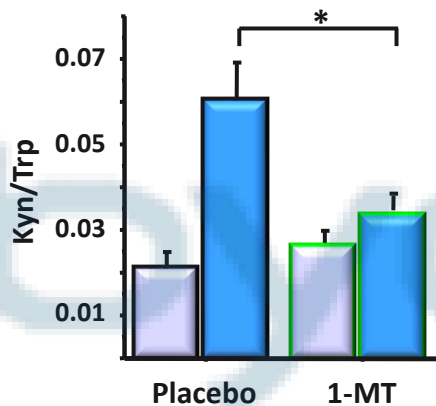
*Microbiote intestinal*

# L'INHIBITION PHARMACOLOGIQUE DE L'IDO BLOQUE LES EFFETS DÉPRESSOGÈNES DE L'INFLAMMATION



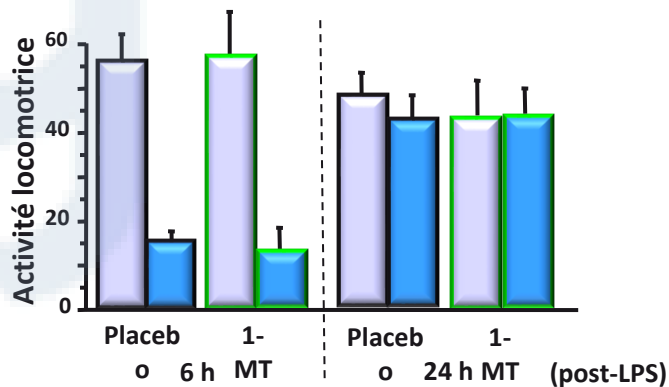
1-MT  
(5 mg/d, 1 wk)

Activation d'IDO dans le cerveau

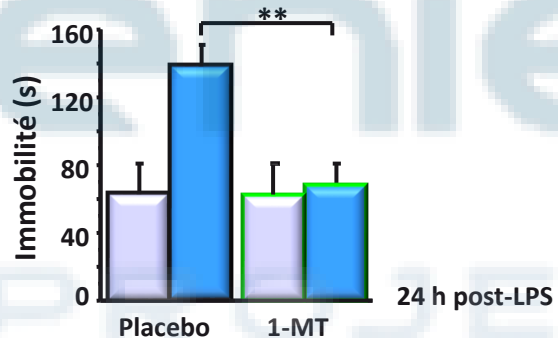


Saline LPS

Comportement de maladie

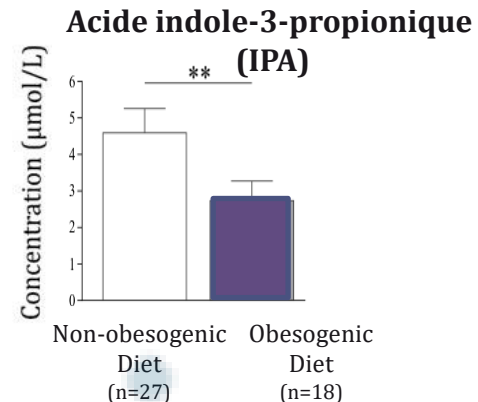
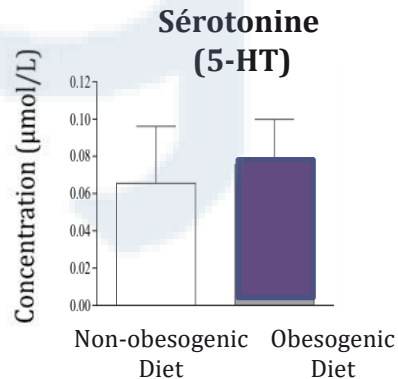
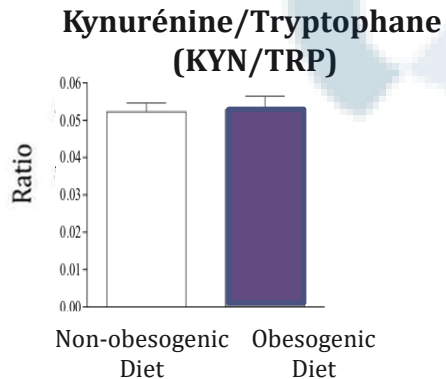
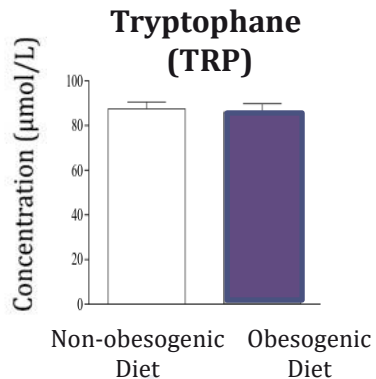


Symptômes dépressifs

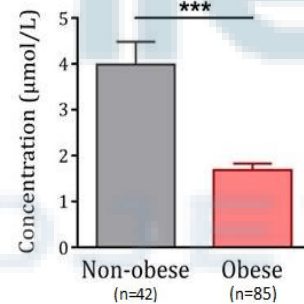
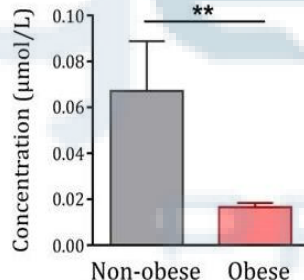
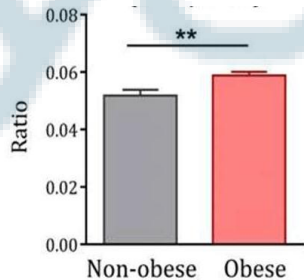
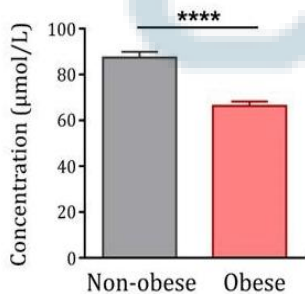


# ALTÉRATIONS DES VOIES MÉTABOLIQUES DU TRYPTOPHANE EN LIEN AVEC LES HABITUDES ALIMENTAIRES ET L'OBÉSITÉ

## Régime alimentaire obésogène (*In prep*) CRP (0.8 vs 1.7 mg/L)



## Obésité (*Cusotto et al. Front Immunol, 2020*) CRP (1 vs 8.8 mg/L)

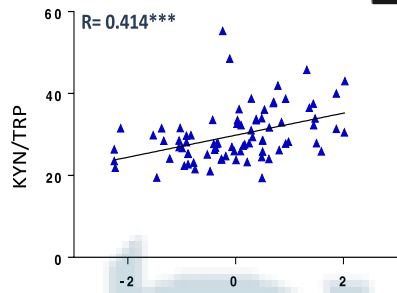


# LES ALTÉRATIONS DU MÉTABOLISME DU TRYPTOPHANE DANS L'OBÉSITÉ CORRÈLENT AVEC LA SYMPTOMATOLOGIE DÉPRESSIVE

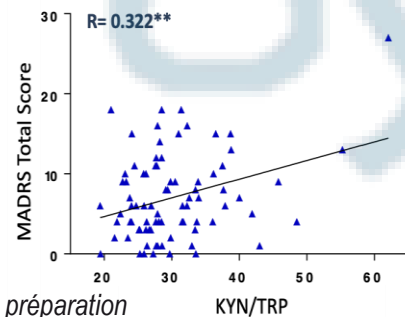


Inflammation

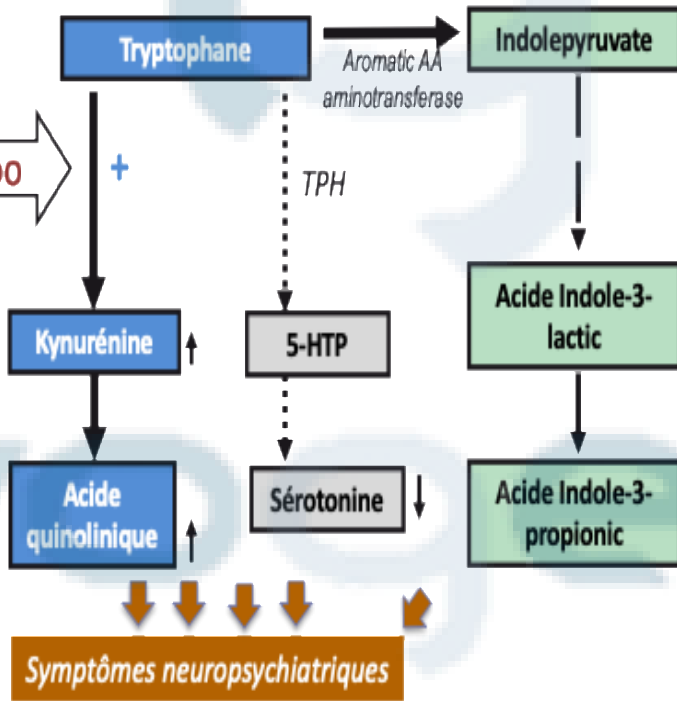
Microbiote intestinal



Inflammatory Profile (hsCRP + hsIL-6)



En préparation



**Table 2.** Interaction effect between hsCRP and IAld on MADRS total scores.

	Adjusted $R^2$	$\beta$	t	p
<i>Model</i>				
1. hsCRP	0.081	0.307	2.08	0.04
2. IAld	0.270	-0.527	-4.01	<0.001
3. hsCRP x IAld	0.220	-0.479	-3.52	0.001

Multiple regression analyses ( $\beta$  coefficients) controlling for comorbidities (hypertension, type-2 diabetes, obstructive sleep apnea, dysthyroidism). hsCRP and IAld were log-transformed for the analyses due to non-normality.  $N = 44$ .

hsCRP high-sensitive C-reactive protein, IAld indole-3-carboxaldehyde.

