



UNIVERSITÉ
PARIS-EST CRÉTEIL
VAL DE MARNE



L'instabilité émotionnelle au cœur du trouble
bipolaire : même lors des périodes
euthymiques.

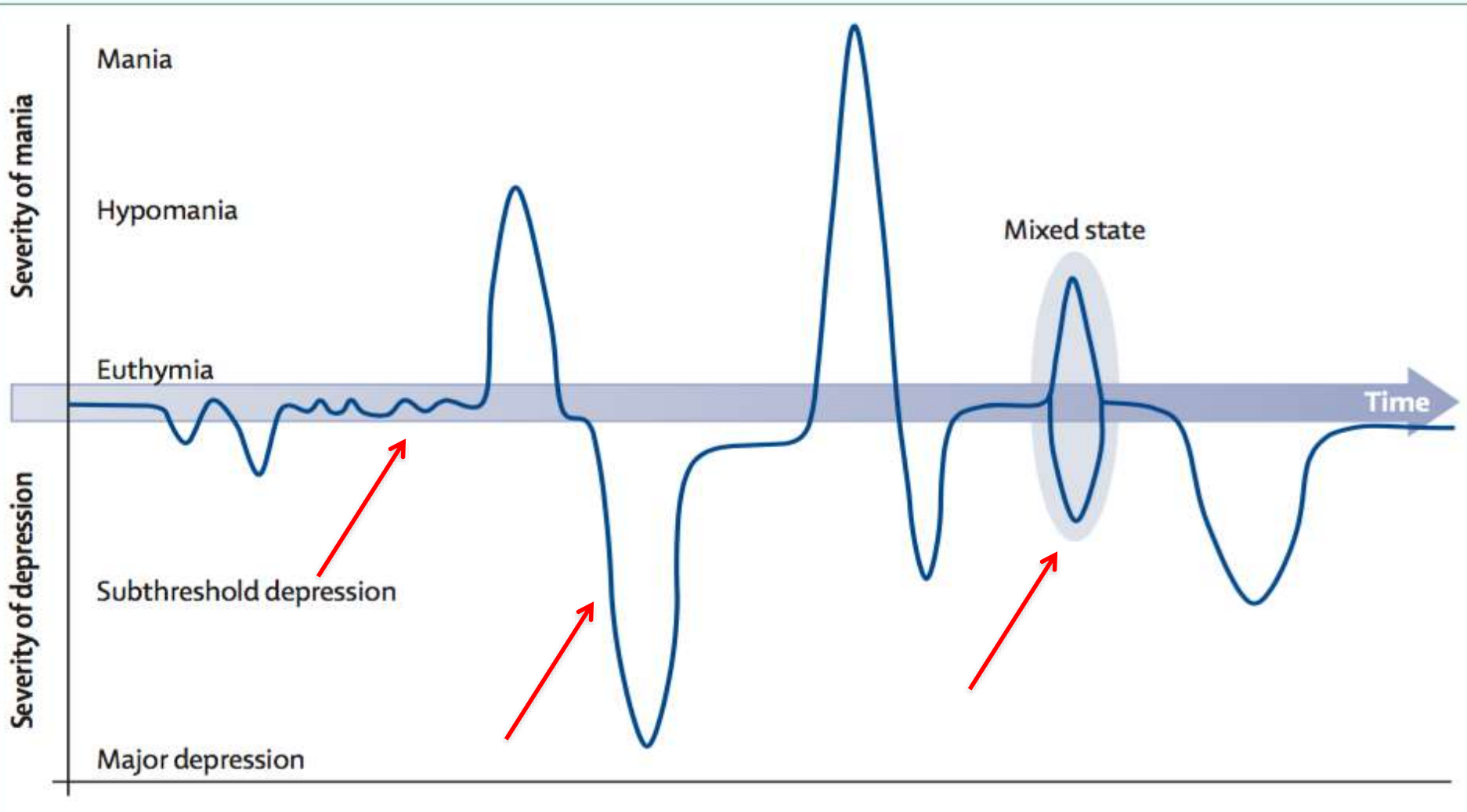
Pr Chantal HENRY

Université Paris-Est
Institut Pasteur

DÉCLARATION DE LIENS D'INTÉRÊTS

- Réunions de conseil pour : Lilly, Lundbeck,
- Conférences: invitations en qualité d'intervenant : Lilly, Lundbeck, BMS, AstraZeneca, Otsuka
- Conférences: invitations en qualité d'auditeur (frais de déplacement et hébergement): Lilly, Lundbeck, BMS, AstraZeneca

Les troubles bipolaires selon l'approche catégorielle



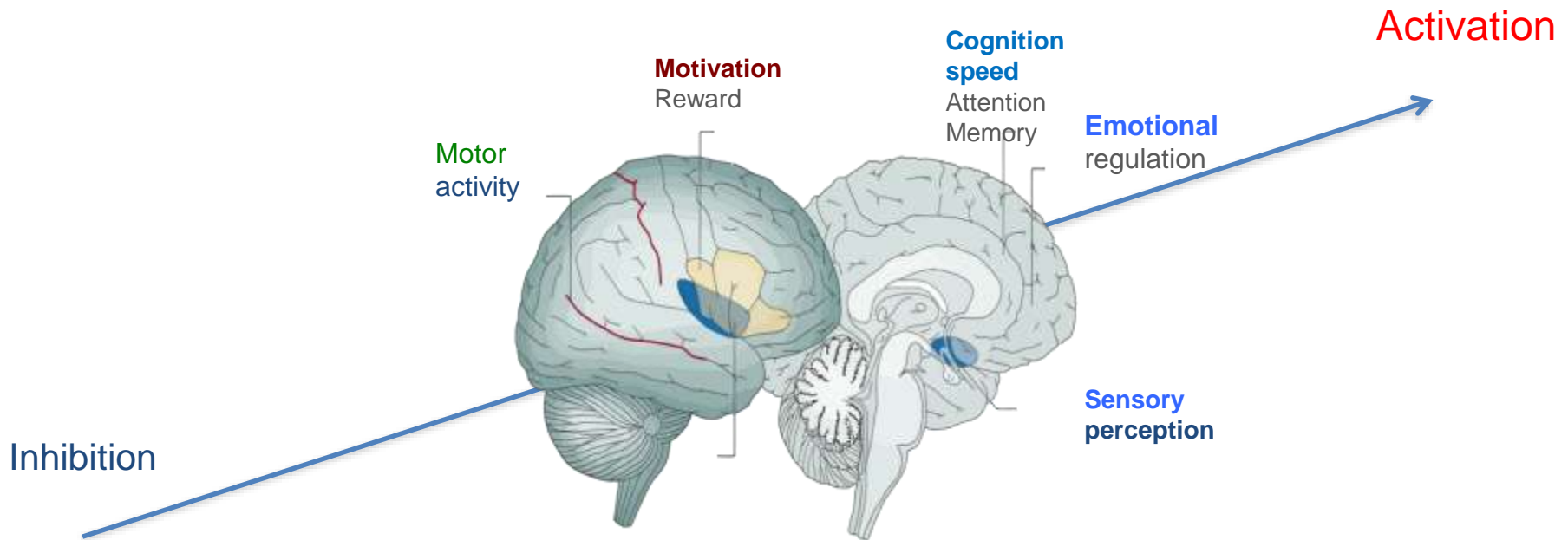
Un nouveau modèle des troubles bipolaires basé sur une approche dimensionnelle (comportements objectivables et quantifiables)

Avantages:

- Dimensions plus en lien avec la physiopathologie
- Possibilité d'étudier ces comportements chez l'homme et l'animal

Un modèle spécifique pour le trouble bipolaire:




