

# YOUTH MENTAL HEALTH: FROM NEUROSCIENCE TO CLINICAL APPLICATIONS



Laboratory for Adolescent and  
Youth Emotion Regulation  
(LAYER)

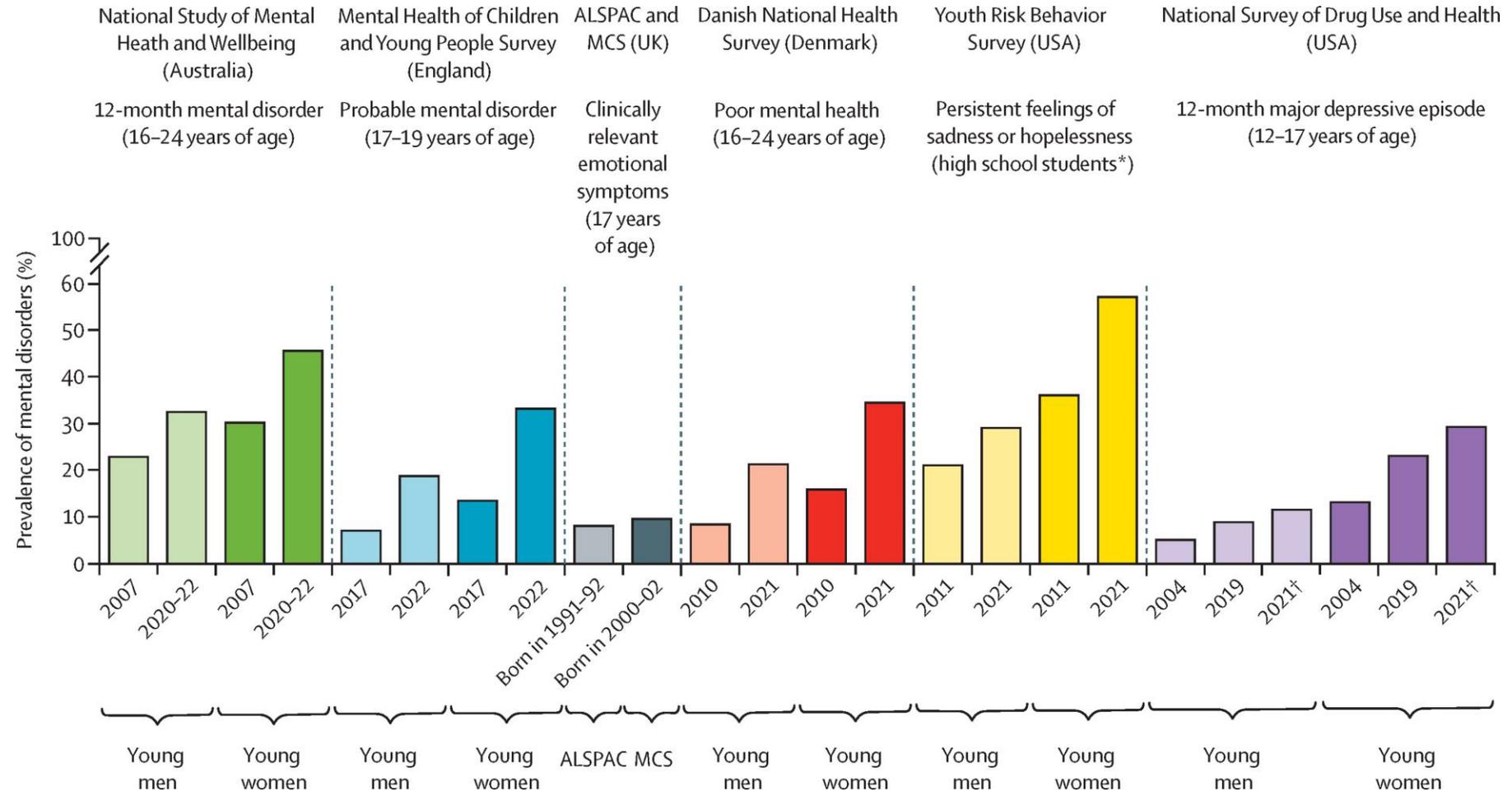
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***NeuroClub***  
***17.12.2024***

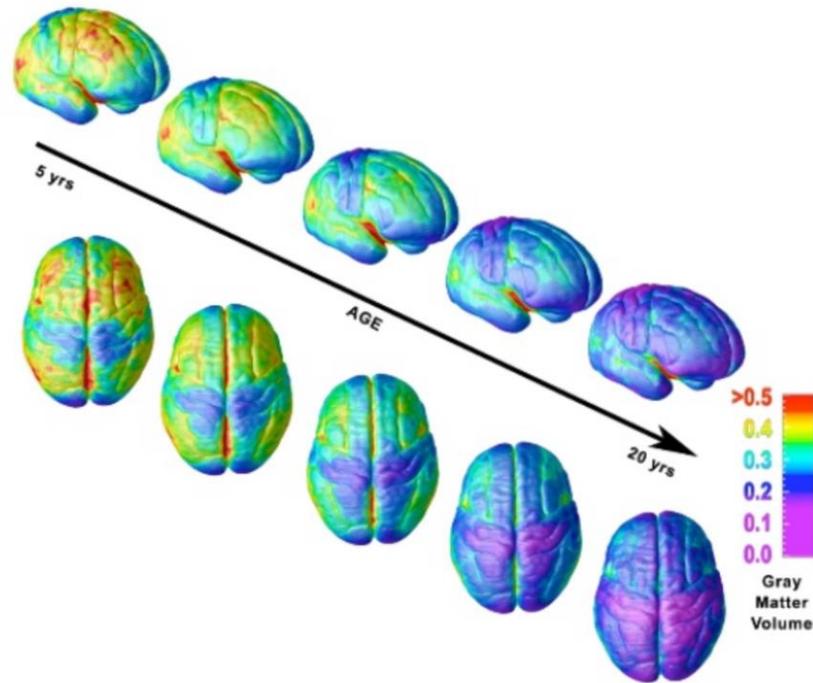
# YOUTH MENTAL HEALTH

- 1/5 youth age 12-25 present with mental ill health
- 2/3 of psychiatric disorders emerge before the age of 25
- Worse since two decades and even more so since COVID19 (rising inequality, unregulated social media, insecurity, climate change)

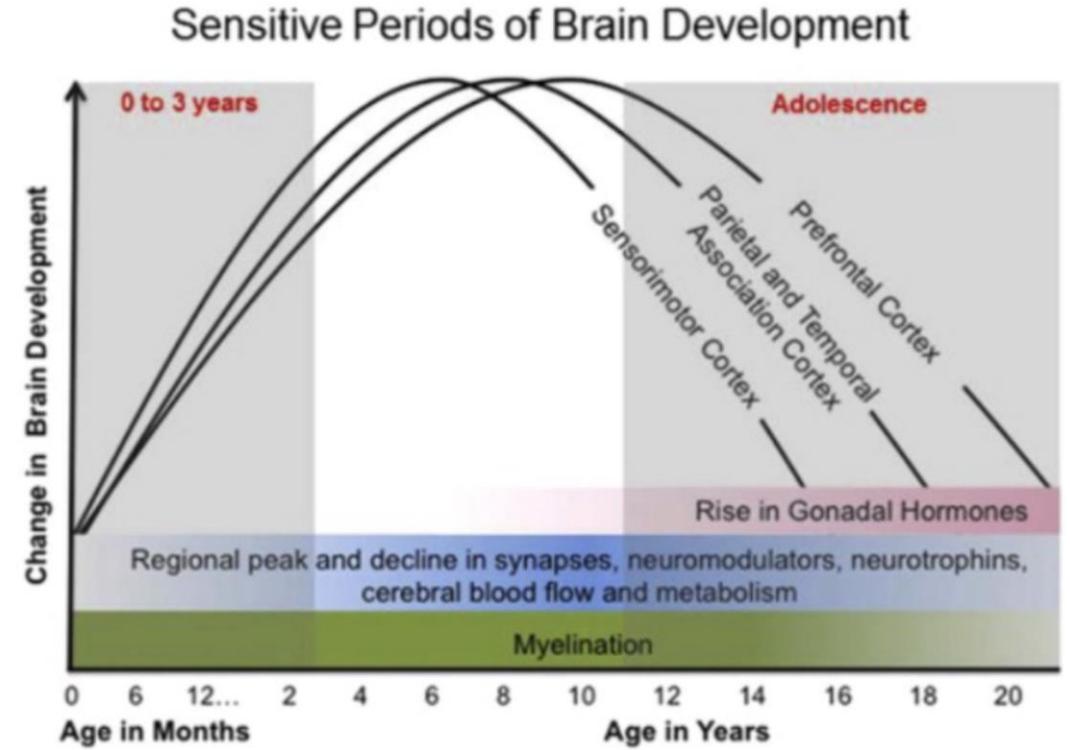


# DEVELOPMENTAL TRAJECTORIES

High variability by region, with posterior-anterior dynamics: the prefrontal regions are the last to specialize, around the age of 20-25.



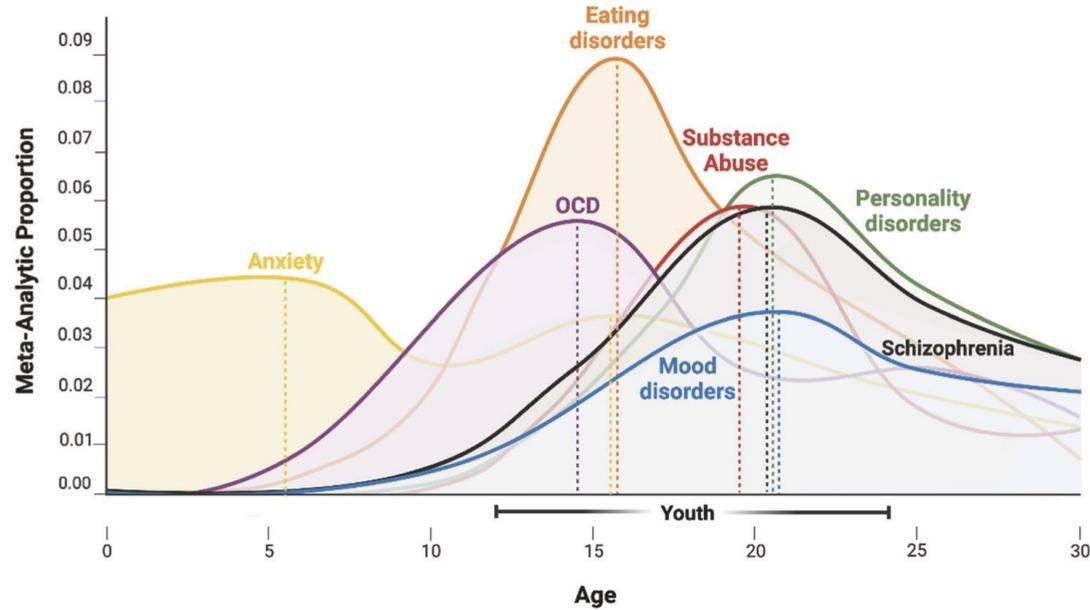
P. Thompson, Laboratory of Neuroimaging, Institute for Neuroimaging and Informatics Keck School of Medicine of USC



Lee & Casey, Neurobiol Stress 2015

Physiological stress reactivity, emotional lability, impulsivity, sensation seeking, sensitivity to peers, lack of mentalization

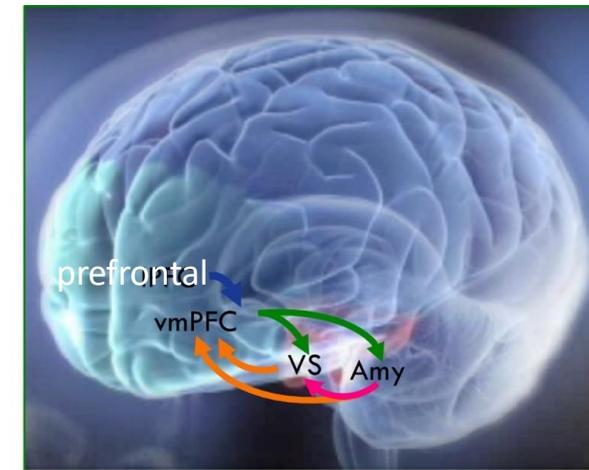
# BRAIN DEVELOPMENT AND MENTAL HEALTH VULNERABILITY



**Fig. 1 Age of onset of mental disorders.** Distribution of age of onset of mental disorders in the general population based on the meta-analysis by Solmi et al. [9]: Meta-analytic epidemiologic proportion (y-axis) for anxiety disorders (5.5/15.5 years), substance use disorders (19.5 years), schizophrenia/psychotic disorders (20.5 years), eating disorders (15.5 years), personality disorders (20.5 years), obsessive-compulsive (14.5) and mood disorders (20.5 years) (ICD-10 blocks). The dotted horizontal lines represent the peak age of onset for each diagnostic category.