Delgado et al., *Int J Obes*, 2022

PROJET

# PERTURBATIONS DU CYCLE DE KREBS DANS L'OBÉSITÉ ET CONSÉQUENCES NEUROPSYCHIATRIQUES : DONNÉES TRANSLATIONNELLES

La diminution des marqueurs plasmatiques du cycle de Krebs chez le sujet en situation d'obésité corrèle avec la fatigue et la baisse de motivation



Données précliniques: souris HFD (régime riche en gras)

Sample size, n	86	
	Mean (SD)	Min-Max
	N (%)	
Age, years, mean (SD)	37.9 (1.2)	18-64
Females, n (%)	73 (85)	
BMI, kg/m <sup>2</sup> , mean (SD)	40.8 (0.5)	33-59
Weight, kg, mean (SD)	111.5 (2.0)	75-163
Current MDD, n (%)	5 (5.8)	
History of MDD, n (%)	32 (37)	

### Obesity-related comorbidities

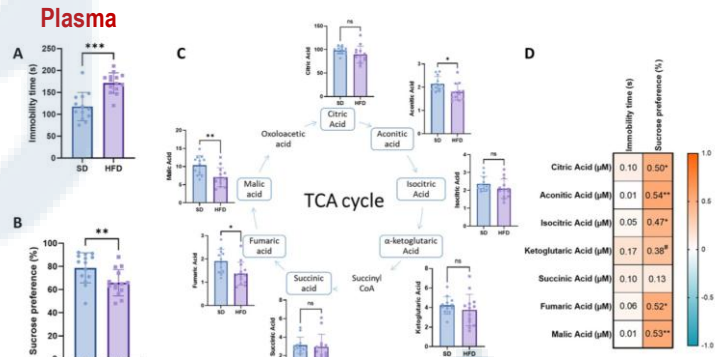
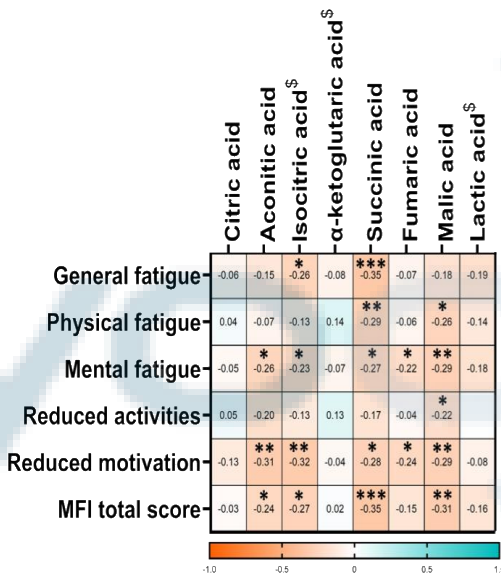
Hypertension, n(%)	16 (19%)
Type-2 diabetes, n(%)	7 (8%)
Dysthyroidism, n(%)	6 (7%)
Obstructive sleep apnea, n(%)	46 (53%)

### Inflammation

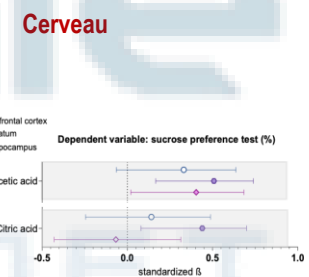
hsCRP <sup>3</sup> (CHU), mg/L (SD)	7.8 (0.7)	0.8-30.7
IL-6 <sup>5</sup> , mean (SD)	3.0 (0.2)	0.9-8.9
TNF-α <sup>5</sup> , mean (SD)	1.1 (0.0)	0.6-2.3
Neopterin <sup>5</sup> , mean (SD)	8.0 (0.2)	4.2-13.0

### Neuropsychiatric profile

• MADRS total score, mean (SD)	6.8 (0.6)	0-28
• STAI TRAIT total score mean (SD)	40.1 (1.1)	23-69
• MFI total score, mean (SD)	48.5 (1.5)	25-88