Projection de certaines dimensions sur un axe inhibition/activation



Construction and validation of a dimensional scale exploring mood disorders: MATHyS (Multidimensional Assessment of Thymic States)

Chantal Henry*^{1,2,7}, Katia M'Bailara^{3,7}, Flavie Mathieu^{2,7}, Rollon Poinso^{3,7} and Bruno Falissard^{4,5,6,7}

5 dimensions of behavior

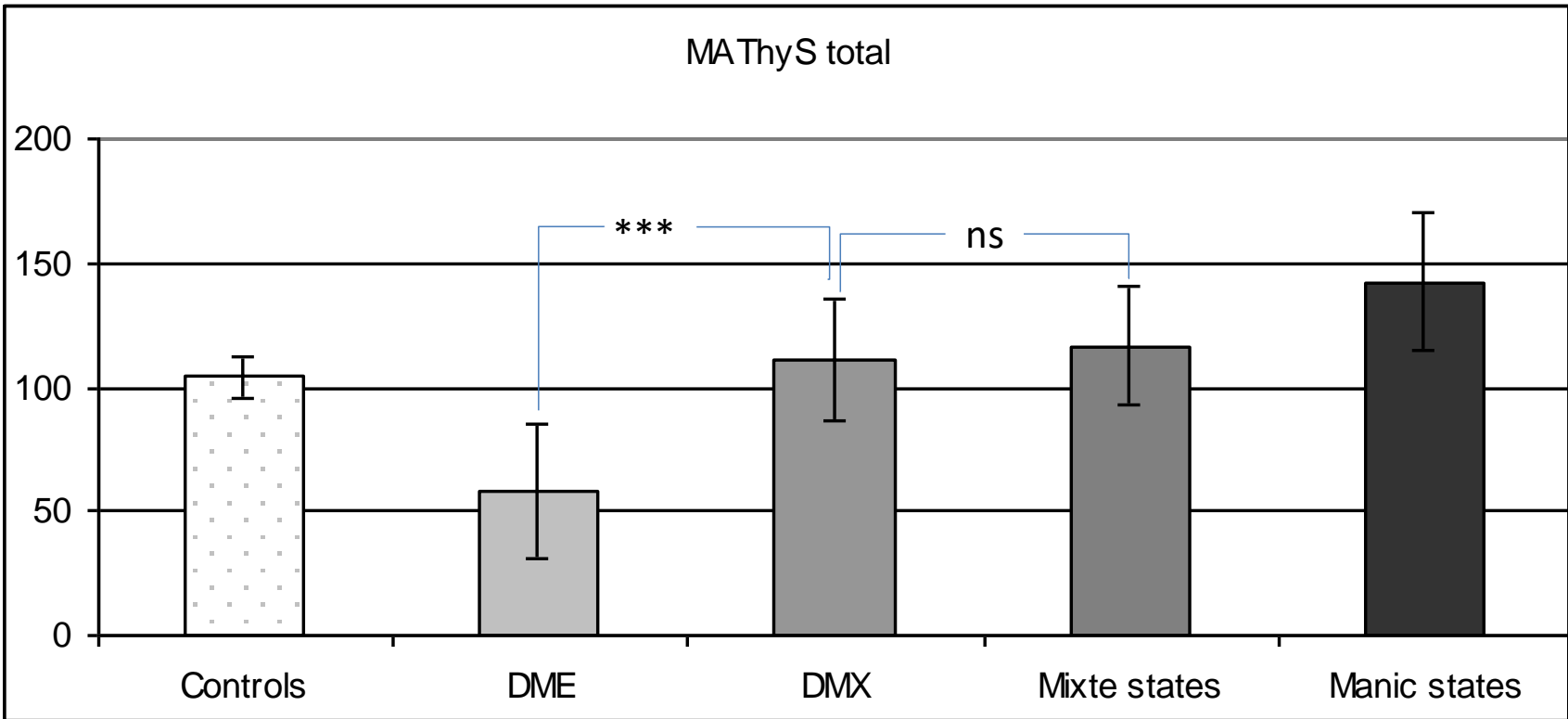
-  Emotional reactivity
-  Motivation
-  Sensory-perception
-  Psychomotor activity
-  Cognition speed
- 

-Can vary from inhibition to activation

-Using a **single tool to characterize all bipolar mood states** (manic, hypo manic, mixed, depressive episodes and sub-threshold symptoms)

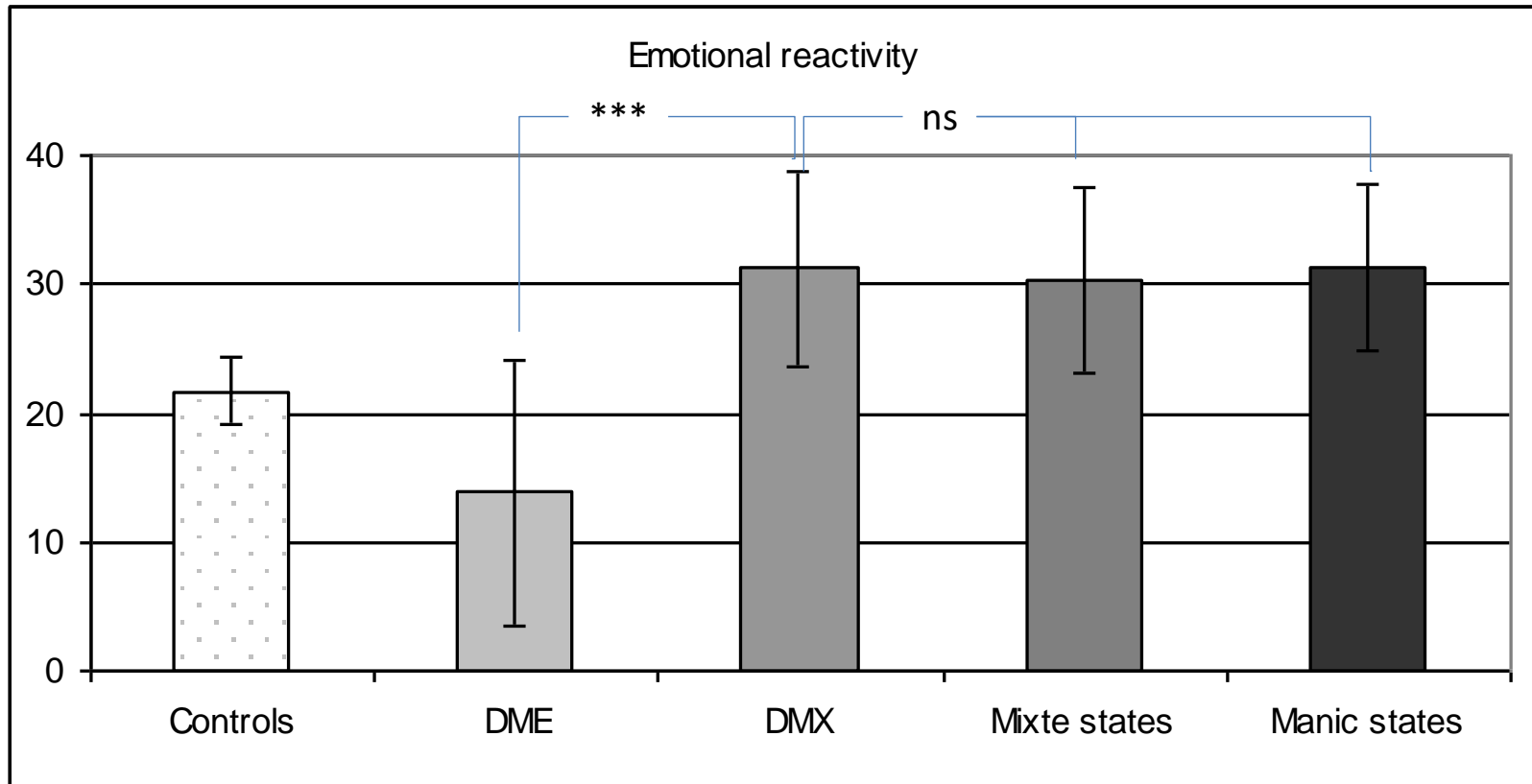
- A total score that measures the global levels of **behavioral inhibition/activation**