This biological maturation is influenced by all kinds of factors: hormonal, external stressors, biological, cultural and sociological context.

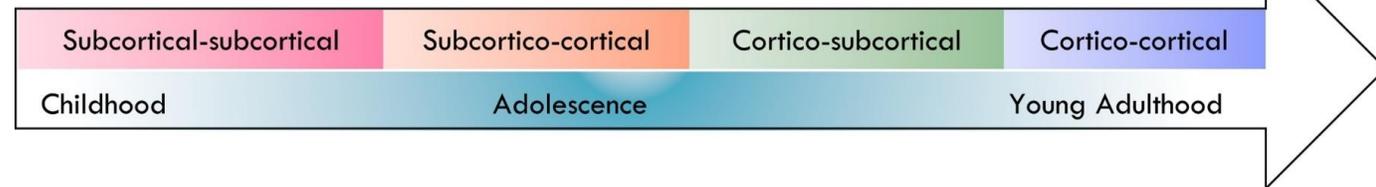
→ **Adolescence as a window of vulnerability and opportunity**



Uhlhaas et al. Molec Psy 2023

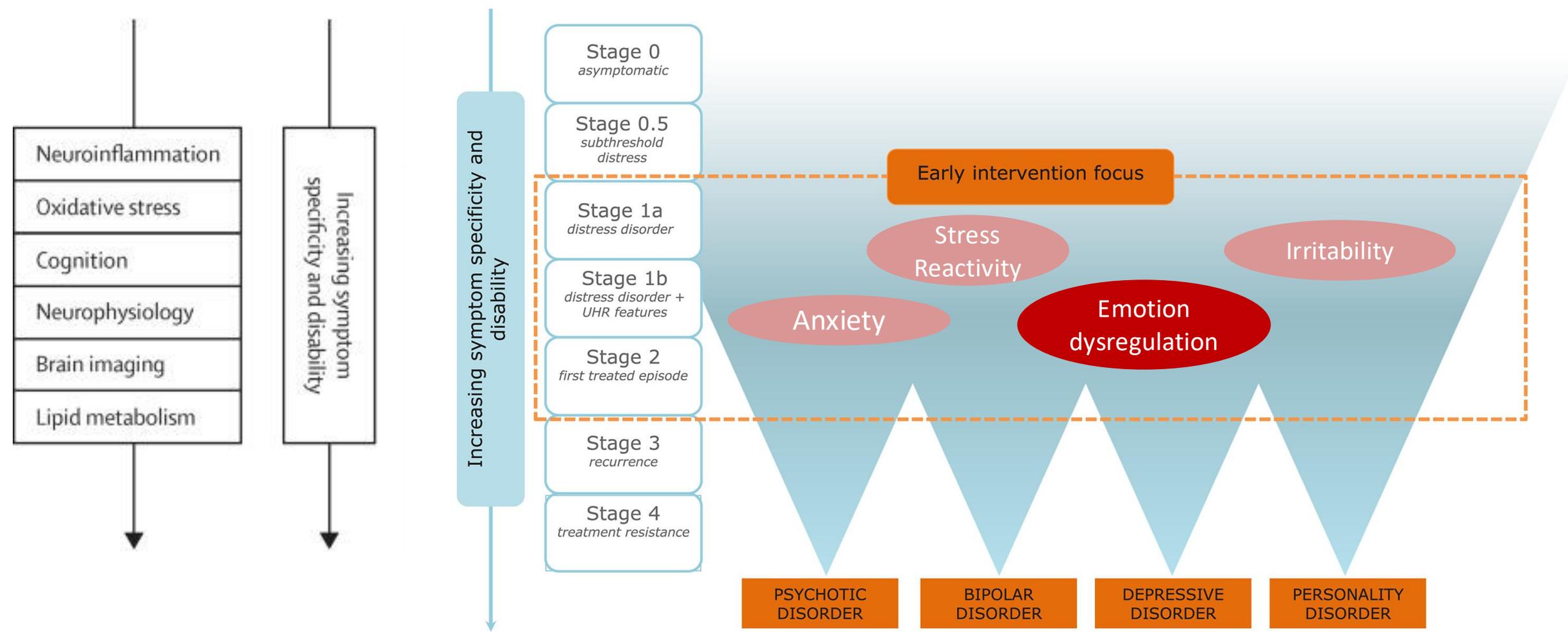
*Adolescent mental health--opportunity and obligation.*

*Lee et al. Science 2014*



*Casey et al. Development of the emotional brain, Neurosc. Letters 2019*

# EARLY INTERVENTION: TRANSDIAGNOSTIC CLINICAL STAGING



Ivanova, Celen & Piguet; Stage-specific interventions for emotion dysregulation disorders in adolescents, Swiss Arch Neurol Psychiatr Psychother 2021  
 Hartman et al. Early Intervention in Psychiatry 2017, Nieman DH, McGorry PD, Lancet Psychiatry 2015

# RESEARCH AXIS FROM NEUROSCIENCE TO CLINICAL INTERVENTIONS

## Neurobiological Level

Acute stress response

Chronic stress response  
Maladaptive development

Pathological stress and emotion regulation networks, immune response, ...

## Clinical Level

Transient distress (non psychiatric)

Subthreshold symptoms (sleep, emotion dysregulation,...)

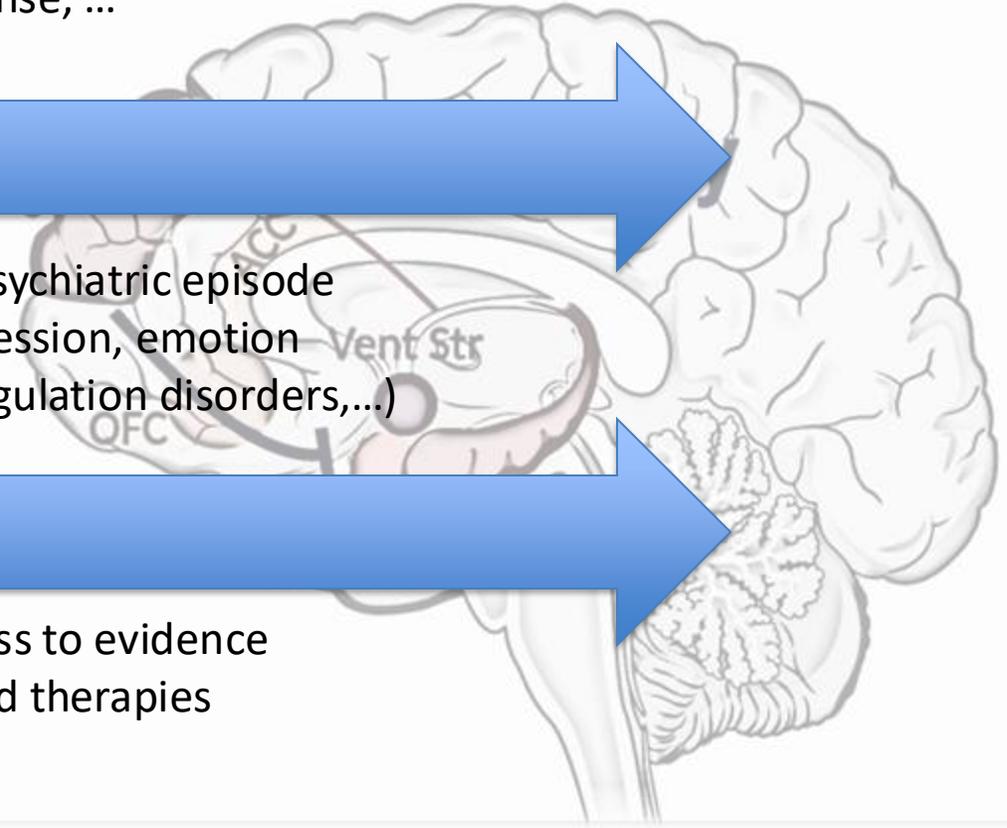
Full psychiatric episode (depression, emotion dysregulation disorders,...)

## Intervention Level

Resilience factors: mental health literacy, stress reduction tools

Early intervention : mindfulness, emotion regulation skills groups

Access to evidence based therapies



Transdiagnostic markers of emotion dysregulation in adult patients and offspring (Bipolar, ADHD, borderline personality)

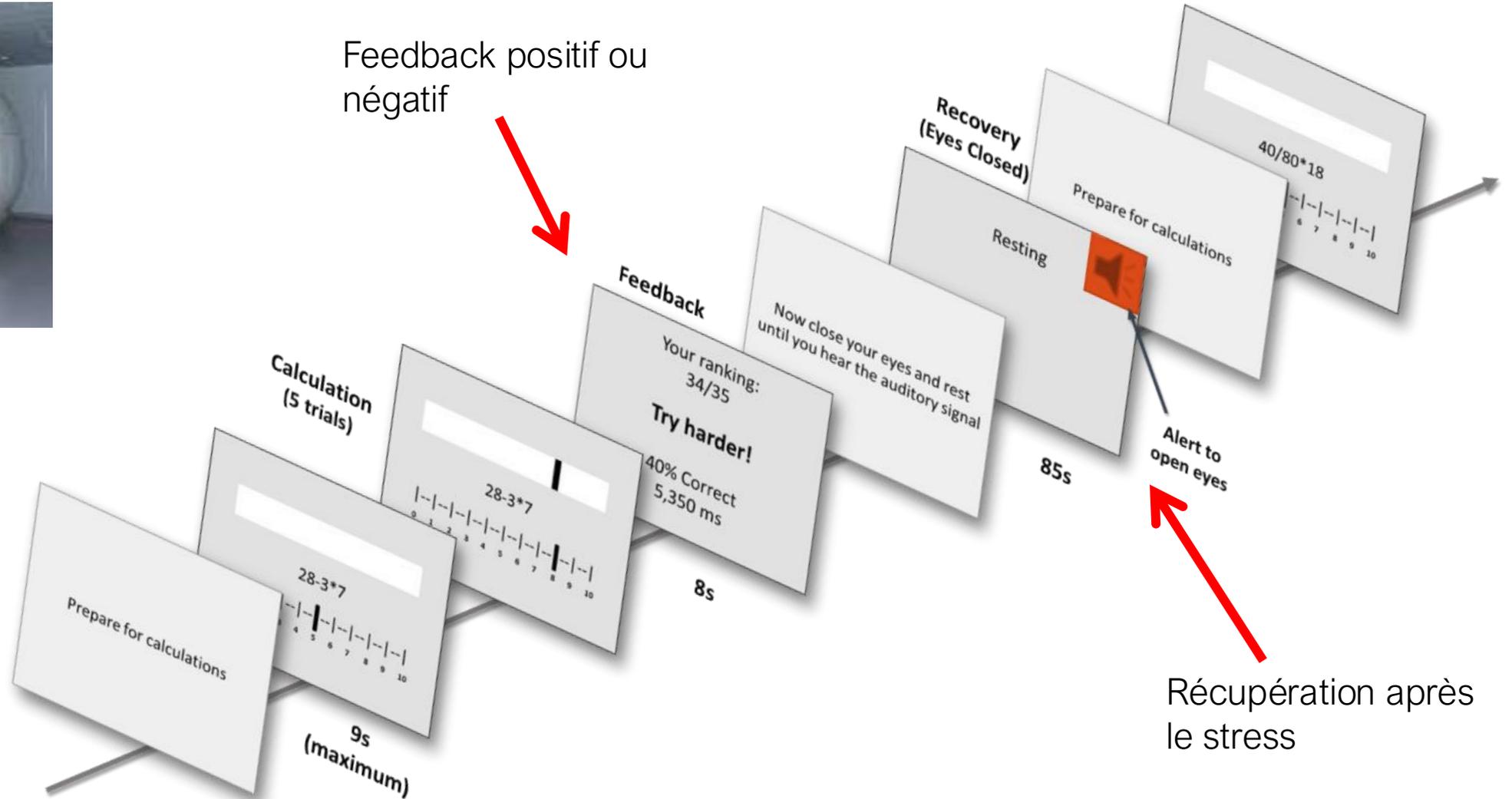
- **During psychosocial stress task (MIST)**
- **During resting state**
- **Associated with biological markers**