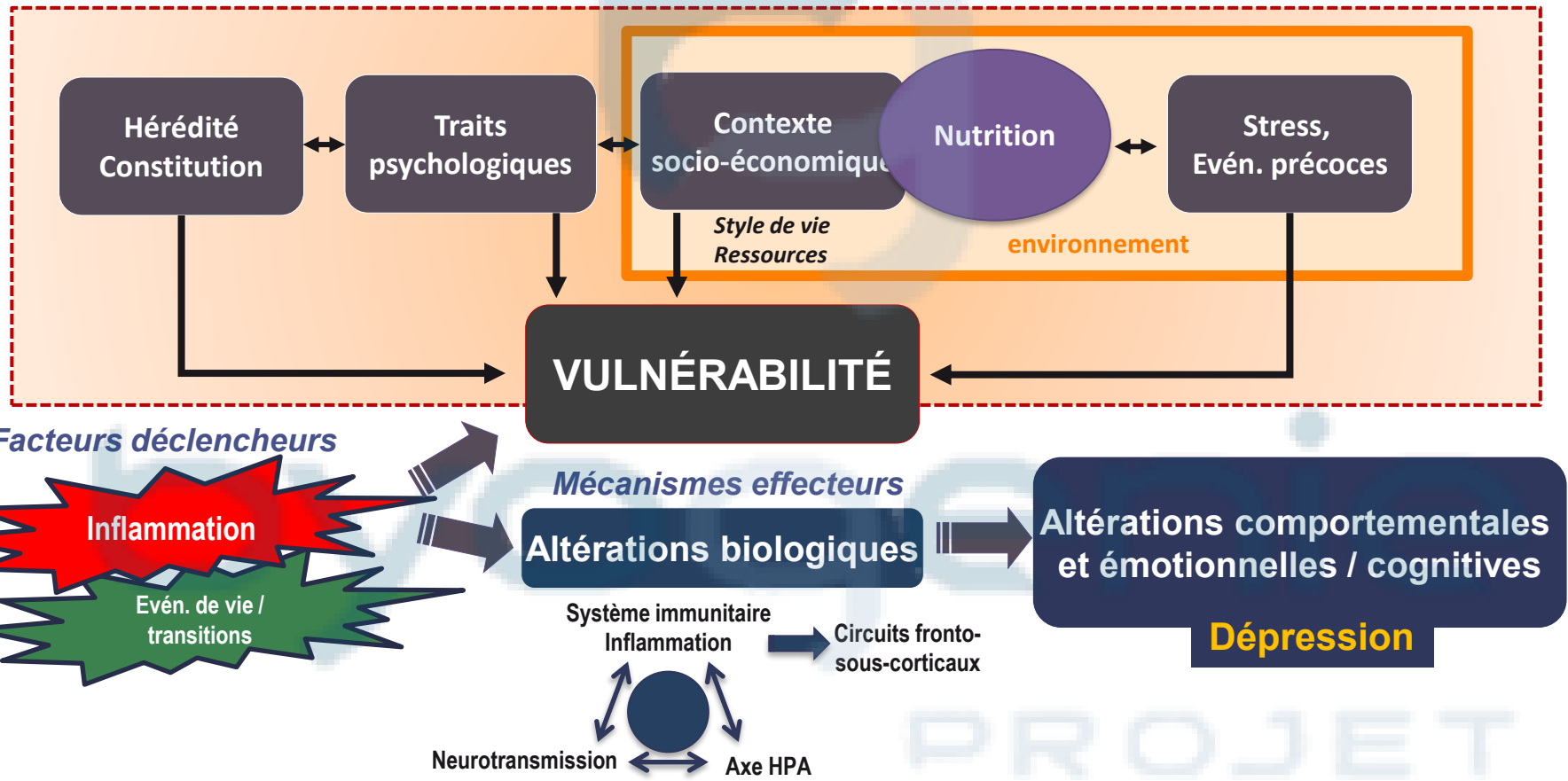


	TCA cycle metabolites (µM)	SD, n=14	HFD, n=15	p
Prefrontal cortex	Citric Acid	8.12 (2.78)	5.73 (2.01)	
	Aconitic Acid	0.23 (0.06)	0.25 (0.06)	
	α-ketoglutaric acid <sup>2</sup>	0.15 (0.07)	0.16 (0.06)	
	Succinic acid	0.19 (0.13)	0.17 (0.11)	
	Fumaric acid <sup>2</sup>	0.77 (0.12)	0.86 (0.22)	
	Malic acid	2.27 (0.31)	2.43 (0.37)	
	Oxaloacetic acid <sup>2</sup>	0.68 (0.29)	0.56 (0.18)	p=0.06
	Citric Acid	8.65 (1.81)	7.57 (1.39)	
Striatum	Aconitic Acid	0.22 (0.05)	0.21 (0.04)	
	α-ketoglutaric acid <sup>2</sup>	0.13 (0.06)	0.11 (0.03)	
	Succinic acid	0.24 (0.21)	0.19 (0.14)	
	Fumaric acid	0.79 (0.09)	0.72 (0.10)	p=0.053
	Malic acid	2.21 (0.36)	2.21 (0.27)	
Hippocampus	Oxaloacetic acid <sup>2</sup>	0.70 (0.21)	0.51 (0.09)	**
	Citric Acid	7.77 (2.18)	7.47 (1.48)	
	Aconitic Acid	0.21 (0.05)	0.20 (0.041)	
	α-ketoglutaric acid	0.19 (0.03)	0.17 (0.03)	
	Succinic acid <sup>2</sup>	0.05 (0.02)	0.09 (0.05)	**

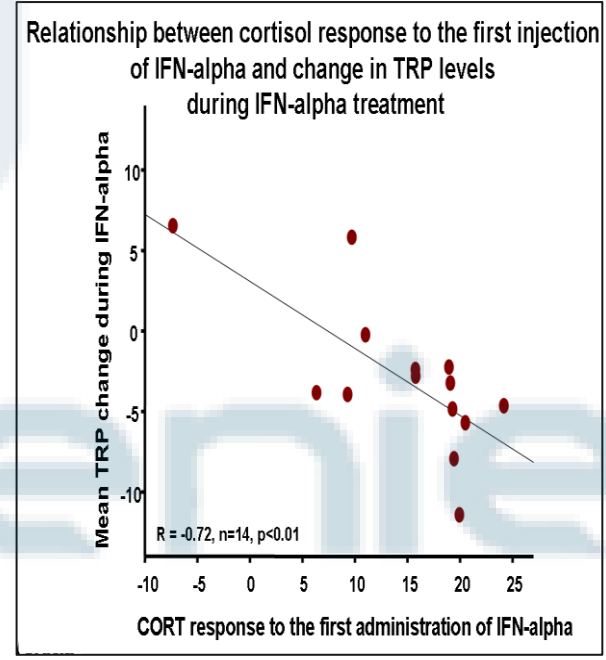
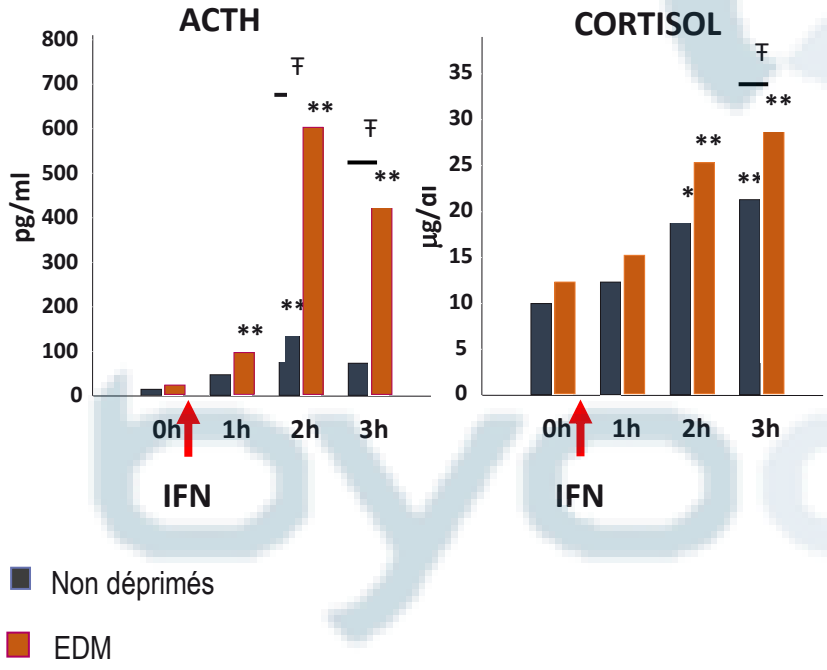


Continuous variables are presented as mean and standard deviation and compared using an independent Student's t-test. Abbreviations: TCA cycle: Tricarboyllic acid cycle; SD: Standard Diet; HFD: High-Fat Diet; µM: micromolaire; PFC: Prefrontal cortex; Str: Striatum; HC: Hippocampus. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001; †log10

# VULNÉRABILITÉ AUX EFFETS NEUROPSYCHIATRIQUES DE L'INFLAMMATION



# HYPER-RÉACTIVITÉ DE L'AXE CORTICOTROPE : UN MARQUEUR DE VULNÉRABILITÉ AUX EFFETS DÉPRESSOGÈNES DE L'INFLAMMATION



# Pituitary-Adrenal and Autonomic Responses to Stress in Women After Sexual and Physical Abuse in Childhood

JAMA, August 2, 2000—Vol 284, No. 5 (Reprinted)