MATHYS: niveau global d'activation/inhibition



ns non sign
*** $p < 0.0001$

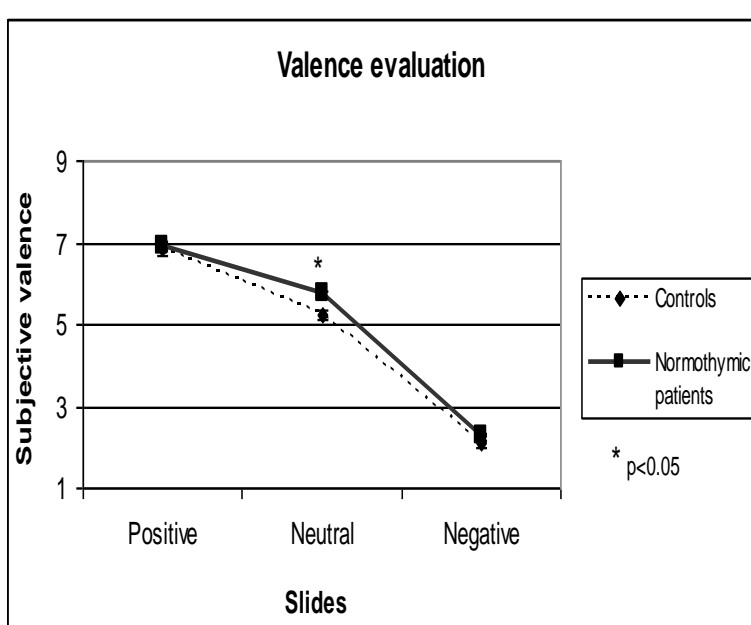
MATHYS: réactivité émotionnelle



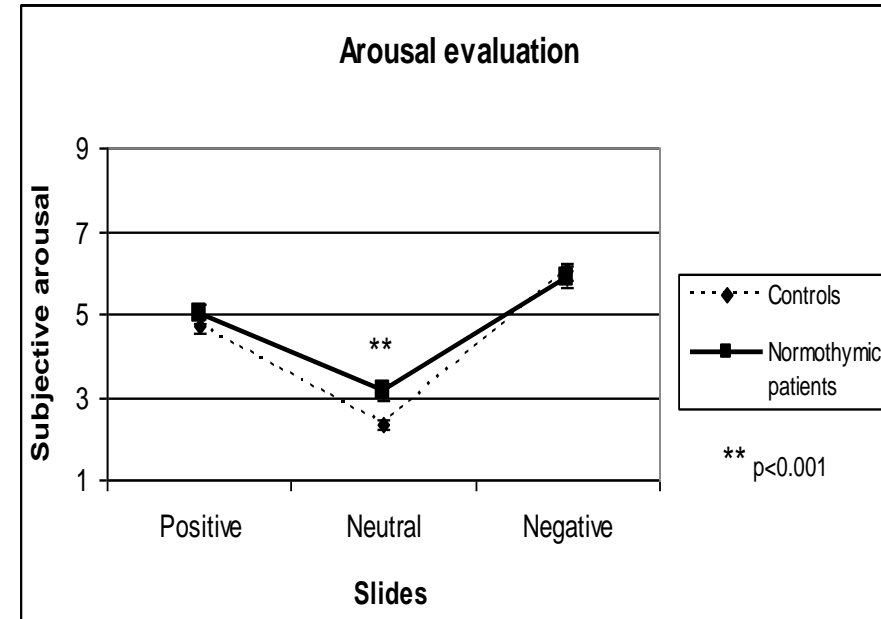
ns non sign
*** $p < 0.0001$



Réactivité émotionnelle chez des patients bipolaires en période de normothymie

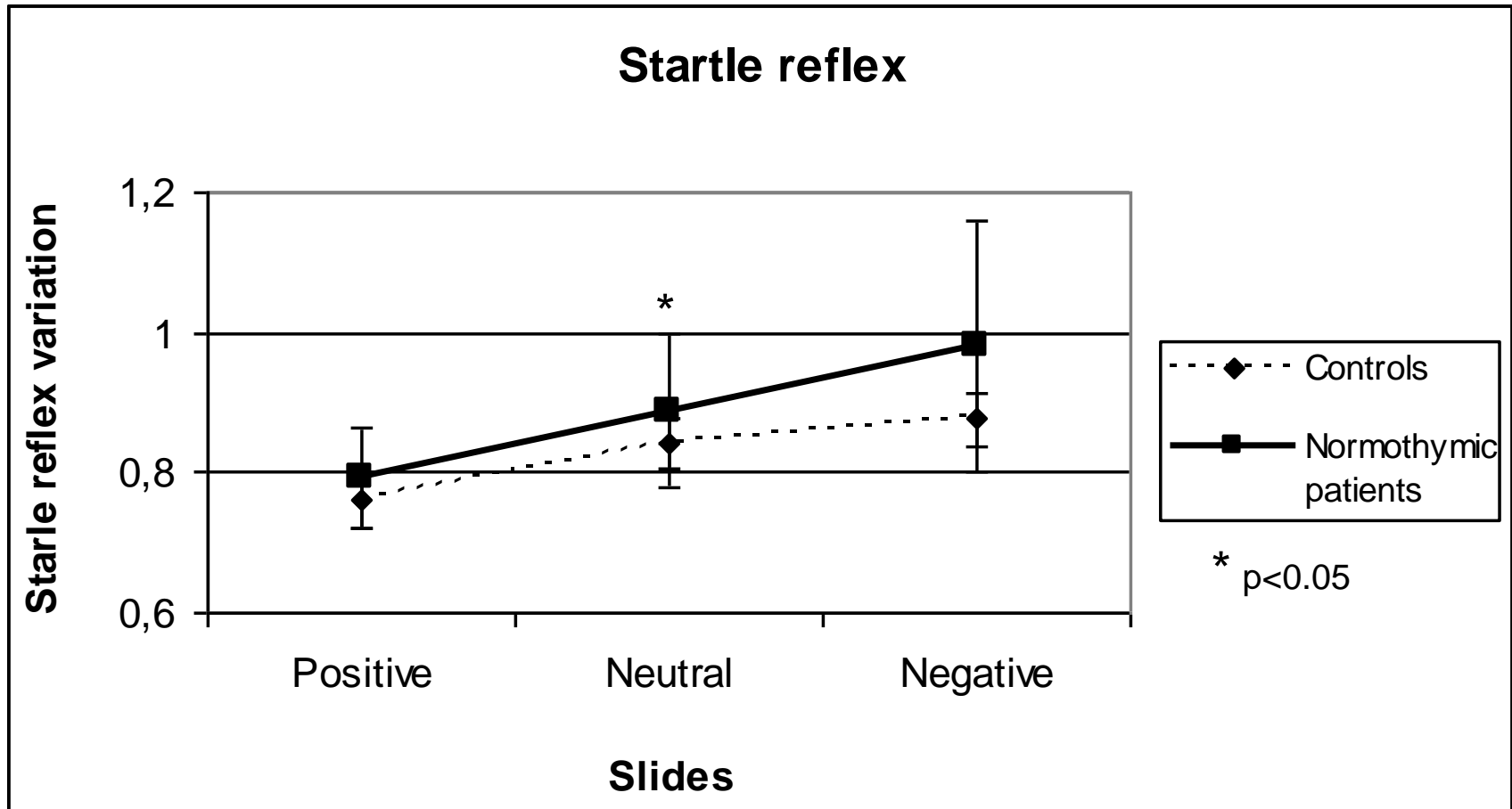


Neutral pictures were assessed as more pleasant by BP



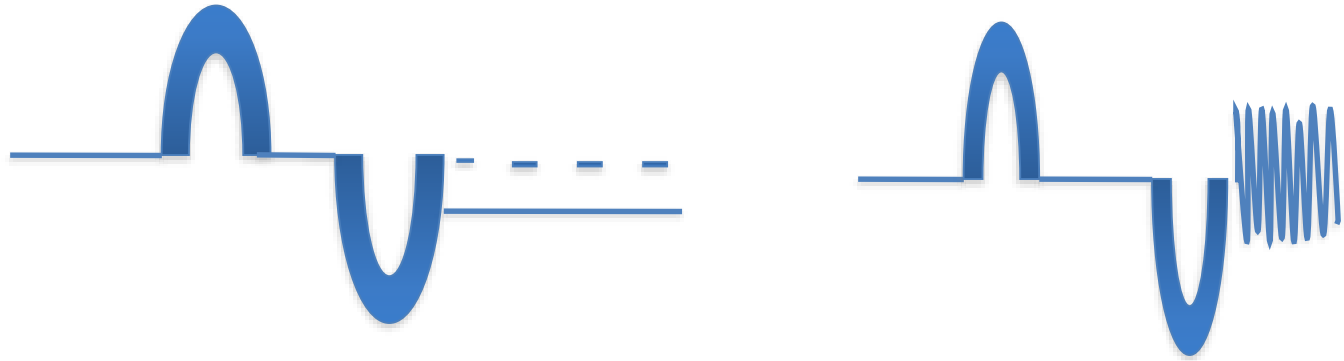
Neutral pictures trigger a higher arousal in BP

Réactivité émotionnelle chez des patients bipolaires en période de normothymie



Global inhibition-activation levels in remitted or mildly depressed bipolar patients (N= 1123)

Clinical presentation



MATHyS

Motor activity

Motivation
Reward

Cognition
Attention
Memory

Emotional
regulation

Activation

108-200

Inhibition

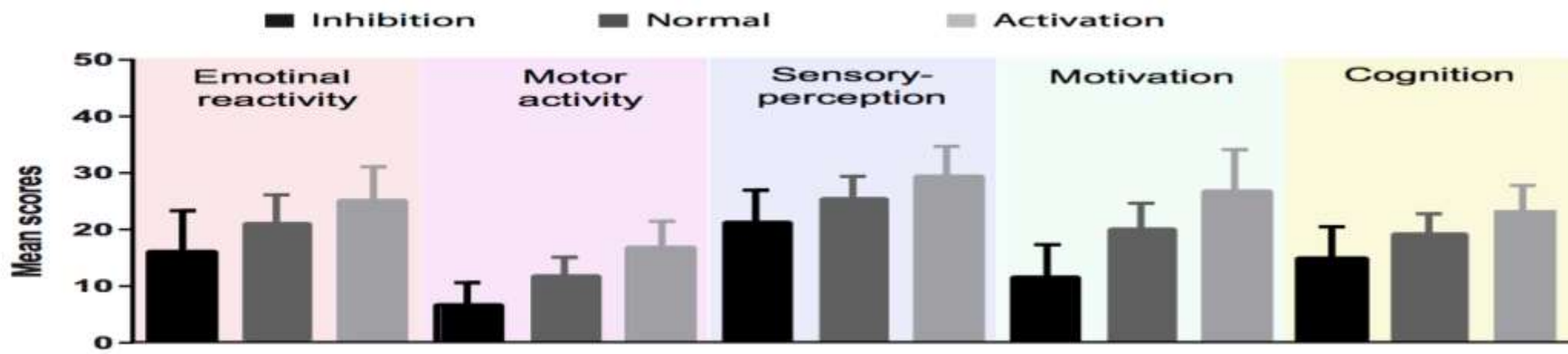
0-92

92-108

Sensory
perception

Global inhibition-activation levels in remitted or mildly depressed bipolar patients (N= 1123)

	Inhibited n = 270	Normal n = 255	Activation n = 598	<i>F</i> or X^2	<i>p</i> *
MADRS score, mean (SD)	13.18 (6.61) ^a	7.98 (6.30) ^b	5.68 (5.6) ^c	15.91	<0.0001
YMRS score, mean (SD)	1.46 (2.16) ^a	1.26 (1.86) ^a	2.36 (2.92) ^b	25.85	<0.0001