Impact of early interventions on stress and emotion regulation

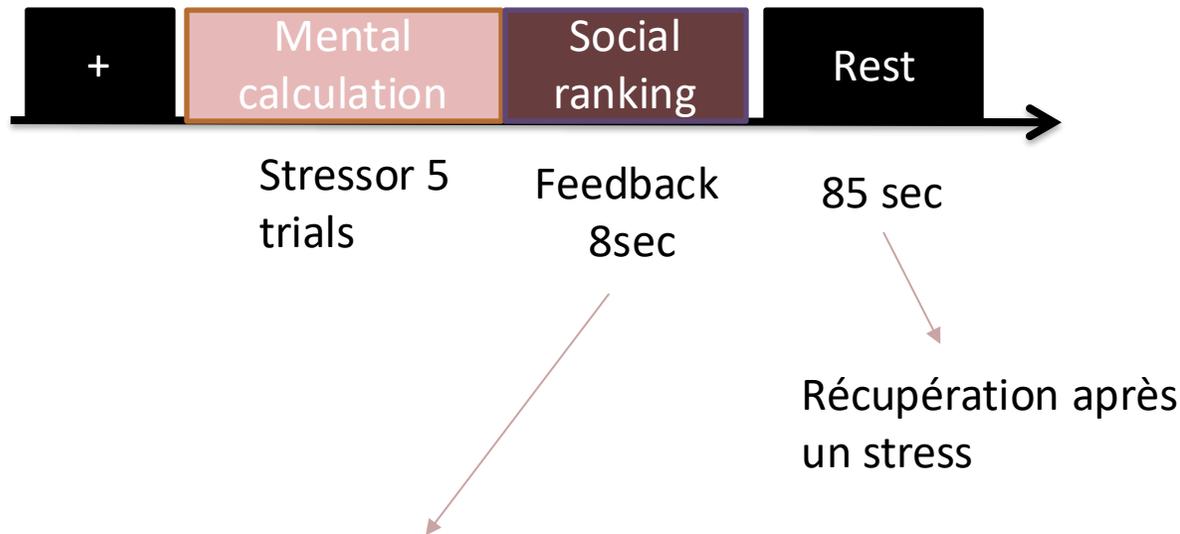
- **Mindfulness translational RCT in adolescents**
- **Mindfulness translational RCT in health care students**
- **Emotion Regulation Skills groups**

# RÉGULATION ÉMOTIONNELLE : MÉTHODES

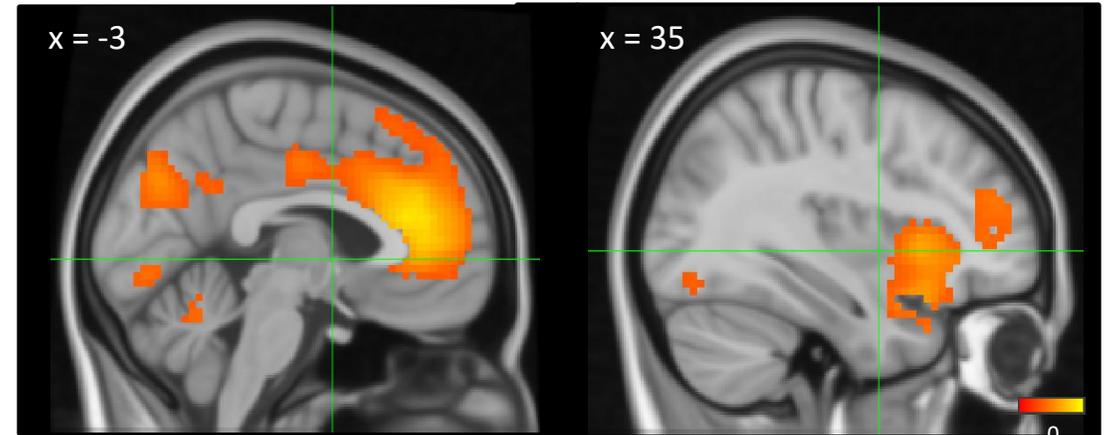




## Montreal Imaging Stress Task



Feedback négatif « essaie de mieux faire »  
Ou feedback positif « bravo! »



N = 47 sujets sains, condition de feedback social versus condition contrôle

Cortex cingulaire: prise de décision, cognition sociale  
Insula: intégration emotion-visceral, salience network

Murray, ... **Piguet**. JAD 2020: Maladaptive emotion regulation traits predict altered corticolimbic recovery from psychosocial stress

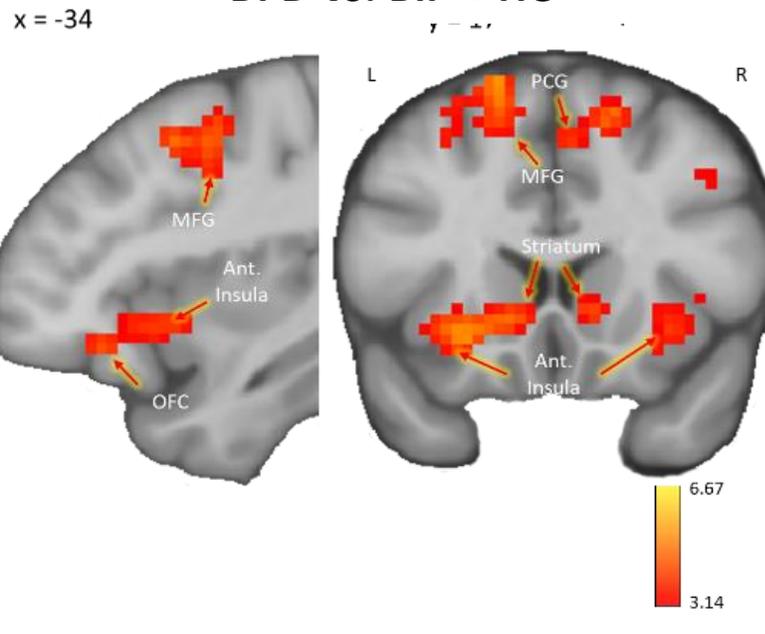
# EFFET SPÉCIFIQUE DU GROUPE LORS DE LA CONDITION DE STRESS



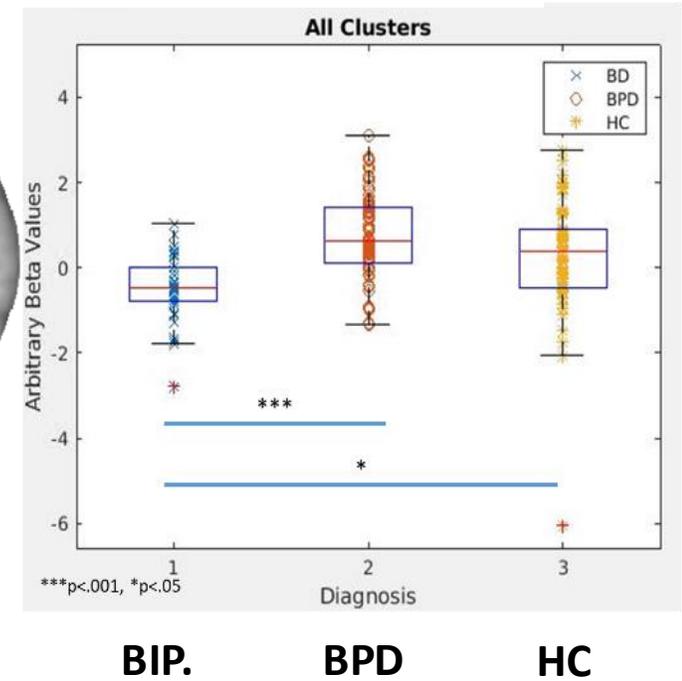
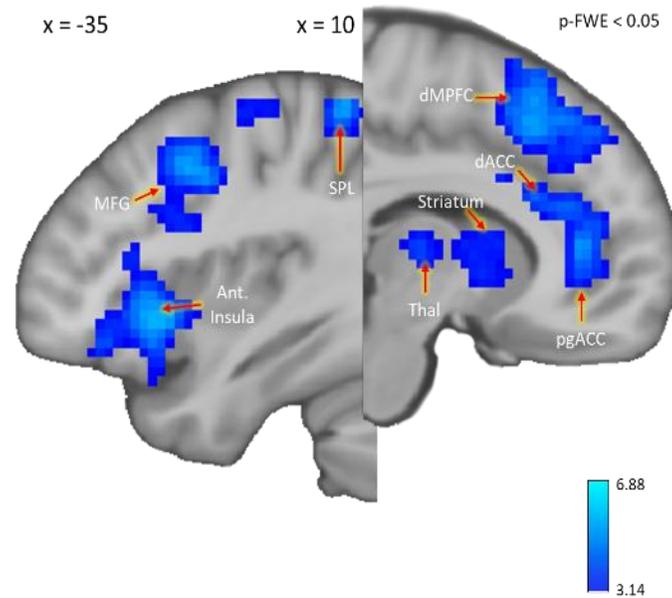
Ryan Murray



## BPD vs. BIP + HC



## BIP vs. BPD + HC



Murray, ... Piguet. Biol Psy CNI 2022

ARTICLE OPEN

Check for updates

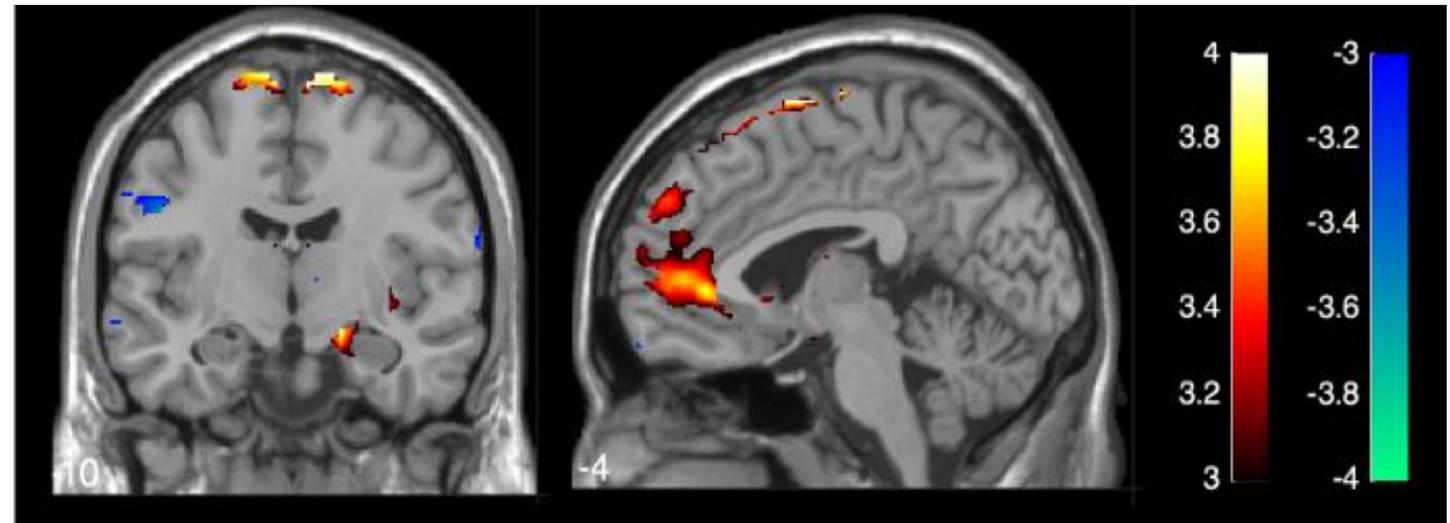
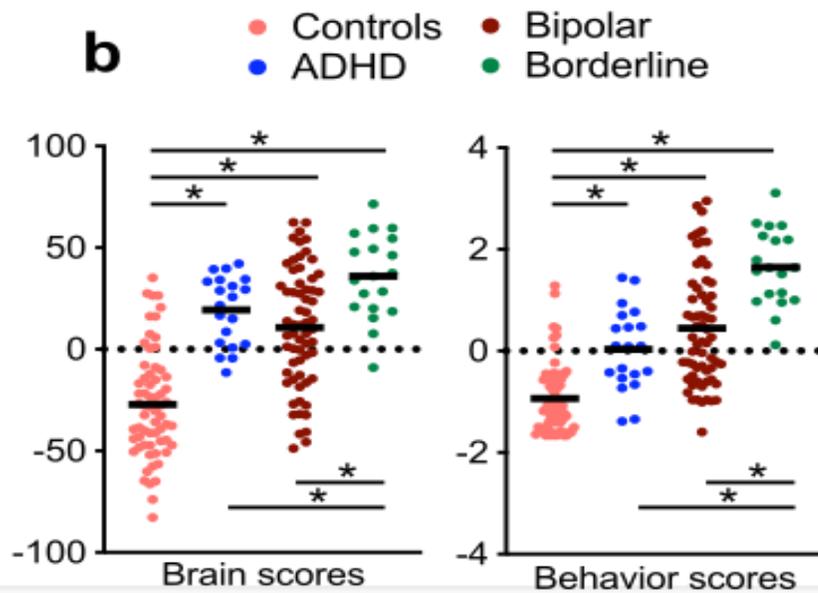
## Fronto-limbic neural variability as a transdiagnostic correlate of emotion dysregulation