Christine Heim, PhD

D. Jeffrey Newport, MD

Stacey Heit, MD

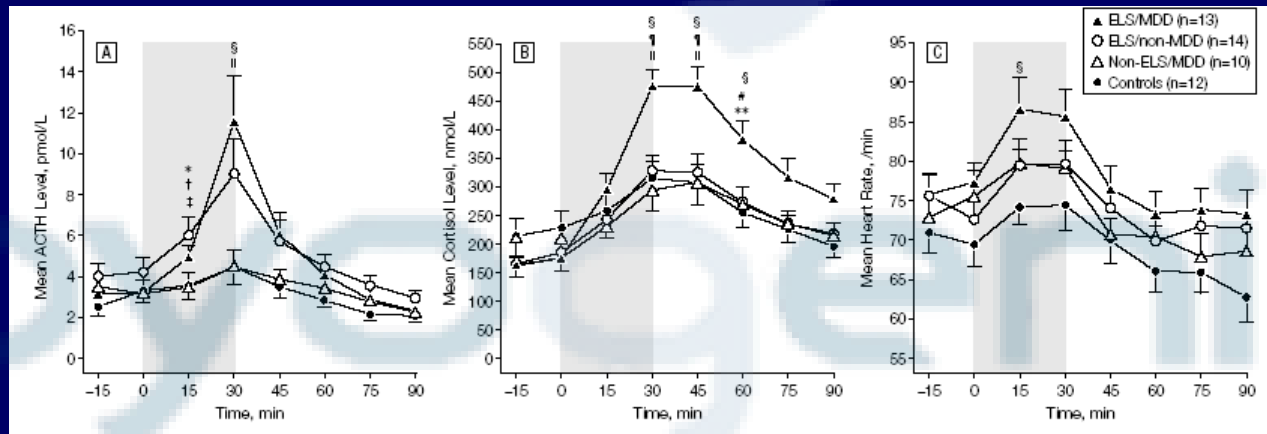
Yolanda P. Graham, MD

Molly Wilcox, BA

Robert Bonsall, PhD

Andrew H. Miller, MD

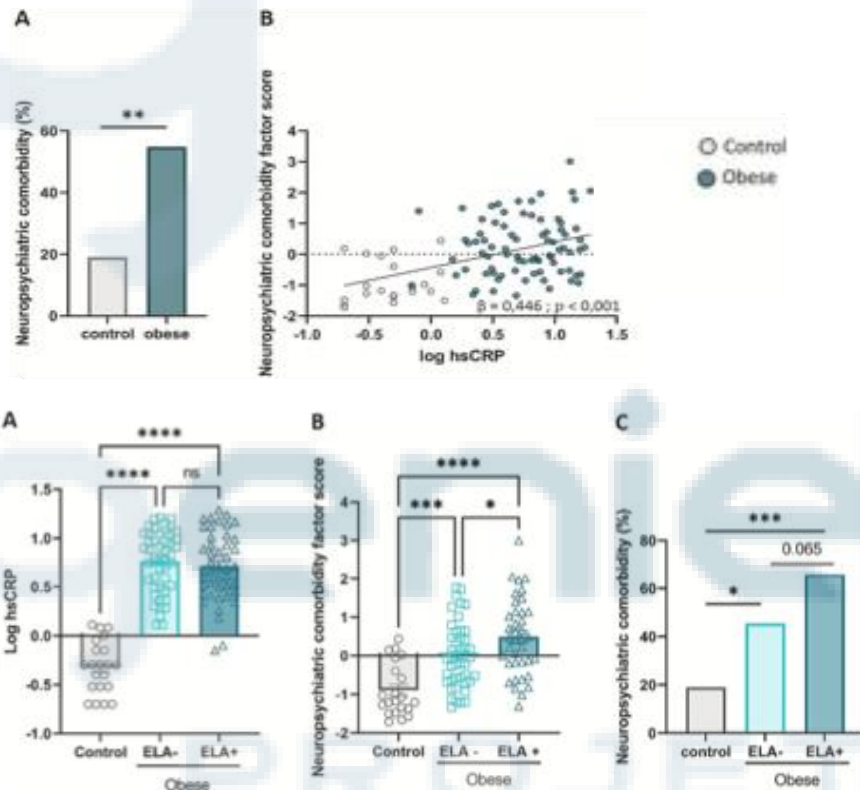
Charles B. Nemeroff, MD, PhD



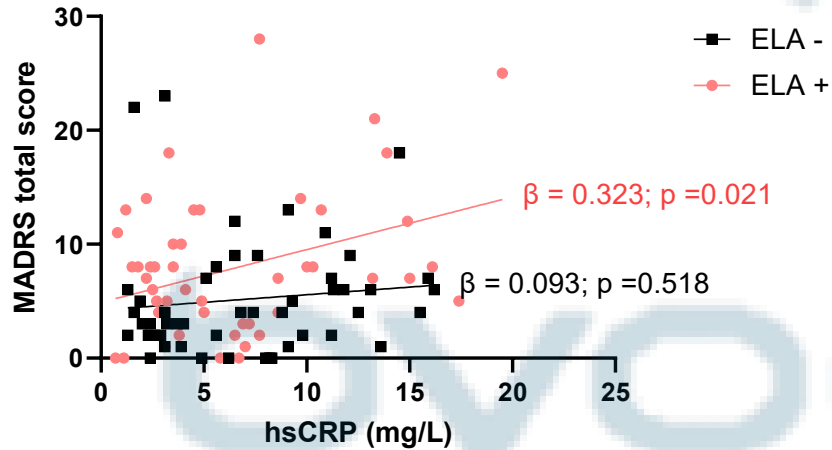
# LE STRESS PRÉCOCE AMPLIFIE LE LIEN INFLAMMATION – DÉPRESSION CHEZ LES SUJETS EN SITUATION D'OBÉSITÉ

Characteristics of study participants.

	Lean subjects	Obese subjects	p
Sample size, n	21	82	
Age, years (SD)	38.67 (8.28)	38.18 (10.79)	0.849
Females, n (%)	18 (85.7)	70 (85.4)	>0.99
HMI, kg/m <sup>2</sup> (SD)	21.75 (1.47)	40.44 (5.10)	<0.001
Weight, kg (SD)	59.75 (7.90)	110.66 (18.45)	<0.001
<b>Inflammation</b>			
hsCRP, mg/L (SD)	0.57 (0.35)	7.18 (4.72)	<0.001
<b>Obesity-related comorbidities</b>			
Hypertension, n (%)	0	15 (18.3)	0.037
Type-2 diabetes, n (%)	0	5 (6.1)	0.580
Dysthyroidism, n (%)	0	5 (6.1)	0.580
Obstructive sleep apnea, n (%)	0	45 (54.9)	<0.001
<b>Neuropsychiatric profile</b>			
Depressive symptoms (MADRS total score (SD))	2.10 (2.53)	6.93 (5.79)	<0.001
Fatigue (MFI total score (SD))	34.76 (10.56)	50.30 (14.30)	<0.001
General behavioral symptoms (NRS total score (SD))	12.86 (10.05)	36.04 (20.36)	<0.001
Current MDD, n (%)	0 (0)	6 (7.32)	0.342
History of MDD, n (%)	8 (38.1)	28 (35.9)	0.853
<b>Childhood adversity</b>			
Childhood adversity exposure, n (%)	7 (33.33)	38 (46.30)	0.284
CTQ scores			
Emotional abuse	10.14 (6.00)	9.37 (4.52)	0.514
Physical abuse	6.24 (2.21)	6.96 (3.90)	0.416
Sexual abuse	6.05 (2.82)	6.85 (4.32)	0.423
Emotional neglect	10.90 (4.38)	12.53 (5.23)	0.192
Physical neglect	6.43 (1.75)	7.76 (3.19)	0.068
CTQ total score	39.76	43.47	0.959



# LE STRESS PRÉCOCE AMPLIFIE LE LIEN INFLAMMATION – DÉPRESSION CHEZ LES SUJETS EN SITUATION D'OBÉSITÉ



Brain, Behavior, and Immunity 128 (2025) 612–619



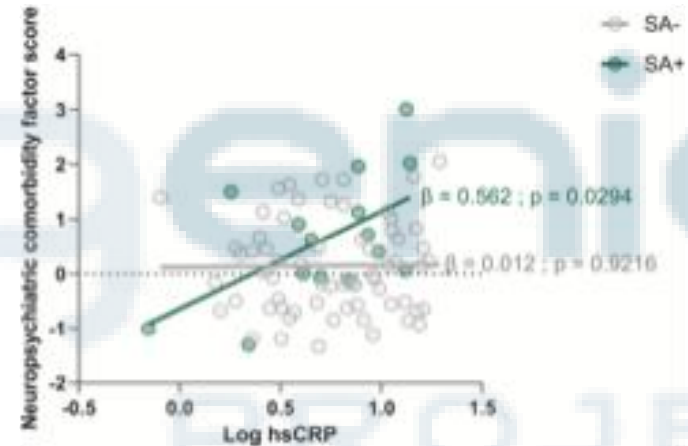
Contents lists available at ScienceDirect

Brain Behavior and Immunity

journal homepage: [www.elsevier.com/locate/ybrbi](http://www.elsevier.com/locate/ybrbi)

Role of early life adversities in inflammation-related neuropsychiatric comorbidity in obesity

Juliette Montet<sup>a</sup>, Sandra Dexpert<sup>a</sup>, Muriel Darnaudéry<sup>a</sup>, Cédric Beau<sup>b</sup>, Damien Forestier<sup>b</sup>, Patrick Ledaguenel<sup>b</sup>, Eric Magne<sup>b</sup>, Bruno Aouizerate<sup>a,c</sup>, Lucile Capuron<sup>a,\*</sup>

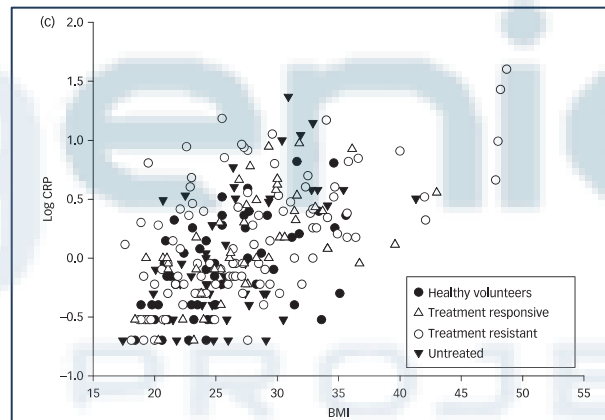
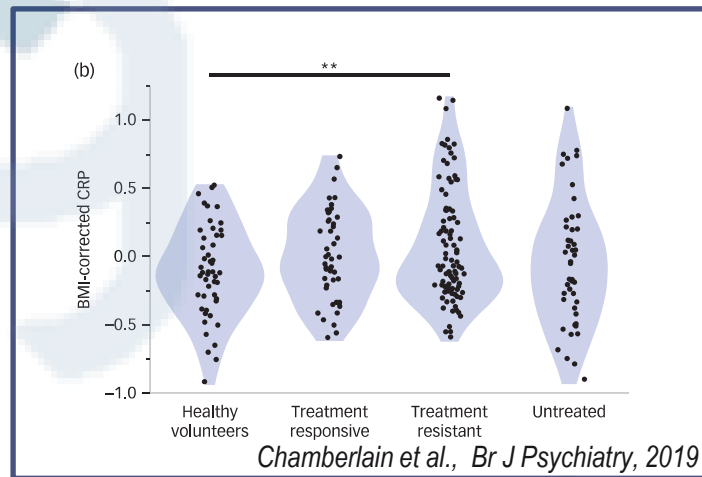
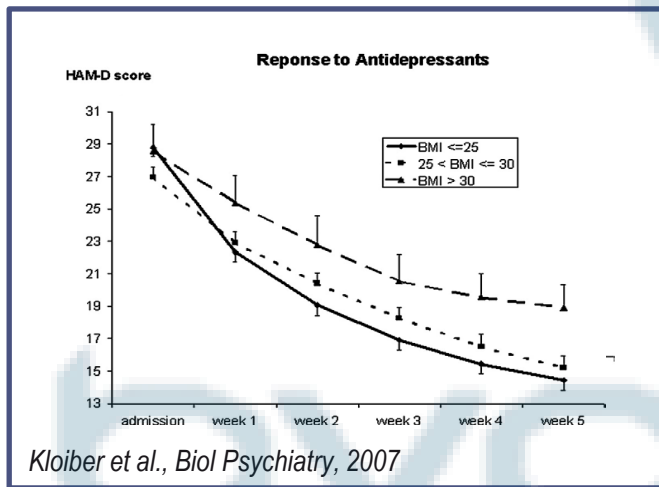