MATHyS total score, mean (SD)	71.71(16.86)	99.99 (3.74)	124.2 (14.53)	1139.97	<0.0001
MATHyS Cognition (SD)	14.9 (5.4) ^a	19.11 (3.5) ^b	23.33 (4.3) ^c	448.2	<0.0001
MATHyS Motivation (SD)	11.5 (5.7) ^a	19.98 (4.5) ^b	26.71 (7.3) ^c	597.1	<0.0001
MATHyS Sensory-Perception (SD)	21.17 (5.6) ^a	25.53 (3.9) ^b	29.34 (5.2) ^c	369.4	<0.0001
MATHyS Motor Activity (SD)	6.63 (3.8) ^a	11.73 (3.3) ^b	16.79 (4.5) ^c	609.2	<0.0001
MATHyS Emotional Reactivity (SD)	16.06 (7.1) ^a	20.68 (5.3) ^b	25.07 (5.9) ^c	290.7	<0.0001



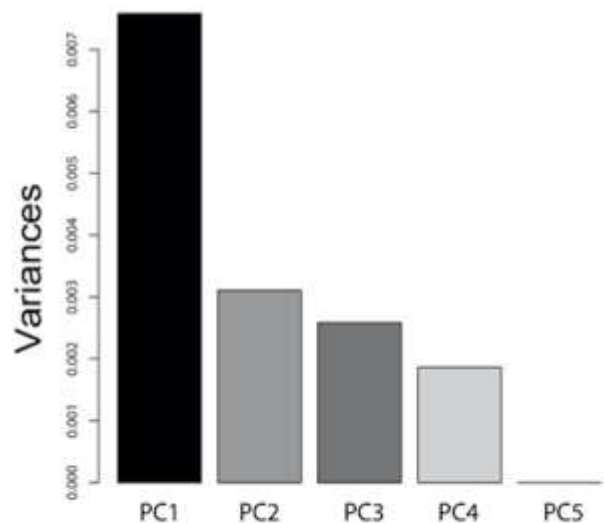
Global inhibition-activation levels in remitted or mildly depressed bipolar patients (N= 1123)

	Inhibited n = 270	Normal n = 255	Activation n = 598	<i>F or X²</i>	<i>p</i> *
Female, n (%)	157 (13.98) ^a	155 (13.8) ^a	357 (31.8) ^b	3.950	0.001
Age, years: mean (SD)	42.20 (12.29)	41.08 (12.9)	40.82 (13.01)	0.199	0.34
Education level, years: mean (SD)	13.91 (2.93) ^a	14.16 (2.77) ^a	13.68 (2.95) ^a	4.211	0.08
Occupation, n (%)					
Unemployed	104 (9.26) ^b	82 (7.3) ^a	70 (6.23) ^a	7.445	<0.001
Diagnosis, n (%)					
Bipolar disorder type I	48 (17.77) ^a	103 (40.39) ^b	385 (64.38) ^c		
Bipolar disorder type II	165 (14.22) ^a	114 (9.83) ^a	159 (13.71) ^b		
Bipolar disorder type NOS	57 (4.91) ^a	38 (3.28) ^a	54 (4.66) ^a	45.11	<0.0001#