Valeria Kebets<sup>1,2,3</sup>, Pauline Favre<sup>4,5</sup>, Josselin Houenou<sup>4,5</sup>, Mircea Polosan<sup>6</sup>, Nader Perroud<sup>1</sup>, Jean-Michel Aubry<sup>1</sup>, Dimitri Van De Ville<sup>2,7</sup> and Camille Piguet<sup>1,5</sup>



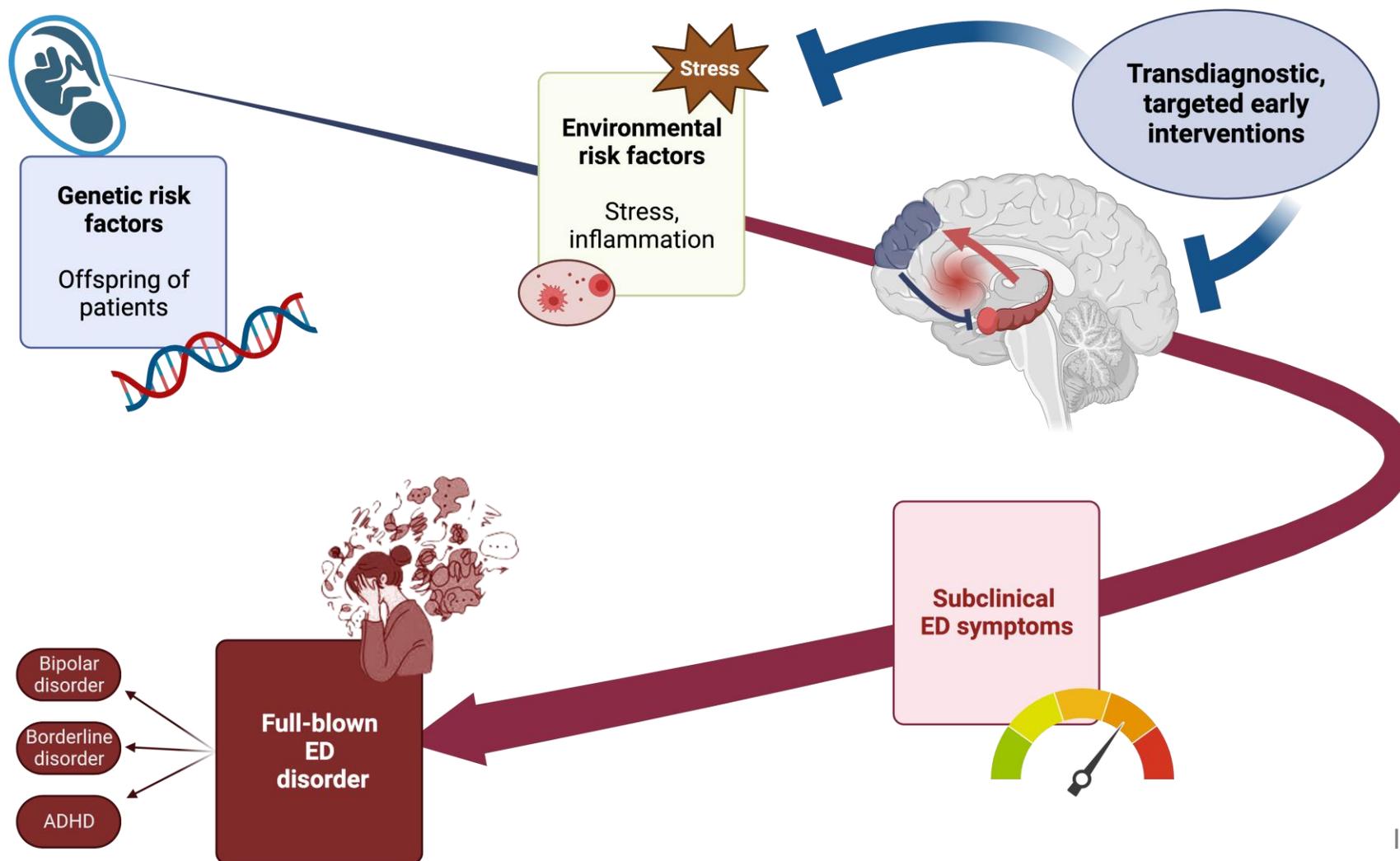
Valeria Kebets

© The Author(s) 2021



Kebets, ... Piguet. Transl Psychiatry 2021

# DYSRÉGULATION ÉMOTIONNELLE: MARQUEUR DE VULNÉRABILITÉ

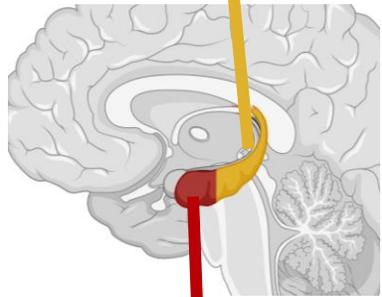
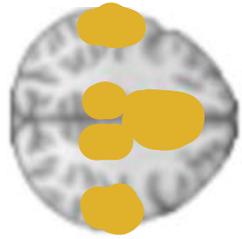


Luigi F Saccaro

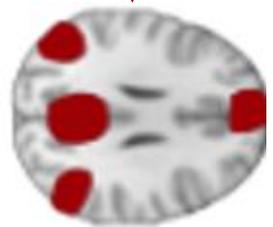
Inspired by Chanen et al. 2016

# TRANSDIAGNOSTIC AND MULTIMODAL PROJECT

micro-coactivation pattern 1 (CAP1)



**MRI connectivity**  
-Functional (micro-CAPs)  
- Structural



micro-coactivation pattern 2 (CAP2)

Depression, anxiety and affective lability scores

Transdiagnostic ED symptoms

ED patients, offsprings, controls

↑ Stress

↑ Inflammation

30 biological markers  
Multiplex-Immunoassay



Luigi F. Saccaro

Early life stress scores



Neuroscience & Biobehavioral Reviews  
Volume 127, August 2021, Pages 184-192

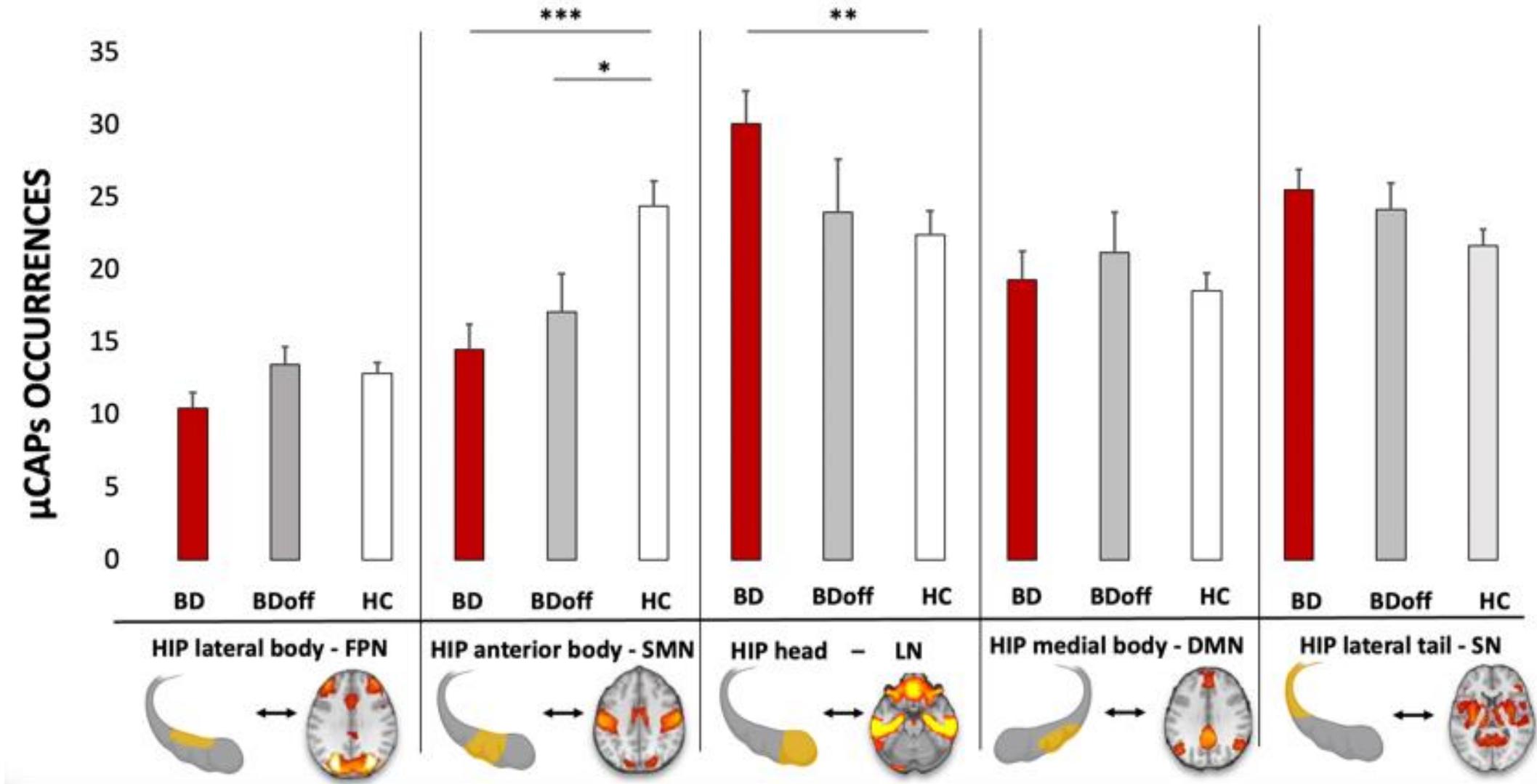


Review article

Inflammation, anxiety, and stress in bipolar disorder and borderline personality disorder: A narrative review

L.F. Saccaro <sup>a</sup>, Z. Schilliger <sup>b</sup>, A. Dayer <sup>c, d</sup>, N. Perroud <sup>c</sup>, C. Piguet <sup>e, e</sup> ✉

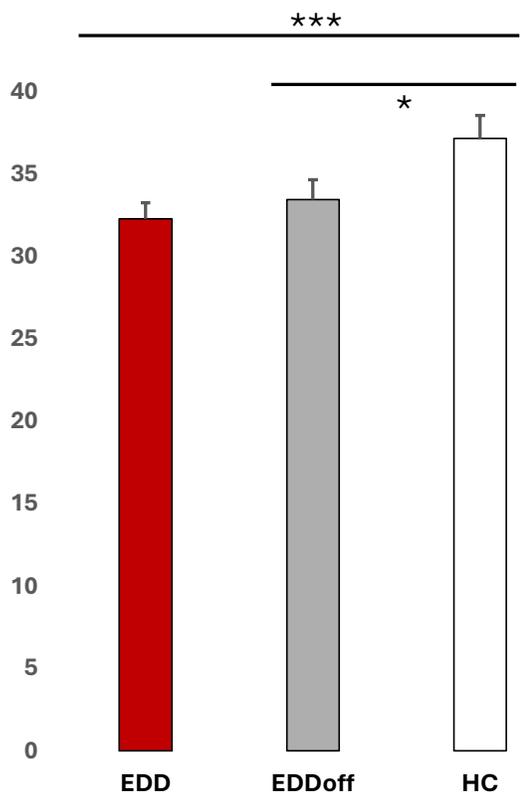
# RESTING STATE: Hippocampal connectivity in BD, BD offspring, and HC