# TRAITEMENT DES SYMPTÔMES NEUROPSYCHIATRIQUES LIÉS À L'INFLAMMATION DANS L'OBÉSITÉ ET LES TROUBLES MÉTABOLIQUES

CONDITION	PREVALENCE
General population	5-10%
Cancer	18-39%
Autoimmune disorders	15-40%
Cardiovascular diseases	15-40%
Chronic illnesses	15-60%
Obesity / metabolic disorders / Aging	20-30%

Inflammation

# L'INFLAMMATION PARTICIPE À LA RÉSISTANCE AUX ANTIDÉPRESSEURS



# A Randomized Controlled Trial of the Tumor Necrosis Factor Antagonist Infliximab for Treatment-Resistant Depression

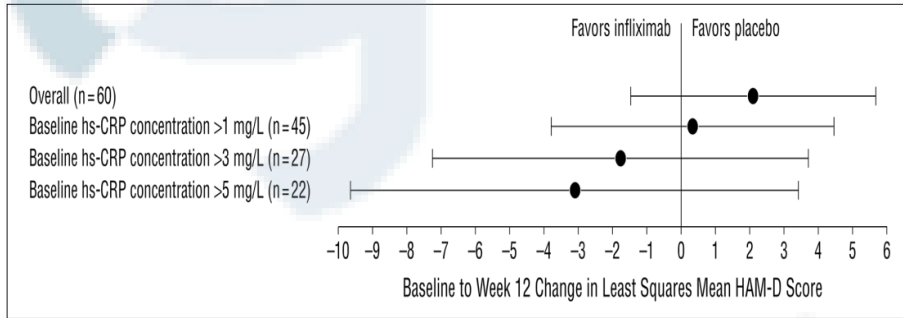
## The Role of Baseline Inflammatory Biomarkers

Charles L. Raison, MD; Robin E. Rutherford, MD; Bobbi J. Woolwine, MSW; Chen Shuo, MS; Pamela Schettler, PhD; Daniel F. Drake, PhD; Ebrahim Haroon, MD; Andrew H. Miller, MD

JAMA Psychiatry. 2013;70(1):31-41

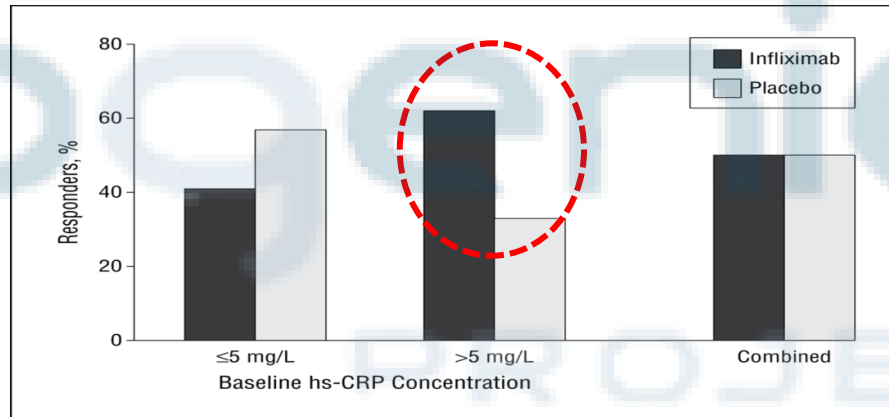
### Clinical Characteristics of the Study Sample

Characteristic	Infliximab (n=30)	Placebo (n=30)
Age (yrs.) – mean (SD)	42.5 (8.2)	44.3 (9.4)
Sex (female) – no. (%)	20 (66%)	20 (66%)
BMI (kg/m <sup>2</sup> ) – mean (SD)	31.2 (6.9)	32.7 (8.0)
Baseline hs-CRP (mg/L) – mean (SD)	6.34 (8.9)	5.45 (8.2)



### Characteristics of TRD Patients with CRP>5mg/L

Characteristic	Infliximab (n=13)	Placebo (n=9)
Age (yrs.) – mean (SD)	41.4 (8.5)	46.2 (9.7)
Sex (female) – no. (%)	10 (77%)	7 (78%)
BMI (kg/m <sup>2</sup> ) – mean (SD)	34.2 (6.5)	38.9 (8.1)
Baseline hs-CRP (mg/L) – mean (SD)	12.5 (10.9)	14.2 (10.8)



# Inflammation as a predictive biomarker for response to omega-3 fatty acids in major depressive disorder: a proof-of-concept study

MH Rapaport<sup>1</sup>, AA Nierenberg<sup>2</sup>, PJ Schettler<sup>1</sup>, B Kinkead<sup>1</sup>, A Cardoos<sup>2</sup>, R Walker<sup>2</sup> and D Mischoulon<sup>2</sup>

Molecular Psychiatry (2016) 21, 71–79

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www.nature.com/mp



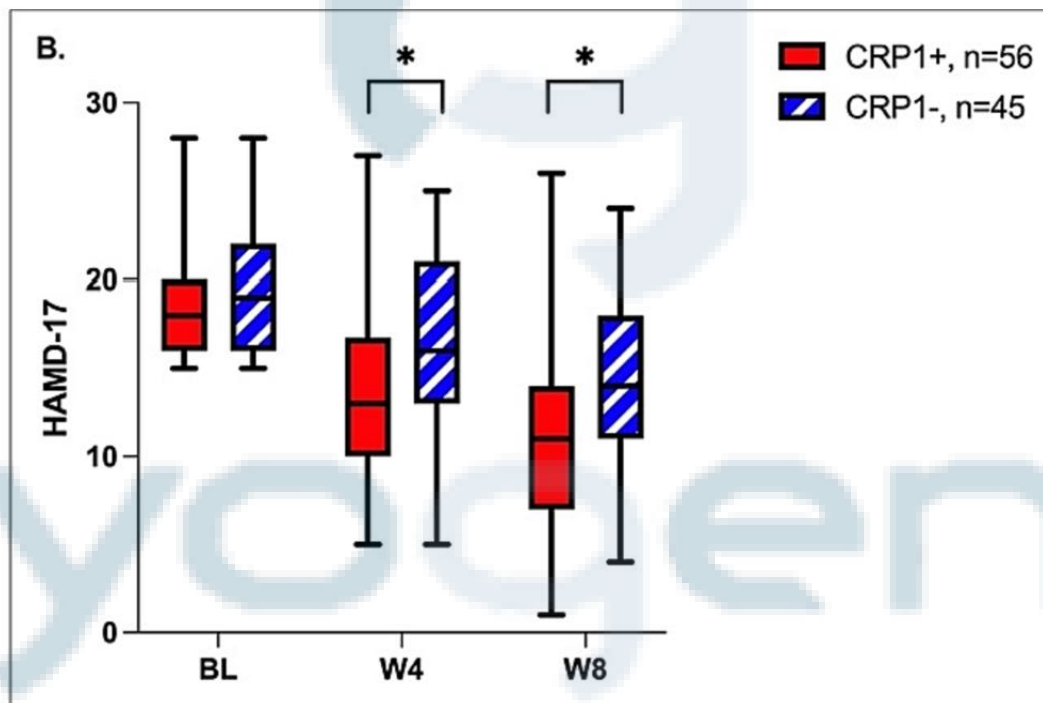
**Table 3.** Change in HAM-D-17 total score from baseline to treatment week 8 for subjects treated with EPA vs PLA with high inflammation on individual biomarkers and pairs of biomarkers at baseline<sup>a</sup>