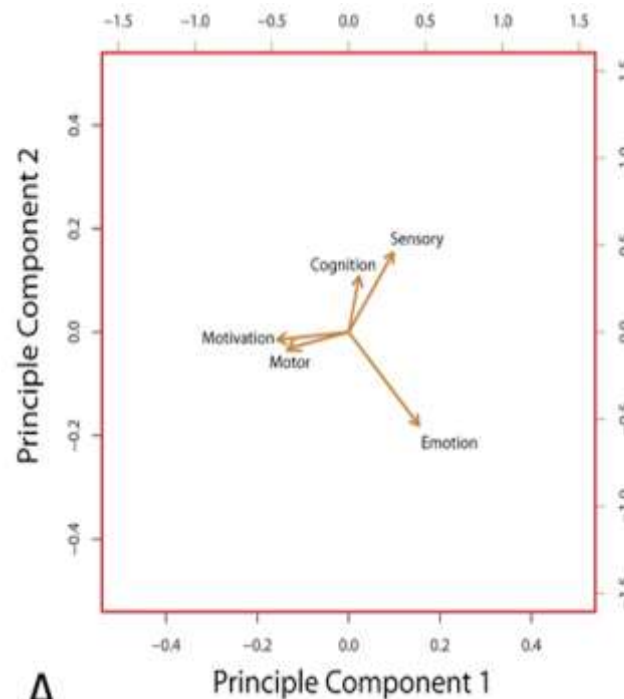
Global inhibition-activation levels in remitted or mildly depressed bipolar patients (N= 1123)

	Inhibited	Normal	Activation	<i>F or X²</i>	<i>p*</i>
	n = 270	n = 255	n = 598		
Age-at-onset, years: mean (SD)	24.63 (10.21)	25.01 (9.94)	24.38 (10.09)	2.135	0.34
Illness duration, years: mean (SD)	16.58 (10.74)	16.10 (11.51)	16.22 (11.08)	1.142	0.56
Total number of episodes, mean (SD)	6.32 (6.26) ^a	6.07 (5.22) ^a	7.07 (6.11) ^b	5.545	0.05
Rapid cycling, n (%)	72 (26.66) ^a	58 (22.74) ^a	84 (14.23) ^b	89.53	<0.001
Number of suicide attempts, mean (SD)	1.85 (2.65) ^a	1.38 (1.89) ^a	2.18 (2.44) ^b	33.03	<0.0001&
FAST score, mean (SD)	27.78(14.93) ^a	16.24(12.86) ^b	19.97(13.46) ^c	146.4	<0.0001
STAI score, mean (SD)	49.11(14.0) ^a	35.78(13.03) ^b	40.06(14.86) ^c	194.23	<0.0001
Anxiety disorders	197 (17.54) ^b	152 (13.54) ^a	164 (14.60) ^a	6.461	0.091
Substance use disorders	146 (13) ^b	111 (9.88) ^a	111 (9.88) ^a	6.162	0.05

Global inhibition-activation levels in remitted or mildly depressed bipolar patients (N= 1123)



B



A

La dimension la plus pertinente est la réactivité émotionnelle
Ne figure pas dans les critères diagnostiques
Motivation et motricité= une même dimension

Quels sont les facteurs liés à cette dysrégulation émotionnelle chronique?

Processus inflammatoires ?

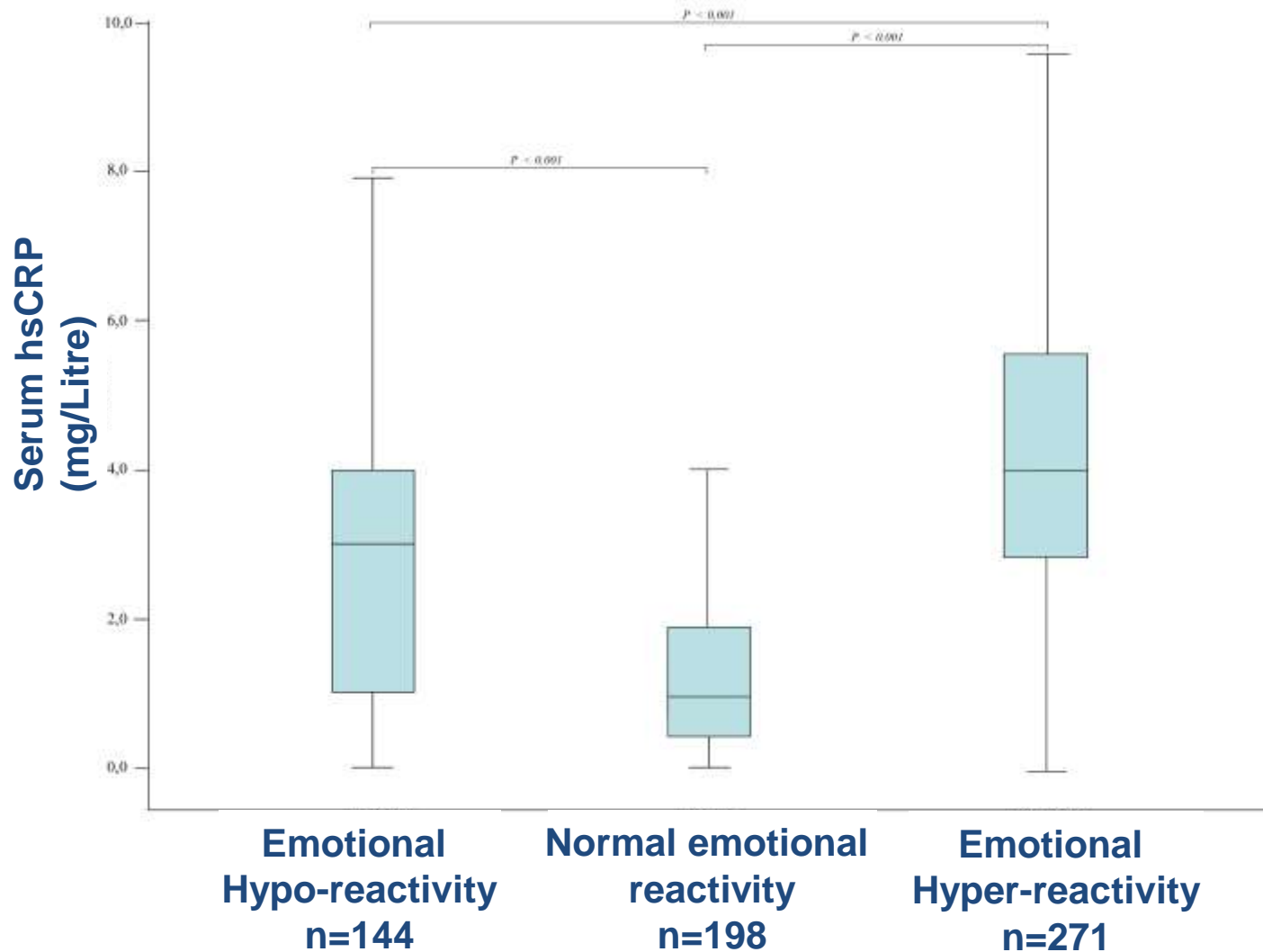
Altérations de certaines structures ou circuits cérébraux ?

Sommeil?