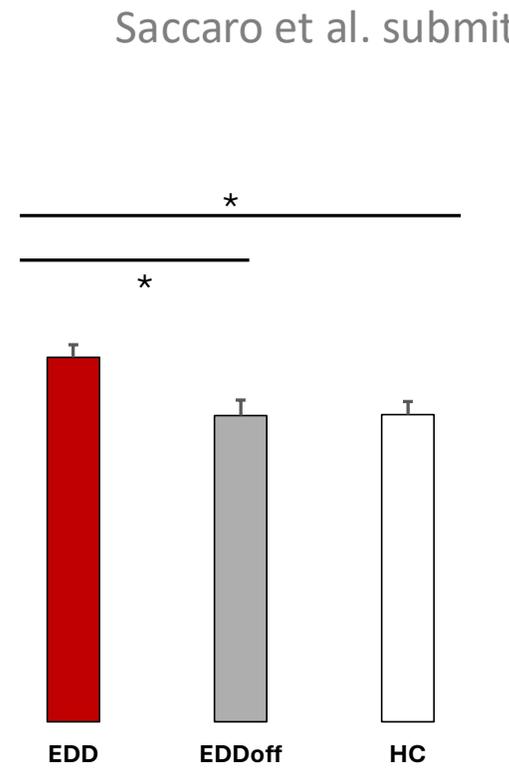
Saccaro et al. Bipolar Disorder 2024

# RESTING STATE: transdiagnostic hippocampal connectivity in ED disorders

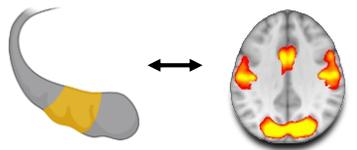
μCAPs OCCURRENCES



Saccaro et al. submitted

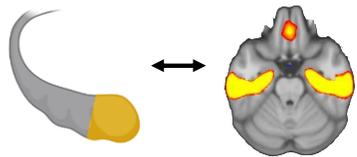


HIP body - SMN

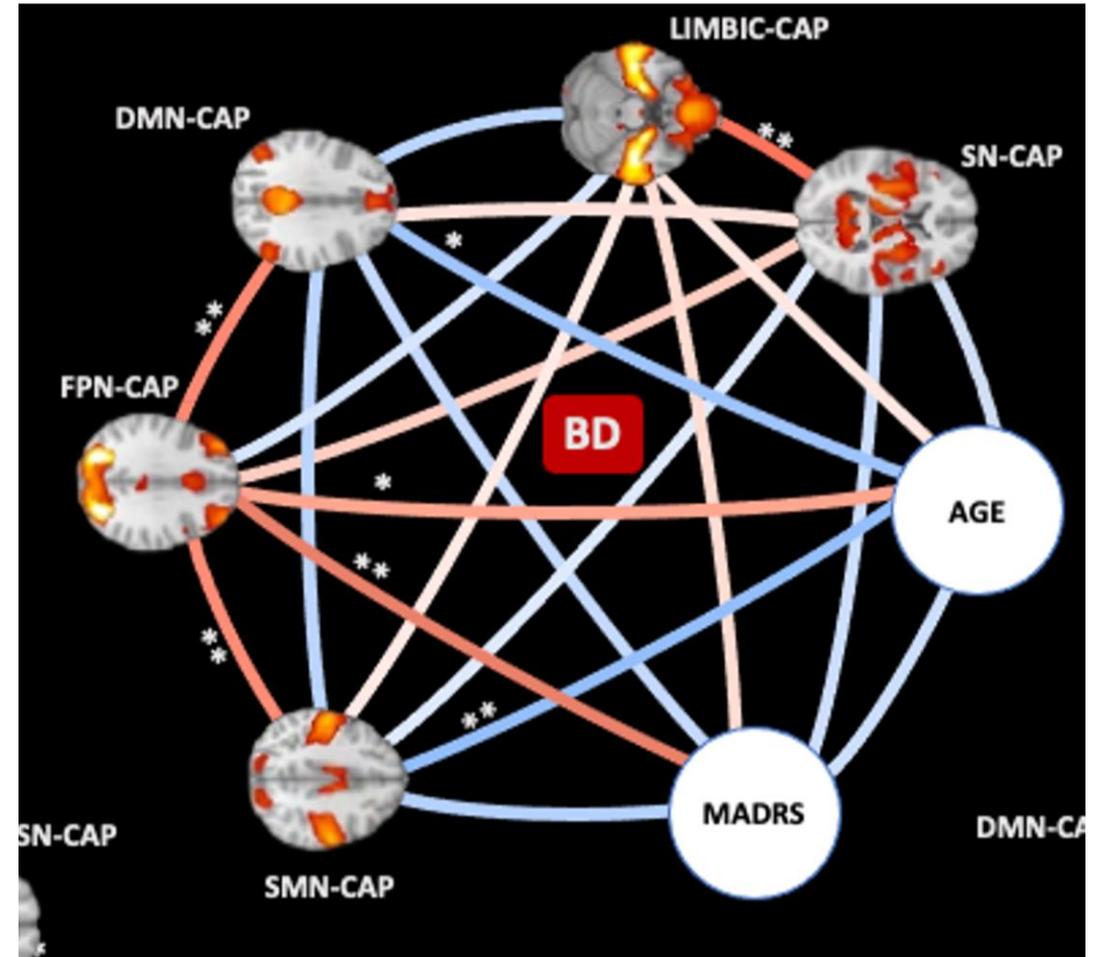


Somatomotor Network

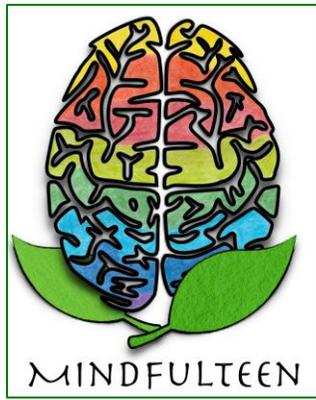
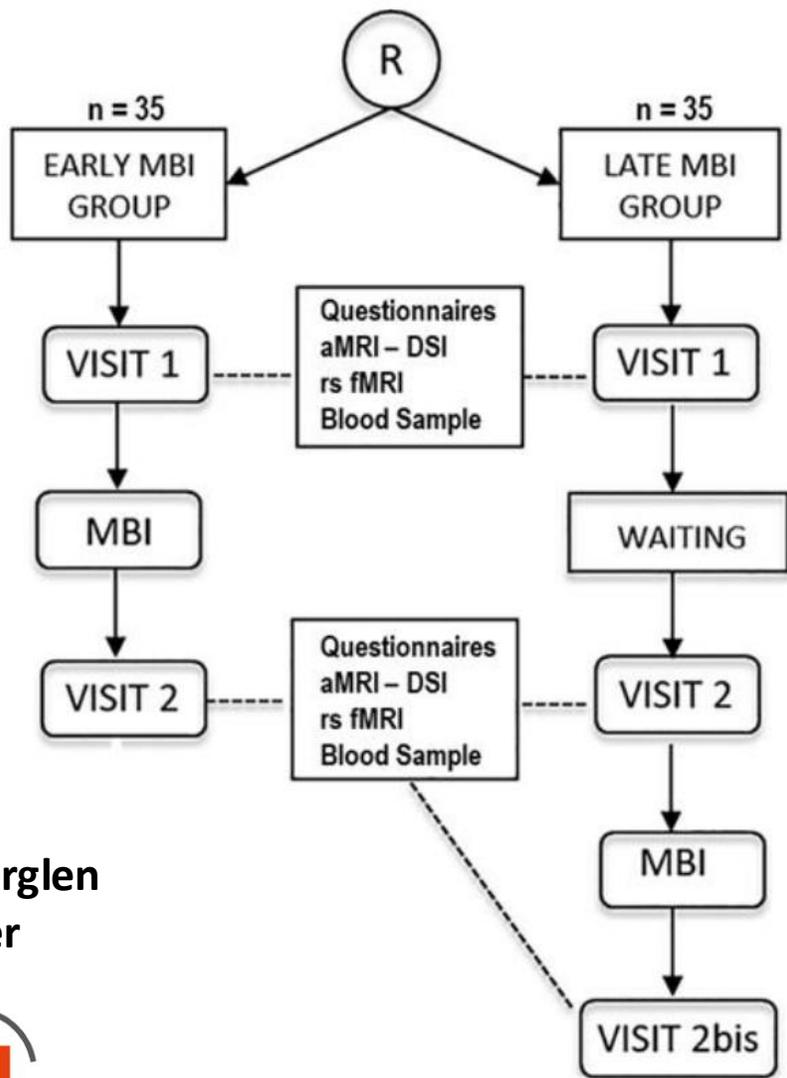
HIP head - LN



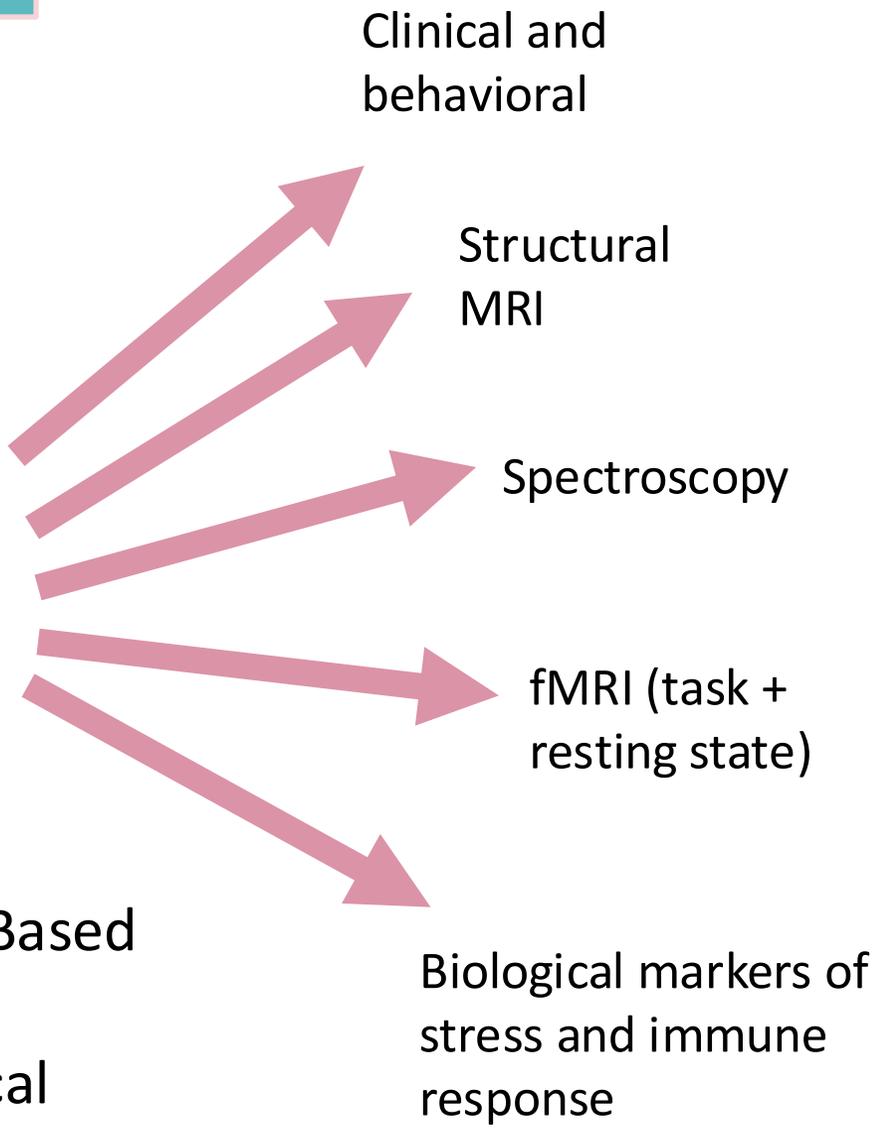
Limbic Network



# IMPACT OF MINDFULNESS ON ADOLESCENTS



RCT 2019-2021  
 8 weeks Mindfulness Based Intervention  
 13-15 yo non-clinical adolescents  
 N = 70