High inflammatory status on	Significance of treatment-by-time interaction			Baseline to week 8		Standardized treatment effect size at treatment week 8			EPA vs PLA at treatment week 8			Significance of treatment-by-time interaction		
				PLA		ES <sup>b</sup>		t		F		P-value		
Individual biomarkers	F	df	P-value	-mean	s.e.m.	N	ES <sup>b</sup>	95% CI	t	df <sup>c</sup>	P-value	F	df	P-value
hs-CRP	1.70	1, 90.6	0.195	-7.99	1.86	8	-0.78	-1.67 to +0.11	-1.84	42.8	0.073	1.70	1, 90.6	0.195
IL-6	0.42	1, 104	0.518	-7.84	1.40	12	-0.37	-1.13 to +0.40	-0.96	54.0	0.341	0.42	1, 104	0.518
IL-1ra	0.31	1, 127	0.580	-9.63	1.61	11	-0.46	-1.18 to +0.27	-1.26	72.1	0.213	0.31	1, 127	0.580
Leptin	1.01	1, 101	0.318	-5.61	1.46	13	-0.62	-1.34 to +0.11	-1.72	63.3	0.090	1.01	1, 101	0.318
Adiponectin	1.69	1, 159	0.195	-8.81	1.06	21	-0.58	-1.20 to +0.04	-1.88	94.9	0.063	1.69	1, 159	0.195
<b>10 Pairs of biomarkers</b>														
hs-CRP+IL-6	4.13	1, 51.9	0.047	-4.44	2.30	4	-1.47	-2.77 to -0.17	-2.65	22.2	0.015	4.13	1, 51.9	0.047
hs-CRP+IL-1ra	1.18	1, 54.2	0.281	-7.05	3.66	2	-0.99	-2.53 to +0.54	-1.42	25.1	0.167	1.18	1, 54.2	0.281
hs-CRP+leptin	0.87	1, 64.6	0.354	-6.30	2.52	5	-0.67	-1.74 to +0.40	-1.34	28.3	0.192	0.87	1, 64.6	0.354
hs-CRP+adiponectin	3.66	1, 47.5	0.062	-3.56	2.33	4	-1.72	-3.10 to -0.34	-2.92	18.9	0.009	3.66	1, 47.5	0.062
IL-6+IL-1ra	0.68	1, 56.1	0.415	-7.41	2.21	6	-0.72	-1.79 to +0.35	-1.35	23.7	0.189	0.68	1, 56.1	0.415
IL-6+leptin	3.94	1, 65.3	0.051	-3.15	1.96	6	-1.30	-2.38 to -0.22	-2.74	32.1	0.010	3.94	1, 65.3	0.051
IL-6+adiponectin	0.28	1, 65.7	0.597	-7.46	2.03	6	-0.52	-1.53 to +0.49	-1.06	27.7	0.300	0.28	1, 65.7	0.597
IL-1ra+leptin	0.60	1, 71.4	0.441	-5.80	2.54	5	-0.73	-1.78 to +0.32	-1.43	32.1	0.162	0.60	1, 71.4	0.441
IL-1ra+adiponectin	0.00	1, 52.9	0.954	10.44	2.33	4	-0.52	-1.67 to +0.63	-0.92	28.1	0.367	0.00	1, 52.9	0.954
Leptin+adiponectin	1.22	1, 72.1	0.274	-5.42	1.86	6	-0.92	-1.92 to +0.07	-1.99	38.2	0.054	1.22	1, 72.1	0.274

## High inflammation per BMI

	hs-CRP	IL-6
Underweight or normal weight (%)	11.8	7.8
Overweight (%)	13.3	15.6
Obese (%)	47.9	54.2

# UN TRAITEMENT ADJUVANT PAR EPA + DHA AUGMENTE LA RÉPONSE AU TRAITEMENT ANTIDÉPRESSEUR CHEZ DES PATIENTS DÉPRIMÉS AVEC UN PROFIL INFLAMMATOIRE (hSCRP $\geq 1$ MG/L)



Patients déprimés non-répondeurs (traitement actuel; durée > 6 semaines).  
 Traitement adjuvant par omégas-3 (2.2 g EPA, 400 mg DHA, 800 mg autres AG, + extraits riches en tocopherol)

# UN FAIBLE STATUT EN OMÉGAS-3 PRÉDIT UNE MAUVAISE RÉPONSE AUX ANTIDÉPRESSEURS

Received: 22 September 2021 | Revised: 7 February 2022 | Accepted: 17 March 2022

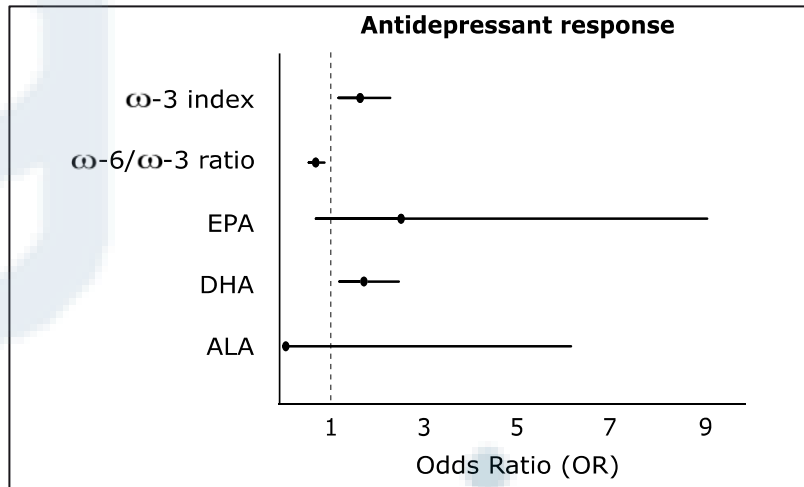
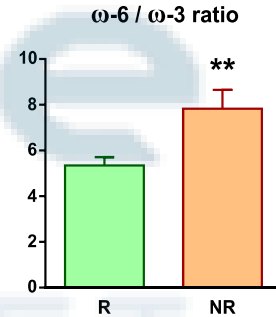
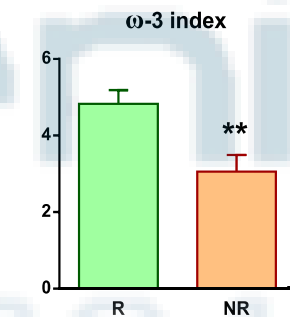
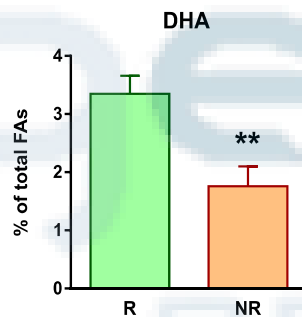
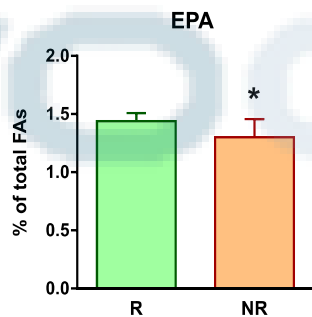
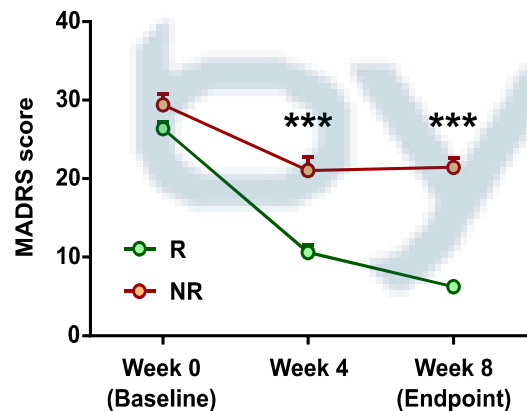
DOI: 10.1002/da.23257

RESEARCH ARTICLE



## Low omega-3 polyunsaturated fatty acids predict reduced response to standard antidepressants in patients with major depressive disorder

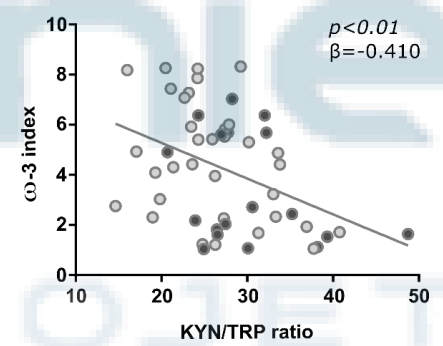
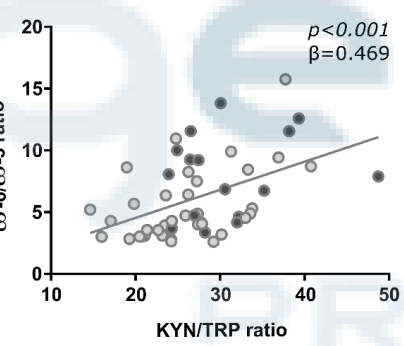
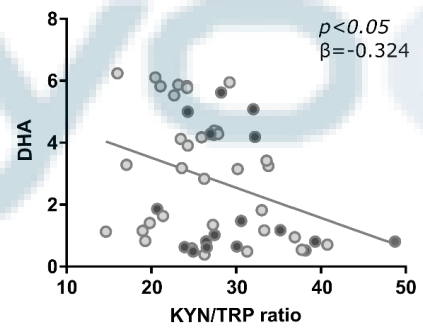
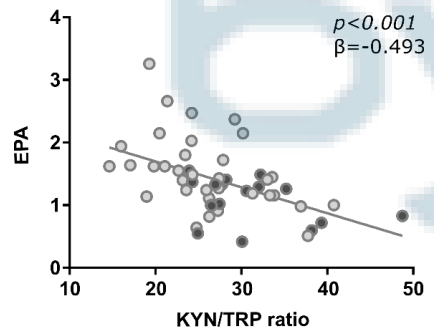
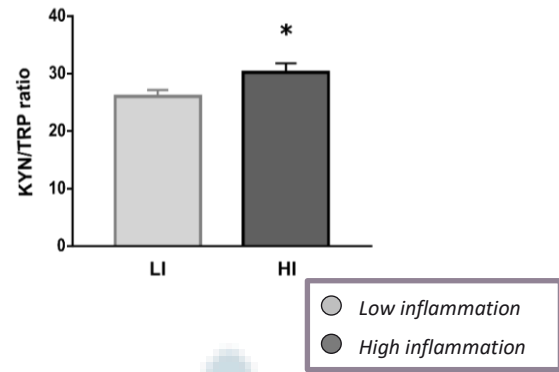
Sofia Cusotto<sup>1</sup> | Inês Delgado<sup>1</sup> | Giovanni Oriolo<sup>2,3</sup> | Jonas Kemper<sup>4</sup> |  
Diane Begarie<sup>5</sup> | Sandra Dexpert<sup>1</sup> | Julie Sauvant<sup>1</sup> | Marion Leboyer<sup>6,7</sup> |  
Bruno Aouizerate<sup>1,8</sup> | Rocío Martin-Santos<sup>2,3</sup> | Martin Schaefer<sup>4,9</sup> |  
Lucile Capuron<sup>1</sup>