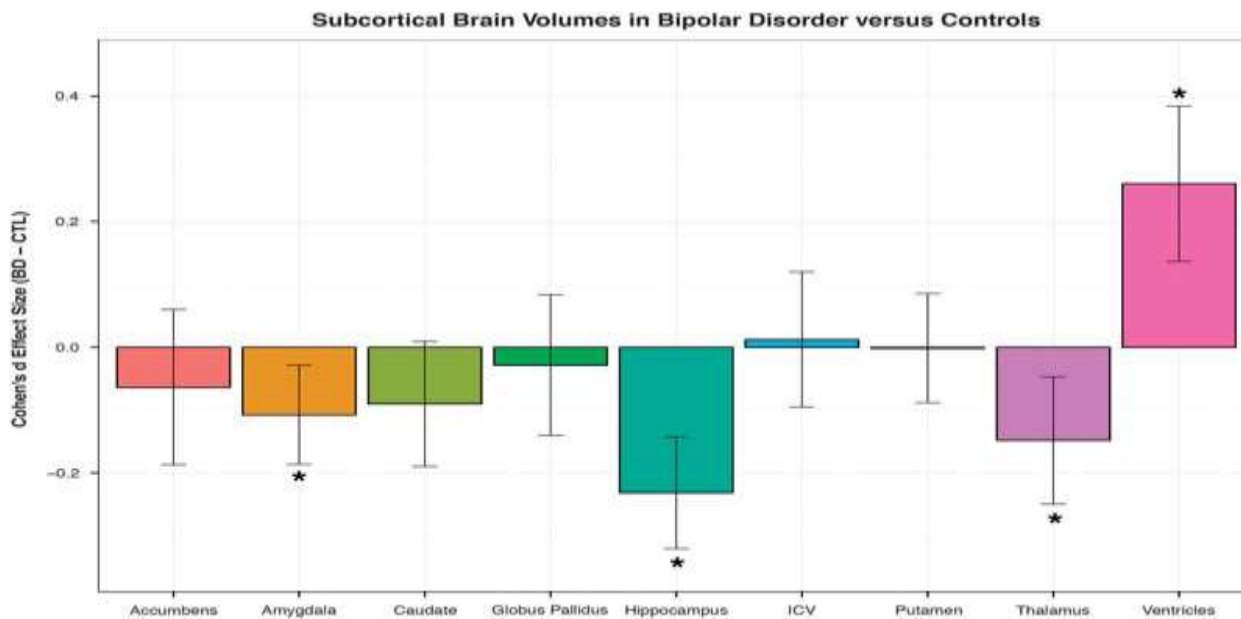
Facteurs génétiques et environnementaux ?

Impact des traitements?

Emotional reactivity and C-reactive protein alterations in remitted bipolar patients



Lien avec le volume de l'amygdale et la connectivité



1710 BD patients
2594 healthy controls

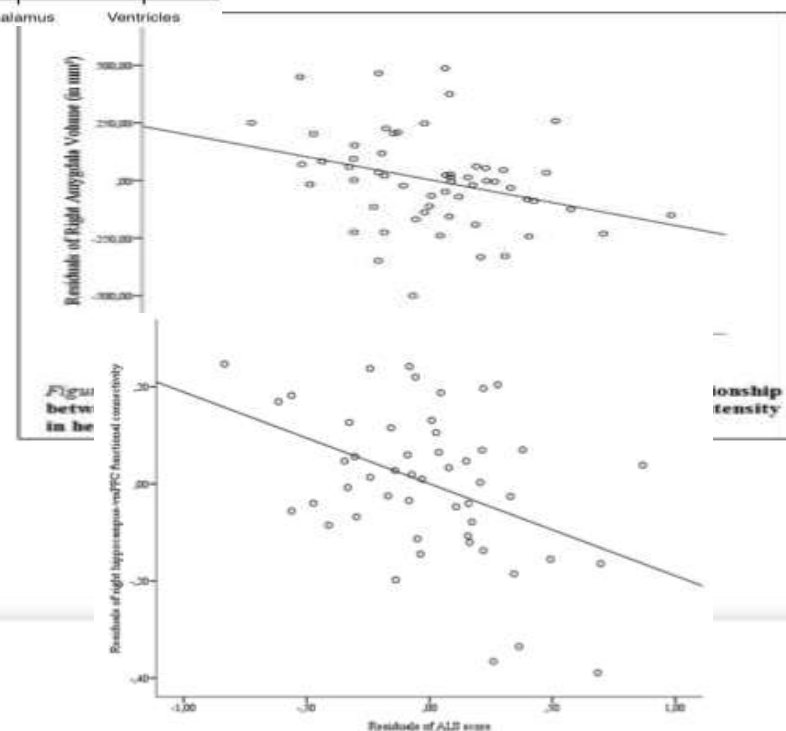
Hibar et al, Mol
Psy, 2016

Affective Intensity Measure/ Affective Liability
Scale

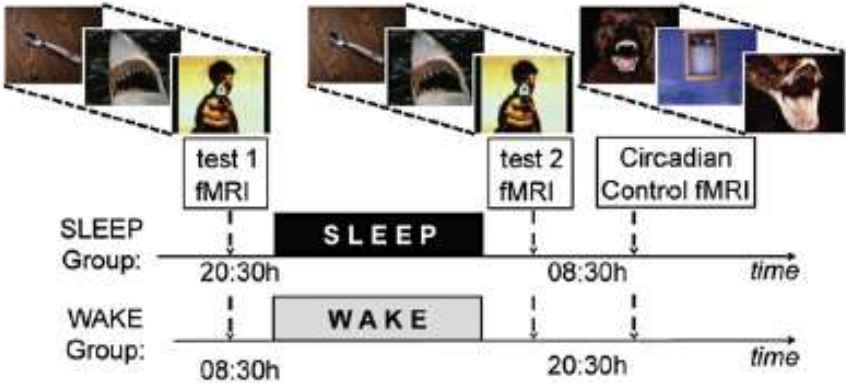
Plus le score AIM est haut (intensité) et plus
l'amygdale est petite

ALS: Connectivité entre l'hippocampe droit et le
PFC ventro-médian est d'autant plus faible que les
sujets sont plus labiles (ALS)

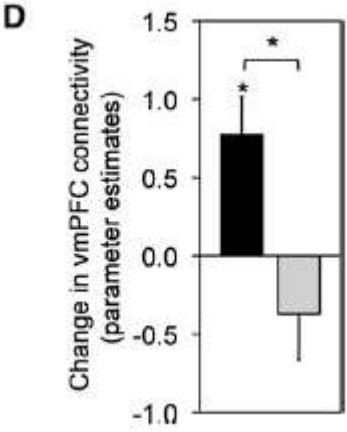
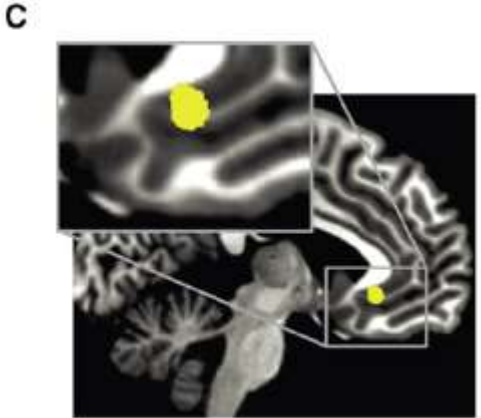
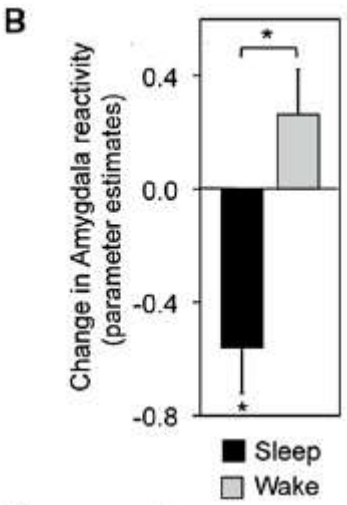
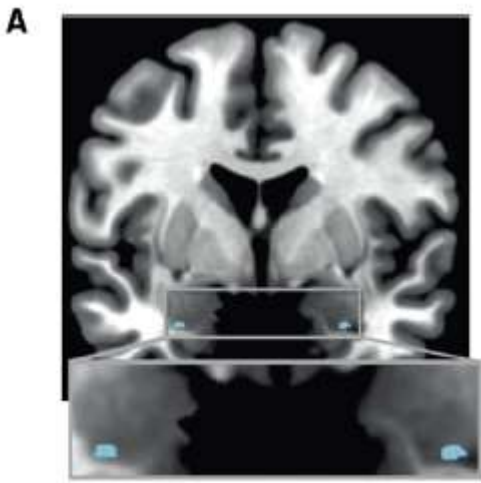
(Trübtschek et al, submitted)