Co-PI  
 Arnaud Merglen  
 Paul Klauser  
 2018



Hôpitaux  
 Universitaires  
 Genève



# MINDFULTEEN STUDY: CLINICAL DATA



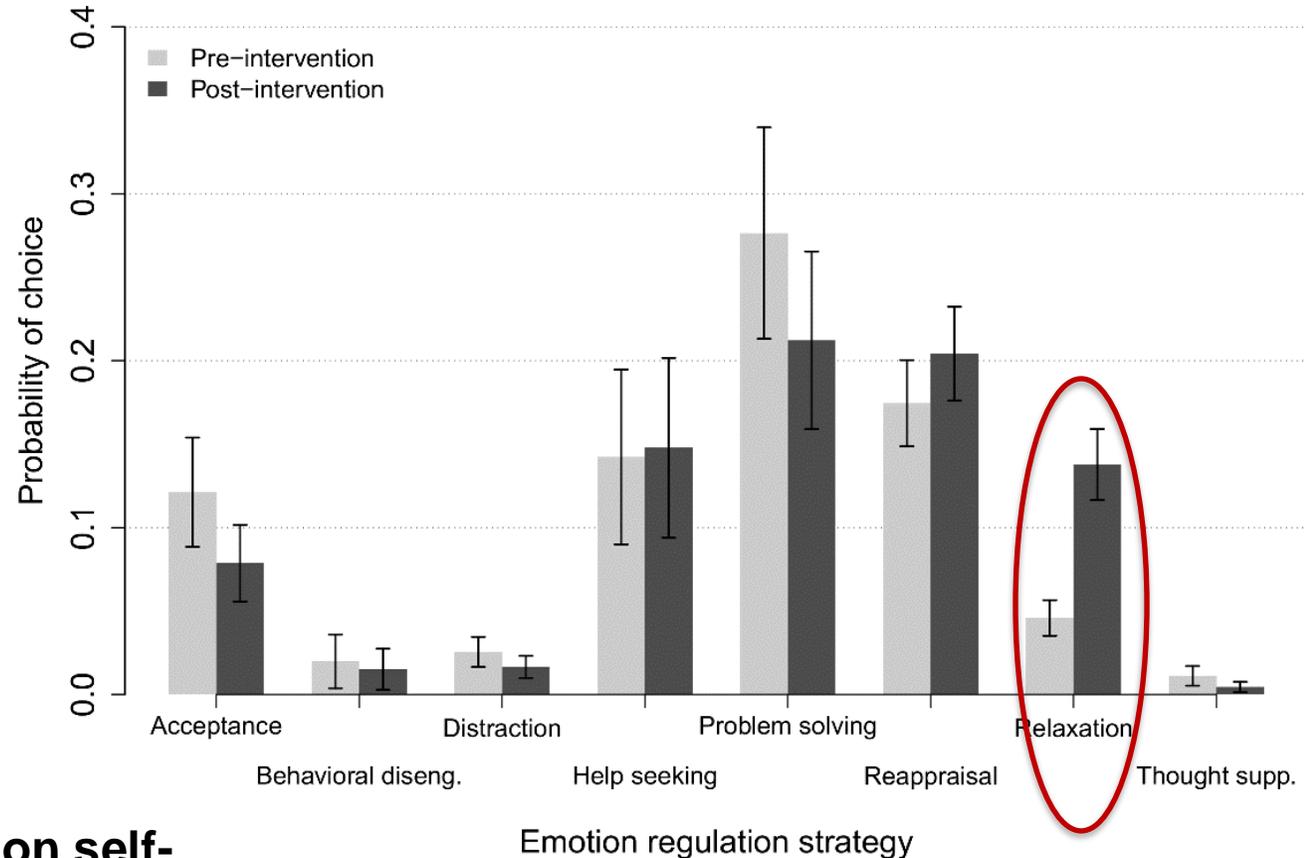
- **70 adolescents recruited**
- Mean age 14 year old (13-15)
- Non clinical (70% no DX)

Very good retention rate  
High satisfaction 8.7/10  
Would recommend the program  
to a friend: 91%

Increased use of "relaxation" as  
emotion regulation strategies

**However: no effect of intervention on self-reported measures except for subgroup with past depressive episode**

Piguet et al. in revision, Mendola et al in prep



Reactivity and Regulation Task  
(Samson et al.)

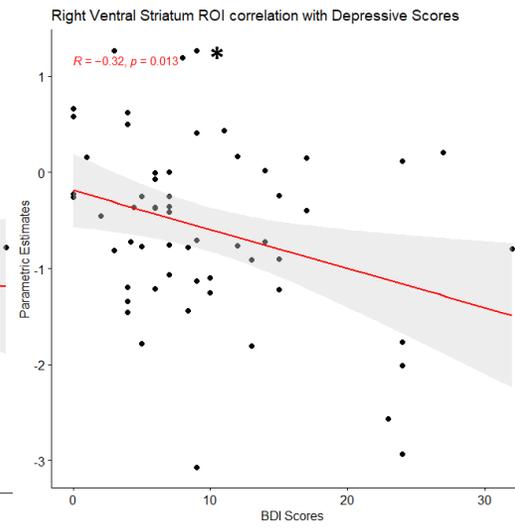
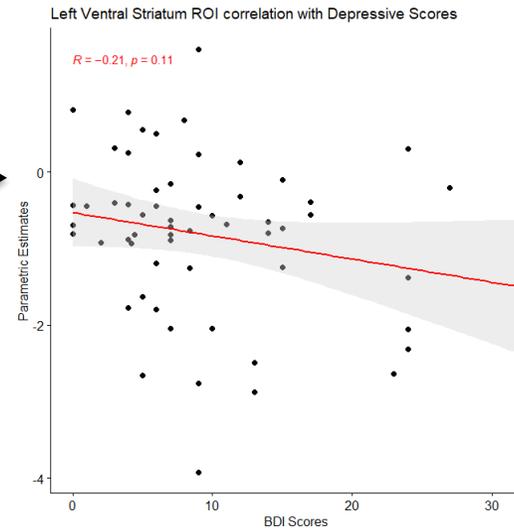
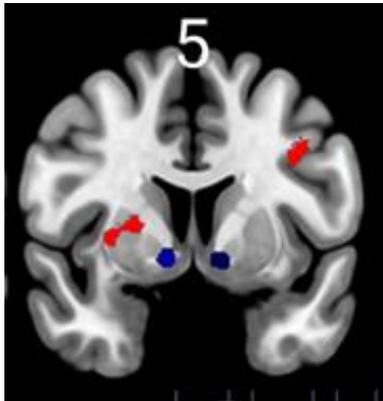
# EFFECT OF MINDFULNESS ON PSYCHOSOCIAL STRESS



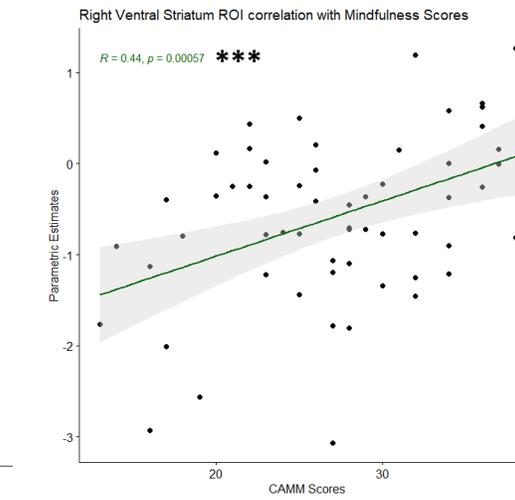
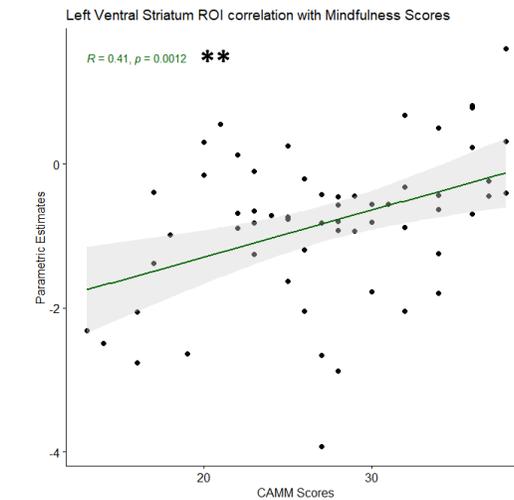
Zeynep Celen,  
Biol Psy CNNI



During acute stress, activity in striatum correlates negatively with depression and positively with trait Mindfulness ( $p < 0.005$ )

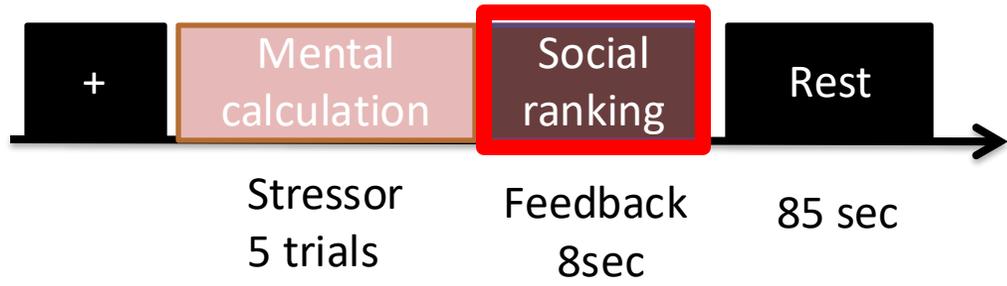


Depressive Symptoms



Mindfulness Trait

# EFFECT OF MINDFULNESS ON PSYCHOSOCIAL STRESS



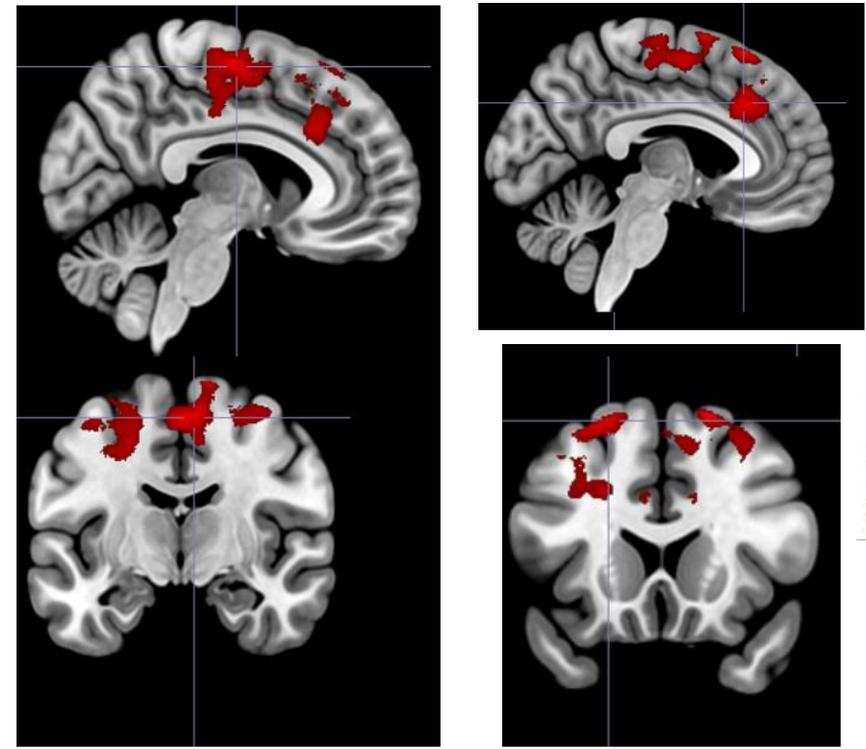
Positive Feedback 😊 + Negative Feedback ☹️

## Social Feedback



- ▶ Supplementary Motor Area
- ▶ Superior Frontal Gyrus
- ▶ dACC

→ Increased activity in social cognition and emotion regulation regions after mindfulness



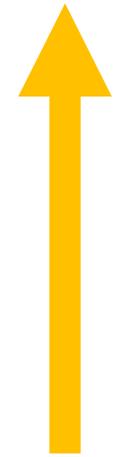
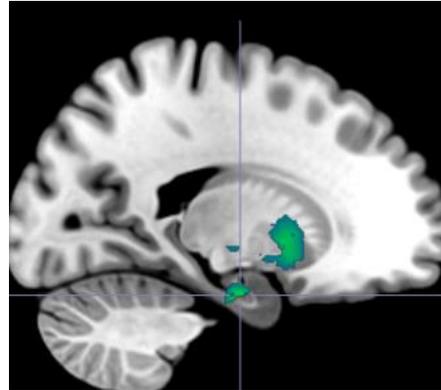
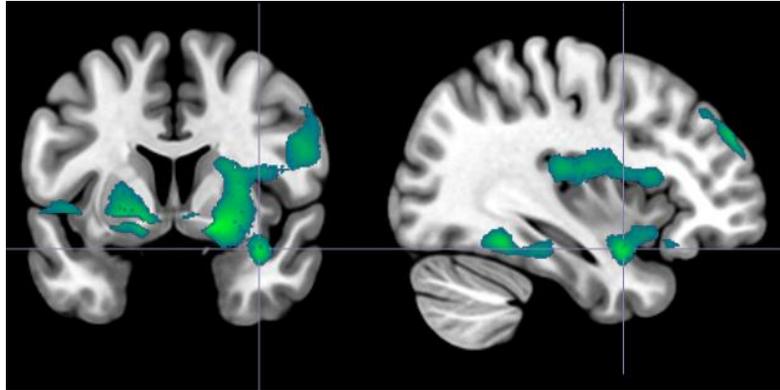
Intervention > Waiting X Social FB > Control FB  
Cluster corrected FWE (p<0.05) p<0.05 cluster forming threshold