# UN FAIBLE STATUT EN OMÉGAS-3 EST ASSOCIÉ À L'ACTIVATION D'IDO CHEZ LES PATIENTS DÉPRIMÉS

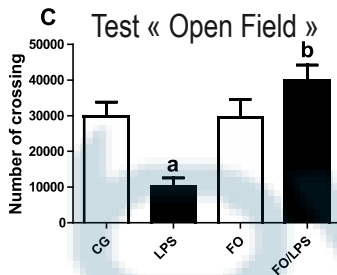
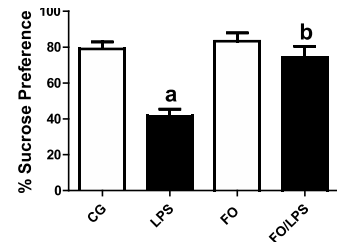
Characteristics	All (n=52)	LI (n=34)	HI (n=18)	<i>p</i> value
Age, years (SD)	40.8 (11.9)	39.6 (11.8)	43.3 (12.0)	0.292
Women, n (%)	33 (63.5)	15 (44.1)	4 (22.2)	0.119
BMI, kg/m <sup>2</sup> (SD)	24.2 (4.2)	23.5 (4.1)	25.5 (4.2)	0.099
hsCRP, ng/mL (SD)	1.7 (2.4)	0.45 (0.15)	4.2 (2.7)	<0.001
<i>PUFA variables</i>				
EPA, % total FA (SD) <sup>a</sup>	1.4 (0.6)	1.5 (0.6)	1.1 (0.3)	<0.01
DHA, % total FA (SD)	2.8 (2.0)	3.1 (2.0)	2.2 (1.9)	0.120
ω-6/ω-3 ratio, value (SD)	6.2 (3.3)	5.6 (3.0)	7.6 (3.4)	<0.05
ω-3 index, value (SD)	4.2 (2.3)	4.6 (2.3)	3.4 (2.2)	0.064

hsCRP threshold = 1 mg/L

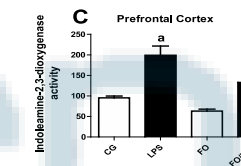
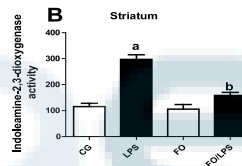
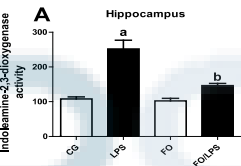
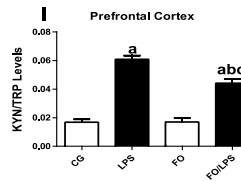
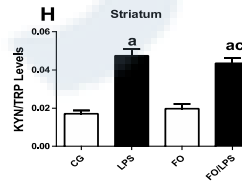
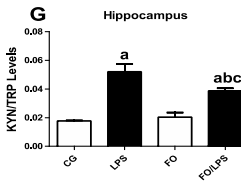
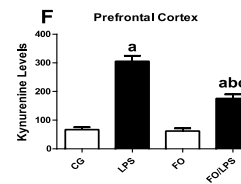
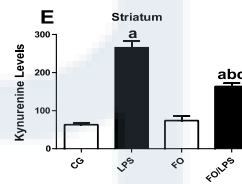
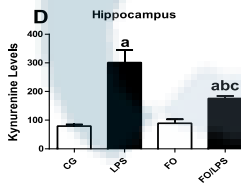


# L'HUILE DE POISSON ATTÉNUÉ LES SYMPTÔMES DÉPRESSIFS INDUITS PAR L'INFLAMMATION VIA LA VOIE IDO/KYN CHEZ LA SOURIS

Test de préférence au sucrose



*a*  $p < 0.05$  vs. *ctrl*  
*b*  $p < 0.05$  LPS vs. FO/LPS  
*c*  $p < 0.05$  FO/LPS vs. FO



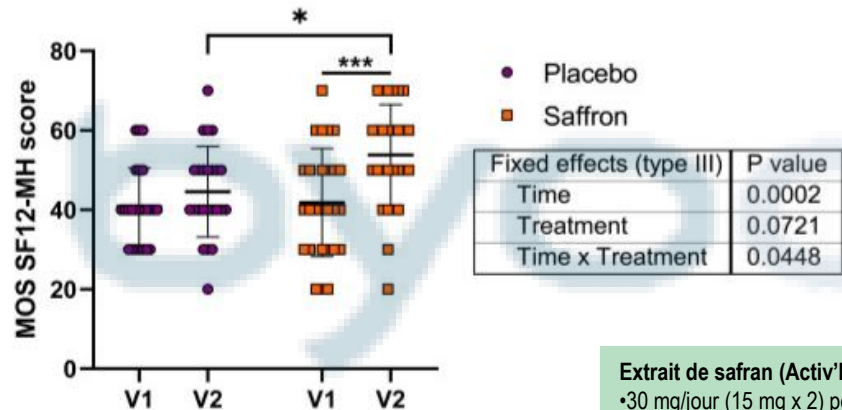
PROJET

Original Research Article

# Effect of saffron extract supplementation on mood in healthy adults with subclinical symptoms of depression: a randomized, double-blind placebo-controlled study

Camille Amadiou<sup>1</sup>, Quentin Leyrolle<sup>1</sup>, Milena Farneti<sup>1</sup>, Andrea Anesi<sup>2</sup>, Eva Bruchet<sup>1</sup>, Juliette Montet<sup>1</sup>, Sandra Dexpert<sup>1</sup>, David Gaudout<sup>3</sup>, Fulvio Mattivi<sup>2</sup>, Line Pourtau<sup>3</sup>, Nathalie Castanon<sup>1</sup>, Lucile Capuron<sup>1</sup>

## MOS SF-12 – Santé Mentale



**Extrait de safran (Activ'Inside) :**

- 30 mg/jour (15 mg x 2) pendant 6 semaines
- Gélules identiques au placebo
- Dose sûre et bien tolérée
- 1 gélule au petit-déjeuner, 1 au dîner

TABLE 1

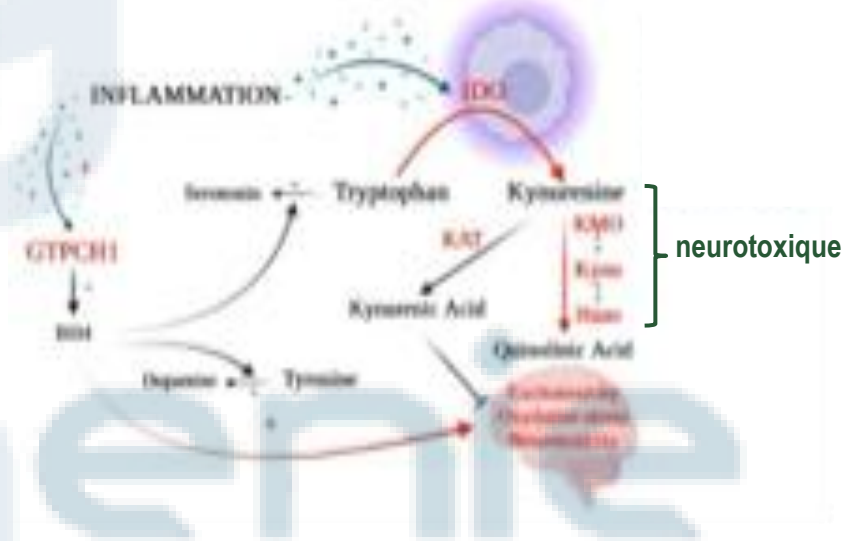
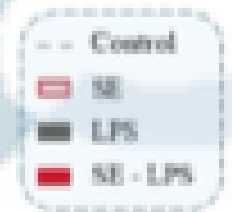
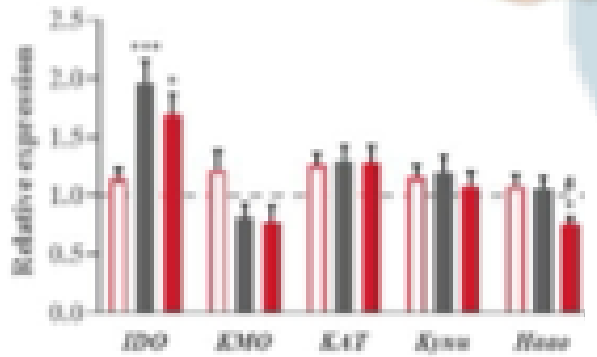
Baseline characteristics of study participants (N = 51).