Sommeil paradoxal diminue l'activation amygdalienne



Chez sujets sains



Serotonin Transporter (5-HTTLPR) Genotype and Amygdala Activation: A Meta-Analysis

Marcus R. Munafò, Sarah M. Brown, and Ahmad R. Hariri

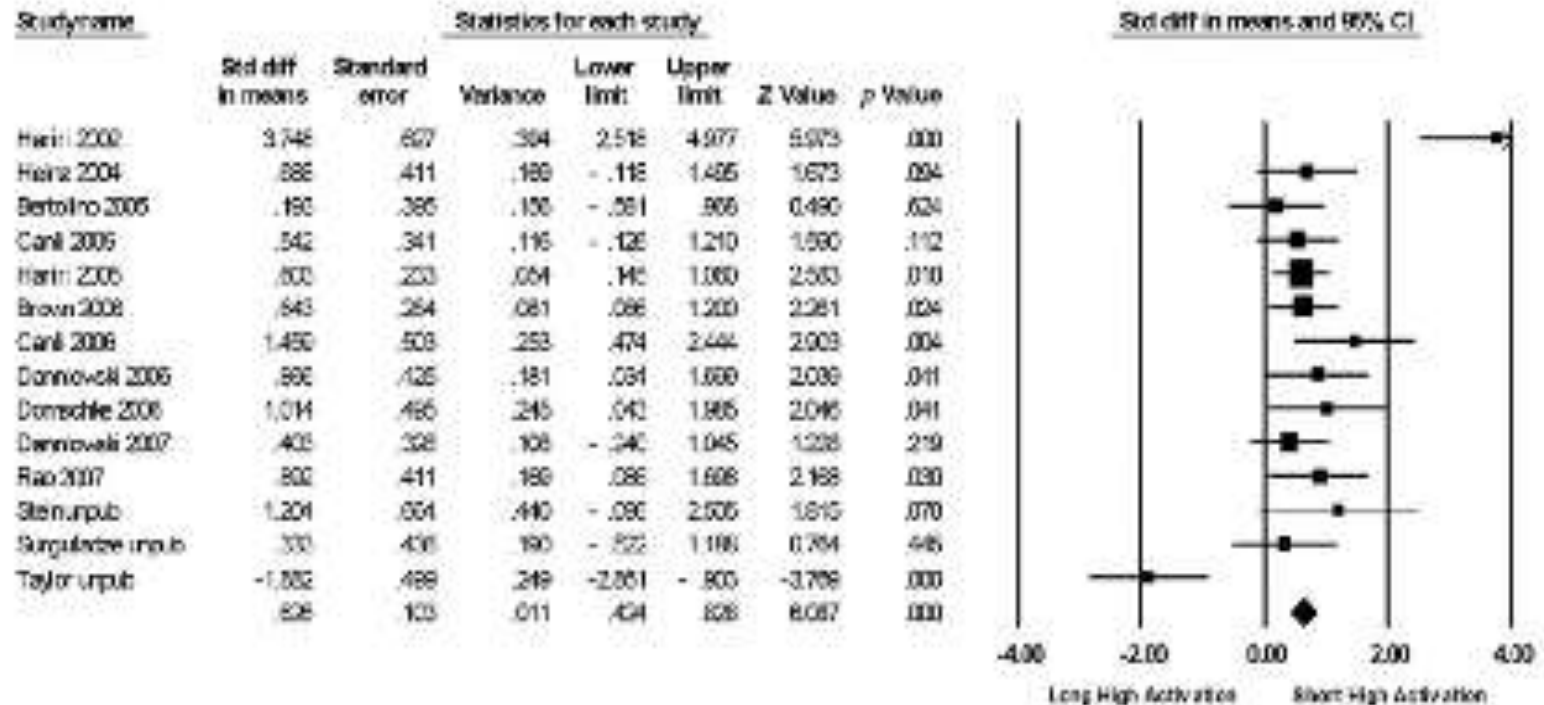
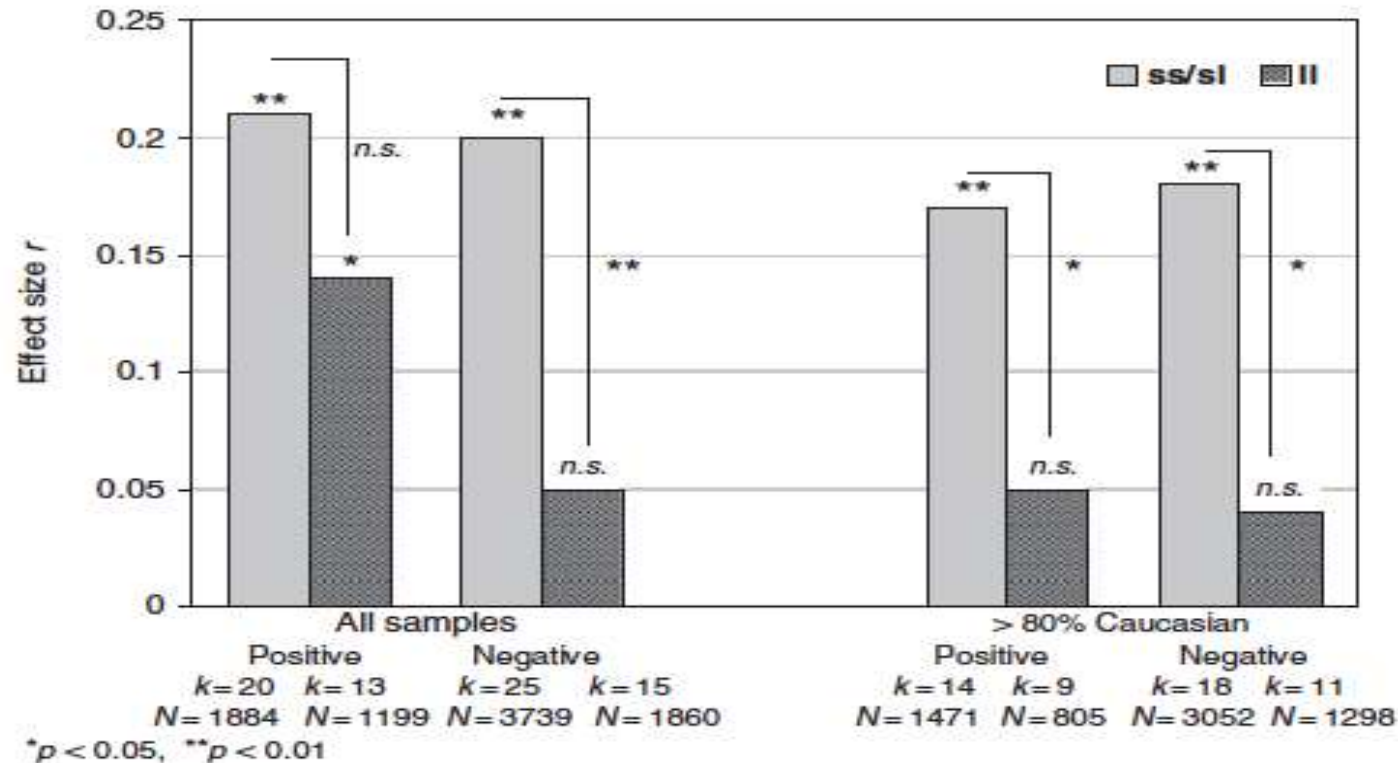


Figure 1.