# EFFECT OF MINDFULNESS ON PSYCHOSOCIAL STRESS



Zeynep Celen, in prep

Positive Feedback 😊

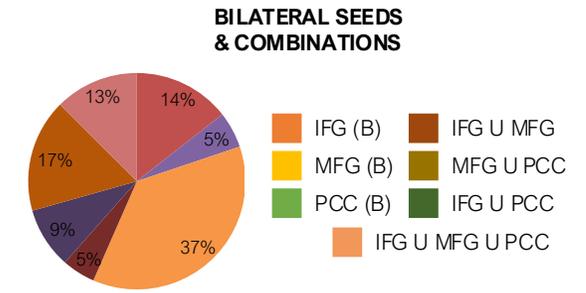
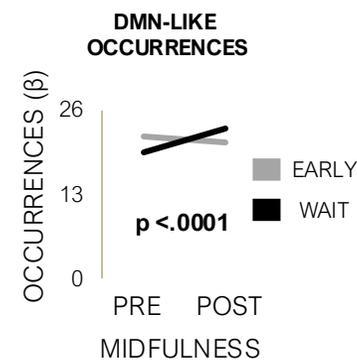
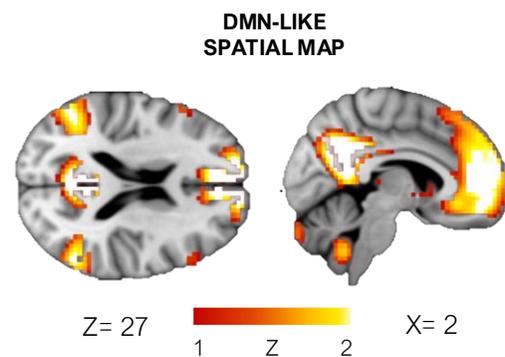
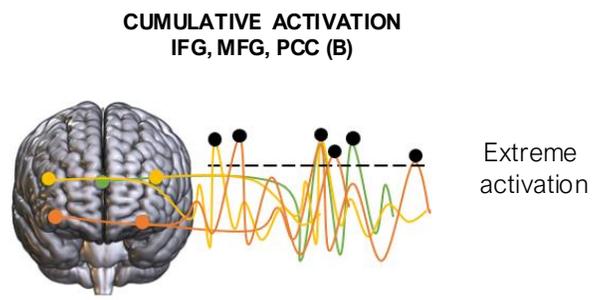


- Increased activity in :**
- Right Putamen
  - Right Middle Temporal Gyrus
  - Left Dorsolateral Prefrontal Cortex
  - Left Hippocampus
  - Hypothalamus
  - Right temporal pole/insula

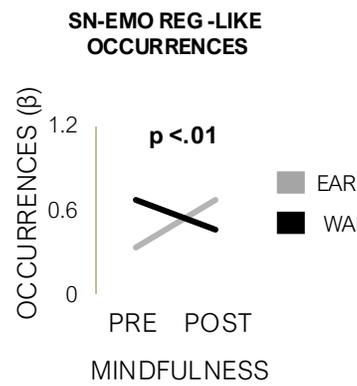
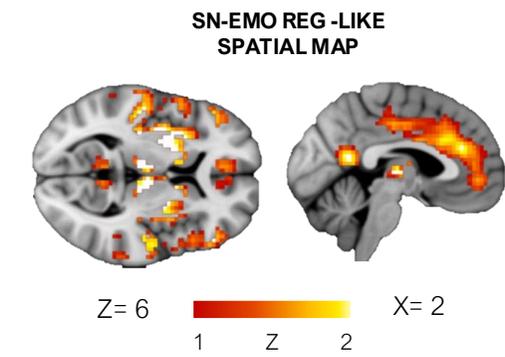
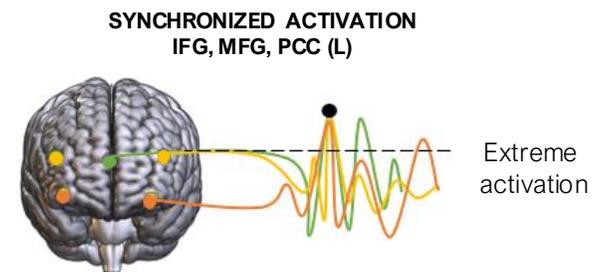
→ **Increased activity in dorsolateral PFC, subcortical structures and insula after mindfulness**

Intervention > Waiting X Positive FB > Negative FB  
Cluster corrected FWE ( $p < 0.05$ )  $p < 0.05$  cluster forming threshold

# REST AFTER STRESS: MAIN EFFECT OF MINDFULNESS TRAINING

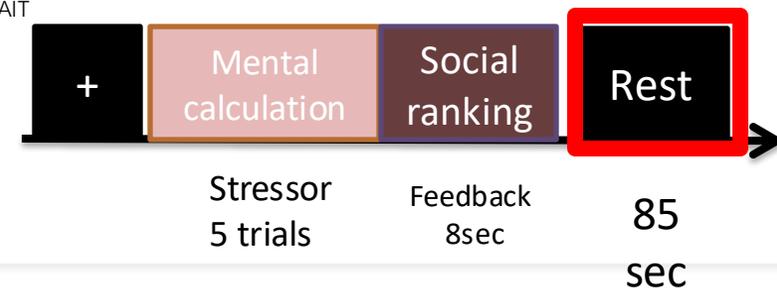


Mindfulness training decreased Default Mode like brain system



Julian Gaviria, in prep.

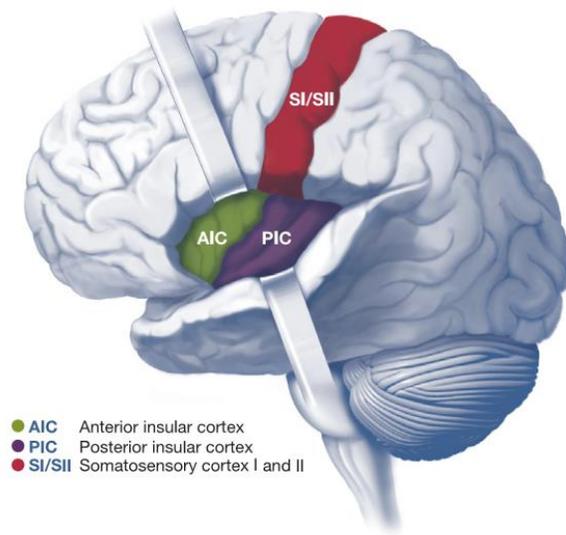
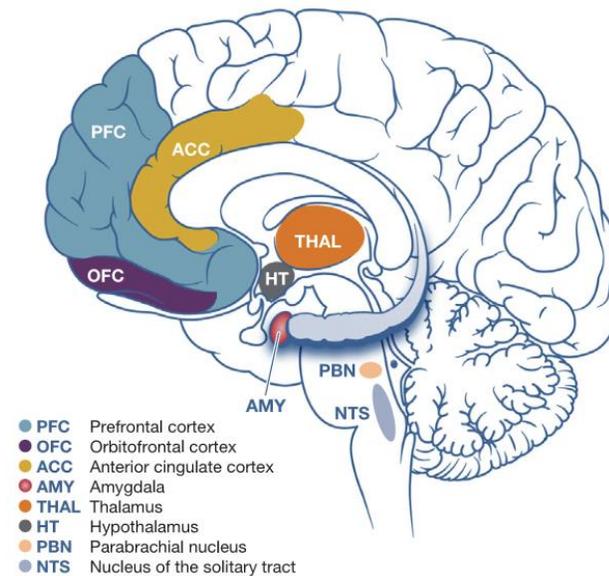
Mindfulness training increased salience-emotion regulation-like brain system



# SUMMARY

- ▶ In offspring of psychiatric patients (“genetic at risk population”), emotion dysregulation is associated with increased connectivity between hippocampus and DMN, and lower connectivity with somato-motor network.
- ▶ In adolescents (“clinically at risk population”), acute stress and low trait mindfulness is associated with decreased striatal activity, correlating with psychiatric vulnerability.
- ▶ Mindfulness intervention decreases DMN but increases relaxation-bodily perception, social cognition and processing of positive feedback.

- ▶ Need to better profile risk for mental disorders, integrating clinical, neuroimaging and biological information
- ▶ Need for developmentally adapted interventions, accessible and targeted for the age and clinical staging
- ▶ Integration of somato-sensory information associated with emotions and stress as a promising target -> interventions that focus on interoception



Trends in Neurosciences

Chen et al. 2021 The Emerging Science of Interoception: Sensing, Integrating, Interpreting, and Regulating Signals within the Self

Transdiagnostic markers of emotion dysregulation in adults patients and offspring (Bipolar, ADHD, BPD)

- During psychosocial stress task (MIST)
- During resting state
- Associated with biological markers

Impact of early interventions on stress and emotion regulation

- Mindfulness RCT in adolescents
- Mindfulness RCT in health care students
- Emotion Regulation Skills groups

First line & youth friendly early interventions for interoception

- Phenotyping of at risk youth for emotion dysregulation disorders
- Personalized stress reduction interventions (e.g. cardiac coherence, VR, etc.)

But also evaluation of more systemic actions !

MERCI POUR VOTRE ATTENTION !



**e-SMILE**  
Empathie, Stress,  
Mindfulness Et Etudes



## Psychiatrie

Jean-Michel Aubry  
Alexandre Dayer  
Nader Perroud  
Françoise Jermann  
Guido Bondolfi  
Stefan Kaiser  
Logos Curtis  
Sarita Goutorbe  
Sandra Ter Pelle

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Zoé Schilliger  
Dan Schechter  
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Julia Fol  
Erik Mendola

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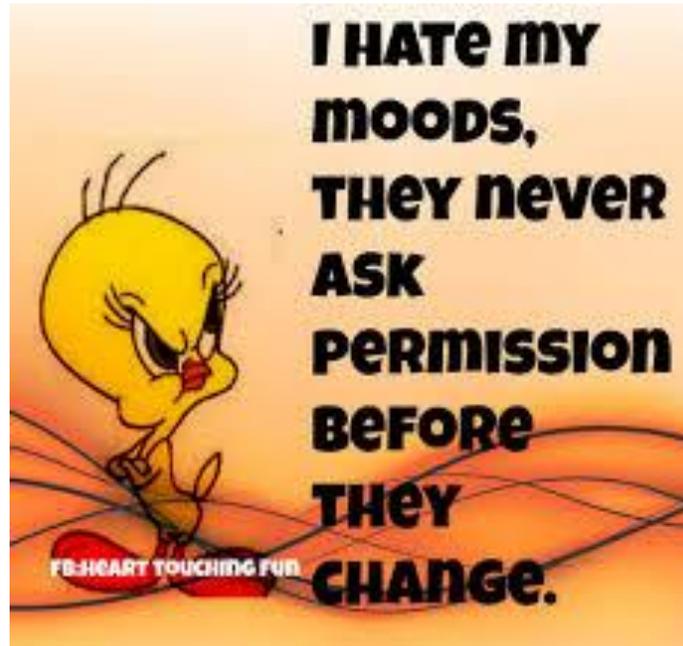
Josselin Houenou  
Pauline Favre  
Luc Mallet

## Campus Biotech

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Ben Meuleman  
Luigi F. Saccaro  
Julian Gaviria  
Eleonore Pham  
Vladimira Ivanova  
Mariana Magnus Smith  
Claire Holman  
Valentine Savary  
Cecimaria Guttierrez  
Sandra Santiago  
Claudia Catel