	Placebo (n = 24)	Saffron (n = 27)
<b>Sociodemographic characteristics</b>		
Age (y)	32.5 ± 8.9	36.6 ± 8.6
<b>Sex</b>		
Male	6 (25.0)	8 (29.6)
Female	18 (75.0)	19 (70.4)
<b>Marital status</b>		
Couple/married	15 (62.5)	16 (59.3)
Single	8 (33.3)	9 (33.3)
Separated/divorced	1 (4.2)	2 (7.4)
<b>Educational level</b>		
Primary	0 (0.0)	0 (0.0)
Secondary	3 (12.5)	5 (18.5)
Superior	21 (87.5)	22 (81.5)
No. of children	1 ± 1	1 ± 1
<b>Clinical examination</b>		
Weight (kg)	65.3 ± 12.5	65.9 ± 9.2
BMI (kg/m <sup>2</sup> )	22.9 ± 3.2	23.5 ± 2.2
SBP (mm Hg)	114.3 ± 12.7	115.9 ± 14.2
DBP (mm Hg)	79.8 ± 9.1	79.5 ± 13.4
Heart frequency (beat/min)	71.4 ± 10.5	74.0 ± 10.6
<b>Smoking</b>		
Never	16 (75.0)	23 (85.2)
Occasional	2 (8.3)	3 (11.1)
<20/ds	4 (16.7)	1 (3.7)
IL-6 (pg/mL)	0.99 ± 0.86	1.24 ± 1.22
hsCRP (mg/L)	1.66 ± 2.49	2.08 ± 2.83
CAR	2.00 ± 4.66	5.13 ± 7.57
<b>Neuropsychiatric symptoms</b>		
NRS total score	39.29 ± 10.36	35.44 ± 14.93
Depression	8.2 ± 3.7	7.6 ± 3.6
Fatigue	58.5 ± 11.9	60.0 ± 12.6
Anxiety	45.2 ± 8.4	46.0 ± 9.3

Values are means ± SD. N = 51. For the IL-6 and the hsCRP, n = 26 in placebo group (extreme value for hsCRP > 30 mg/L). CAR, cortisol awakening response; DBP, diastolic blood pressure; hsCRP, high-sensitivity C-reactive protein; NRS, neurotoxicity rating scale; SBP, systolic blood pressure.

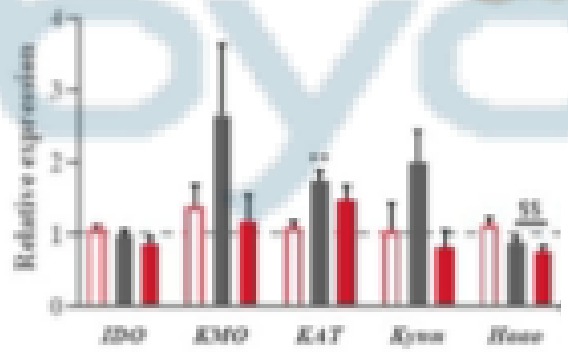
# L'EXTRAIT DE SAFRAN LIMITE L'ACTIVATION CENTRALE DE LA VOIE DE LA KYNURÉNINE INDUITE PAR L'INFLAMMATION CHEZ LA SOURIS

## Cortex frontal



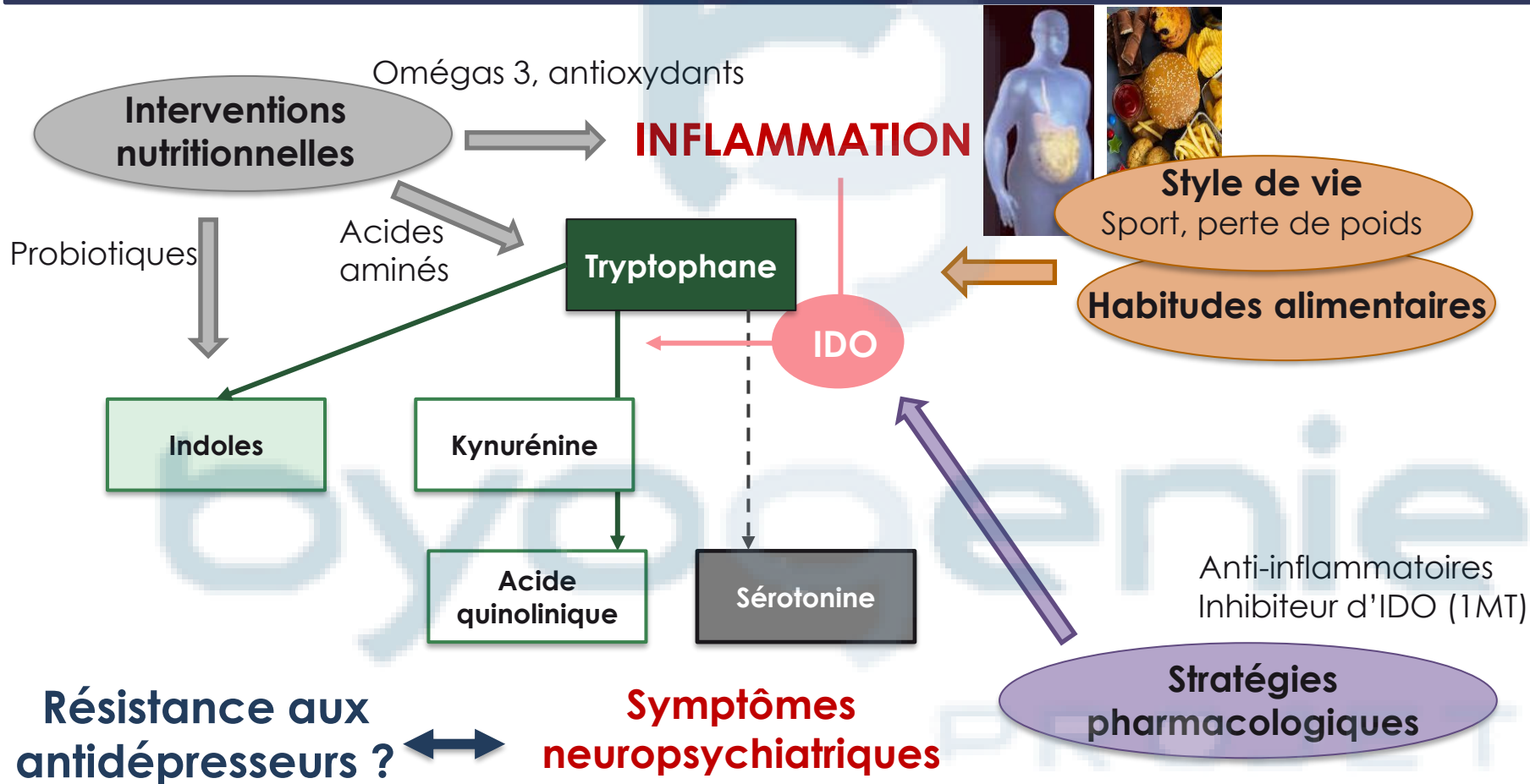
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## Striatum



Effects of oral saffron extract administration (6.25 mg/kg) on LPS-induced activation of KYN and BH4 pathways (2830 µg/kg, ip). Relative expression of Indoleamine 2,3-dioxygenase (IDO), Kynurenine 3-Monooxygenase (KMO), Kynurenine Aminotransferase (KAT), Kynureninase (Kynm), 3-Hydroxyanthranilate 3,4-Dioxygenase (Hao) and GTP-Cyclohydrotase 1 (GTPCH1) measured in the (A) FCx, (B) STR, and (C) HPC 24 h after the LPS challenge. (D) Schematic representation of the activation of the KYN and BH4 pathways in inflammatory conditions. Data are represented as foldchanges normalized to the control group (baseline = 1). Results are shown as mean ± SEM. \*  $p \leq 0.05$ , \*\*  $p \leq 0.01$ , \*\*\*  $p \leq 0.001$  vs. Control; <sup>#</sup>  $p \leq 0.05$  vs. LPS, <sup>§</sup>  $p \leq 0.05$ , <sup>§§</sup>  $p \leq 0.01$  global LPS effect.

# CONCLUSIONS ET IMPLICATIONS CLINIQUES



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# LES RELATIONS IMMUNITÉ – CERVEAU