Meta-analysis of association studies of 5-HTTLPR genotype and amygdala activation. Meta-analysis indicates significant association between 5-HTTLPR genotype and amygdala activation ($p < .001$). Bars represent individual study 95% confidence intervals, with a central block proportional to study size. The summary diamond bar represents the pooled effect size estimate and 95% confidence interval (CI).

Serotonin transporter genotype 5HTTLPR as a marker of differential susceptibility? A meta-analysis of child and adolescent gene-by-environment studies

MH



Disproportionately responsive to positive and negative environmental experiences and exposures.

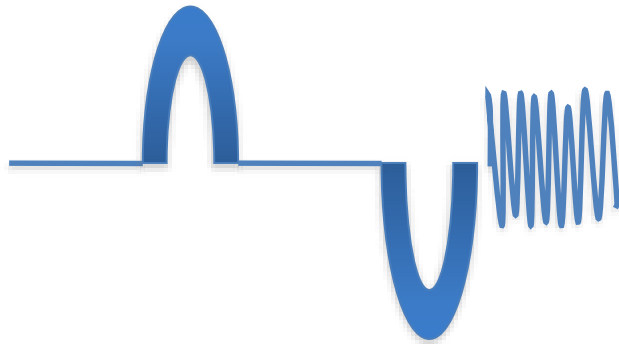
Emotional reactivity and pharmacological treatment

	Emotional Hypo- reactivity n = 144	Emotional Normal reactivity n = 198	Emotional Hyper- reactivity n = 271	<i>F or X²</i>	<i>P</i> *
MADRS score , mean (SD)	7.6 (4.5) ^a	4.4 (4.1) ^b	6.7 (4.6) ^a	24,521	< 0.001
YMRS score , mean (SD)	1.3 (2.0) ^a	1.0 (1.7) ^a	2.5 (2.7) ^b	27,657	< 0.001
MATHyS emotional reactivity score	12.4 (3.4)	19.9 (1.6)	28.9 (3.7)	1363,97	< 0.001
MATHyS total score , mean (SD)	75.7 (21.5) ^a	98 (12.5) ^b	114.2 (22) ^c	189,72	< 0.001
	4 (2.9)	10 (5.5)	7 (2.8)	2,435	0.296
Medications , n (%)					
Antipsychotics	53 (47.3)	77 (51)	89 (42.8)	2,408	0.300
Lithium	45 (40.2)	59 (39.1)	78 (37.5)	0,238	0.888
Anticonvulsants	67 (59.8)	78 (51.7)	125 (60.1)	2,922	0.232
Antidepressants	52 (46.4) ^{a,b}	60 (39.7) ^b	122 (58.7) ^a	13,148	0.001
Benzodiazepines	23 (20.5) ^{a,b}	21 (13.9) ^b	56 (26.9) ^a	8,905	0.012

Cross-sectional study

Antidépresseur au long cours et instabilité émotionnelle ?

	Lifetime AD \geq 5years		P	P
	No (n=582)	Yes (n=189)		
Gender				
Male	265 (45.5)	61 (32.3)	0.001	0.002
Female	317 (54.5)	128 (67.7)		
Age, mean (sd)	38.3 (12.7)	44.4 (10.2)	<0.0001	<0.0001
Bipolar Disorders				
Type I	301 (51.7)	72 (38.1)	0.0022	0.004
Type II	215 (36.9)	96 (50.8)		
NOS	66 (11.3)	21 (11.1)		
MADRS score, mean (sd)	8.7 (8.1)	11.2 (8.3)	0.0002	0.002
YMRS score, mean (sd)	2.3 (3.8)	1.8 (2.6)	0.13	
Rapid cycling, n(%)	66 (12.6%)	25 (14.3)	0.58	
AIM, mean (sd)	3.7 (0.7)	3.8 (0.7)	0.02	0.07
ALS, mean (sd)	1.2 (0.7)	1.4 (0.6)	0.01	0.025

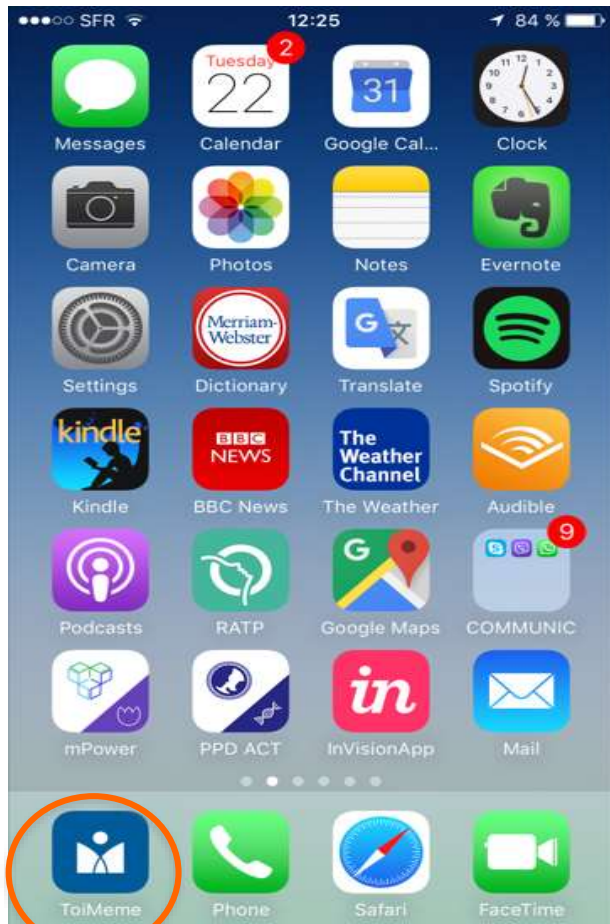


Femme
Facteur génétique
BP I
Troubles du sommeil
AD au long cours
Inflammation



Homme
BP II
Inflammation

App



Conclusion

- Une approche dimensionnelle pour mieux définir l'instabilité émotionnelle au cours de la période de « normothymie »
- Mieux comprendre sa physiopathologie pour mieux la contrôler
- L'impact de la pharmacologie
- Une amélioration de la dysrégulation émotionnelle chronique pourrait être un marqueur précoce de l'efficacité des thymorégulateurs
- Nouveaux outils pour mieux la caractériser
- Recherche translationnelle

International School for Translational Psychiatry – TRANS-PSY

Paris, June 26 to July 1, 2017



A one-week course intended for PhD students and clinicians from France and overseas who are seeking to develop knowledge and experience in the field of Translational Psychiatry. The course is taught in English.

Objectives: The course will focus on the dimensional approach of psychiatric disorders and on the core features of fundamental behaviours, including emotional regulation, cognition and memory that intersect diagnostic categories of psychiatric disorders.

The course provides an overview of putative mechanisms from molecular to social and environmental factors and their potential impact on behaviour alterations, from normal to pathological. The course also addresses how mobile technology and big data approaches can be implemented in the field of mental health research and clinical practice.

Co-directors of the course

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Closing date for applications: April 15, 2017