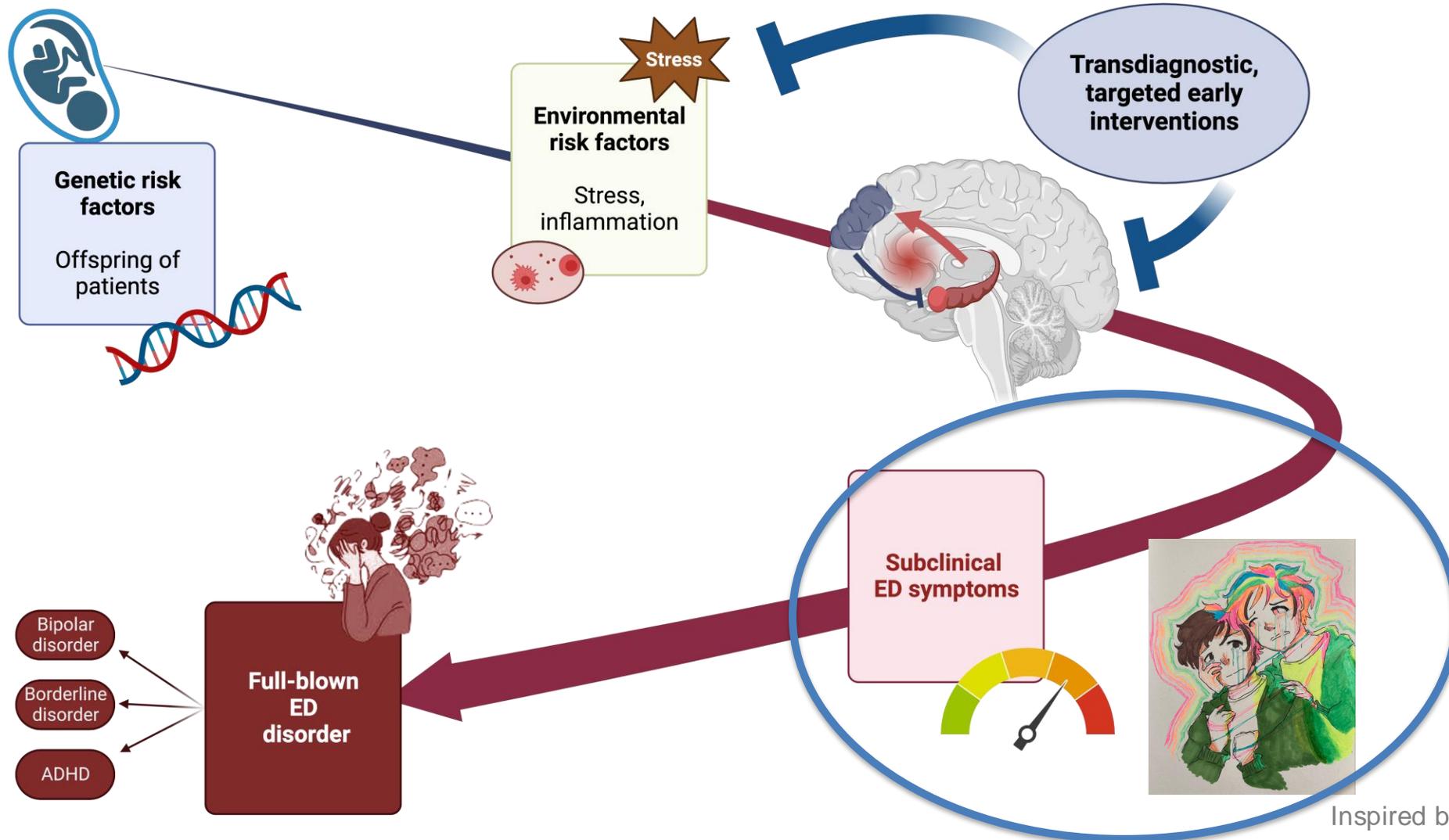


# QUESTIONS



@willowisp

# EMOTION DYSREGULATION AS VULNERABILITY MARKER



Inspired by Chanen et al. 2016

# DETERMINANTS DE LA SANTE MENTALE

## PRÉVENTION PRIMAIRE, SELECTIVE ET INDIQUÉE SELON LES GROUPES DE VULNÉRABILITÉ

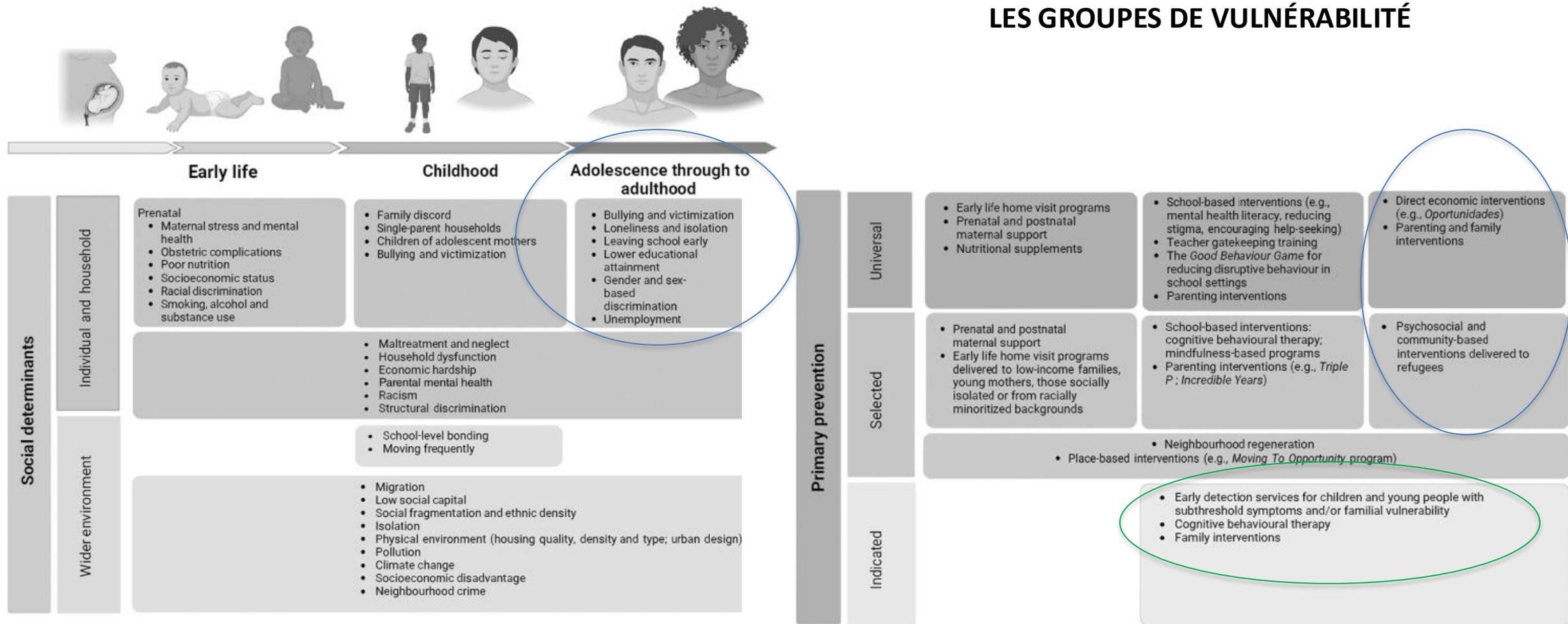
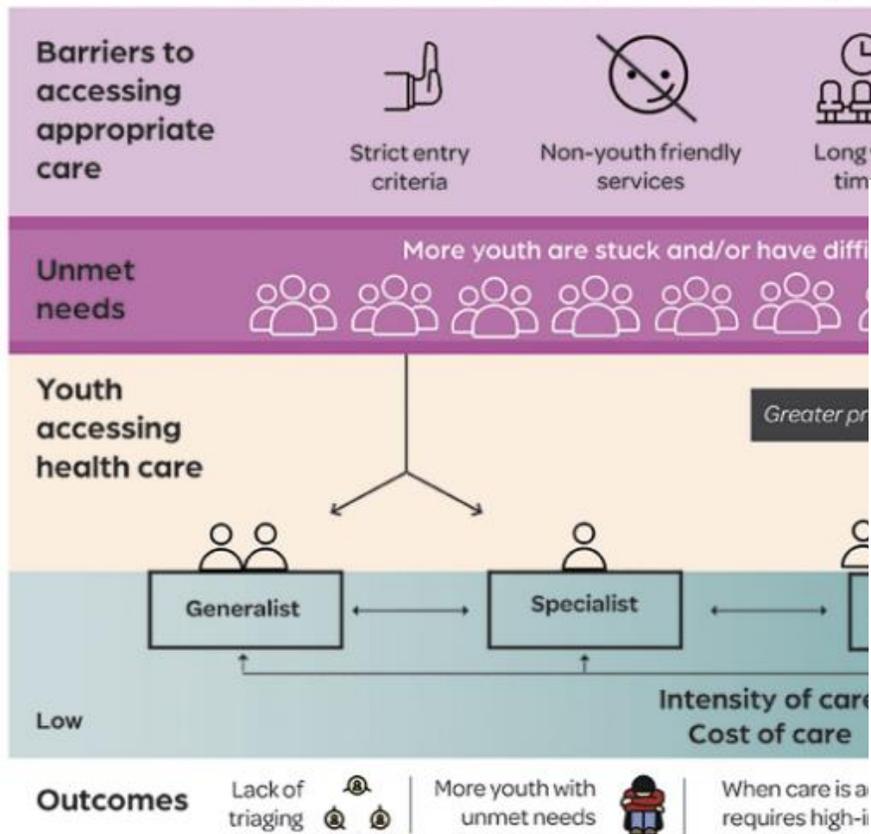


Figure 2 Summary of the social determinants of mental health and disorder and of the main primary prevention strategies

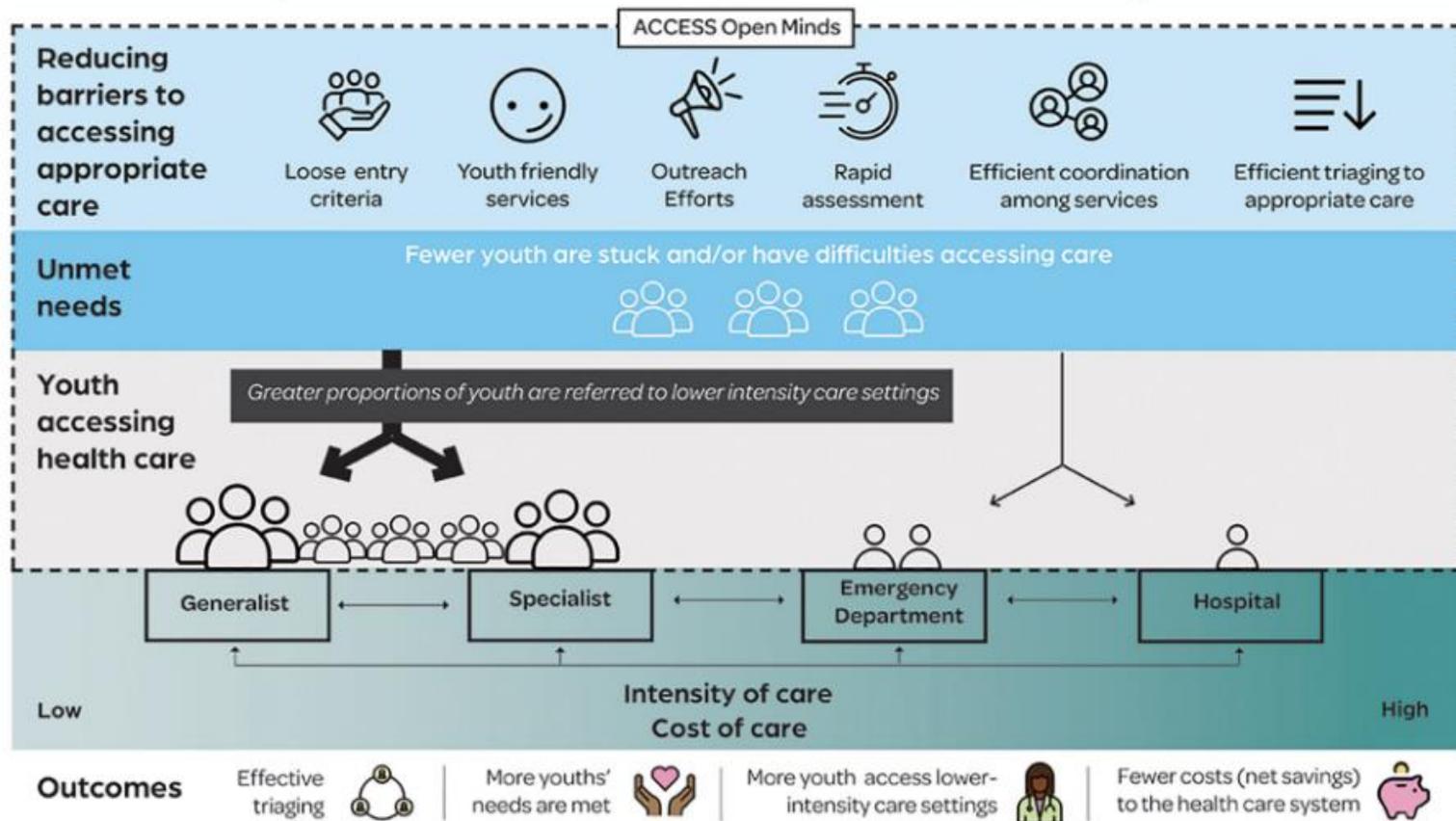
A

## Traditional access to mental health care for youth



B

## Improved access to mental health care for youth



Shah et al. Frontiers in Psychiatry 2023

