Social Neuroscience of Grief
Conference 2023

Loss of a loved one and mental health: Findings from the subcortical limbic system

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Overview

(1) Introduction

(2) Loss of a loved one and subcortical limbic volumes in healthy and clinical populations

(3) Loss of a loved one and subcortical limbic volumes - moderation by adult attachment style and childhood trauma

(4) Conclusion

Introduction

The loss of a loved one

The disruption of an attachment bond

Presented studies

Assessment	Retrospective (questionnaire) e.g., List of Threatening Experiences questionnaire (Brugha & Cragg, 1990)
Loss	Bereavement, relationship breakup
The loved one	First degree relative (parent, sibling, child) Close friend or close relative Romantic partner or spouse
Time of loss	Previous 5 years, lifelong

Loss experiences and mental health

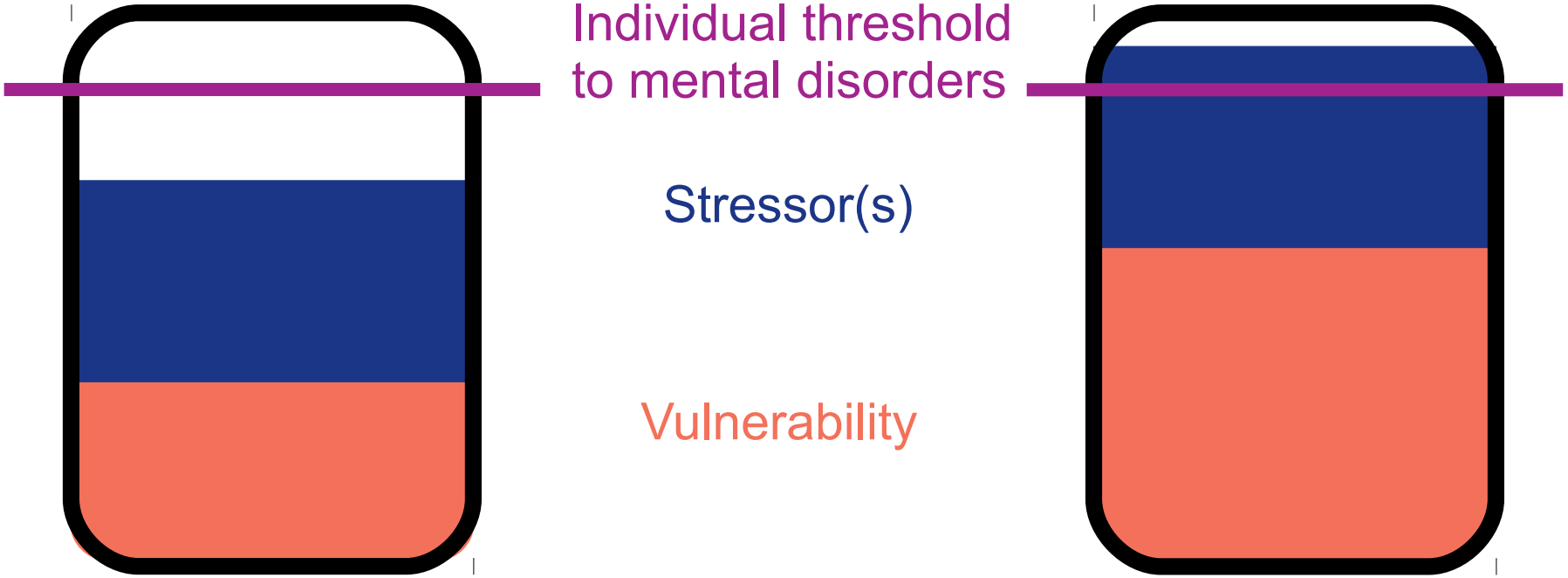
Loss as a stressful and painful experience

Increased prevalence of mental disorders after loss experiences

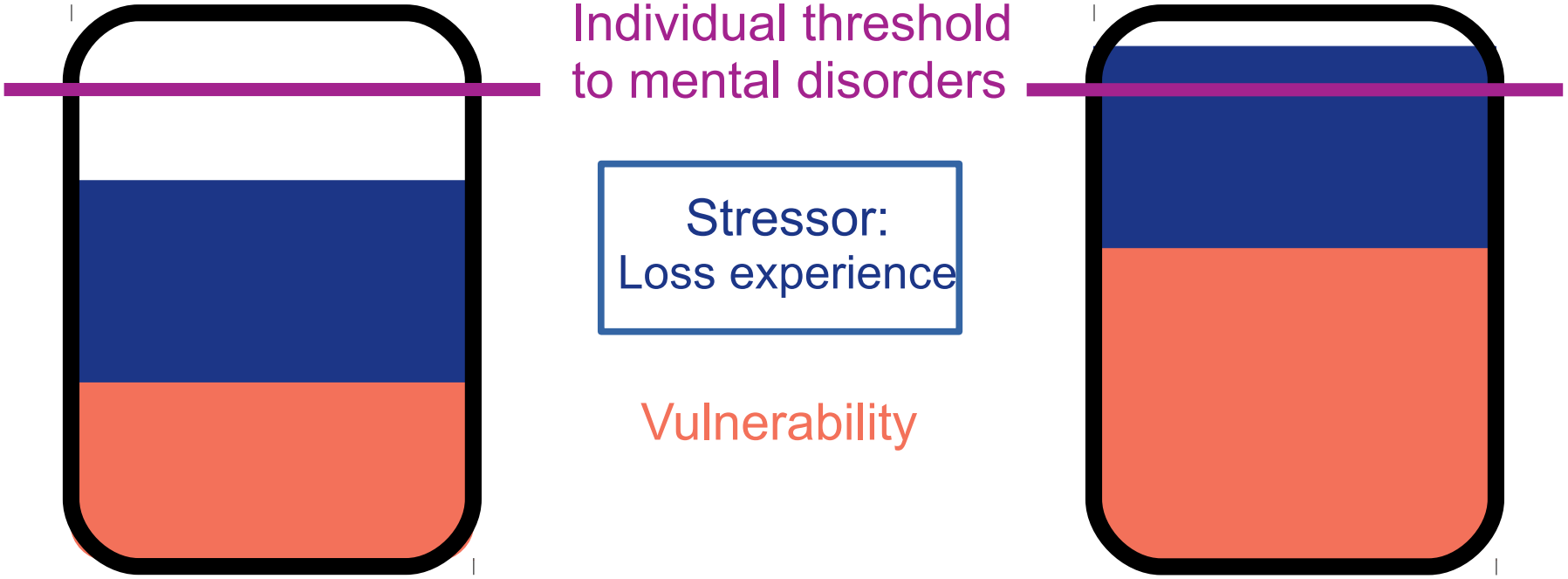
	After loss
Anxiety disorders	~ 30%
Major depressive disorder (MDD)	~ 27 %
Schizophrenia	OR 1.4-2.1
Prolonged grief disorder	~ 10%
Chronic pain disorder	?

Diagnoses of mental disorders according to the International Classification of Diseases (ICD) or the Diagnostic and Statistical Manual of Mental Disorders (DSM)

Vulnerability-stress model of mental disorders



Vulnerability-stress model of mental disorders



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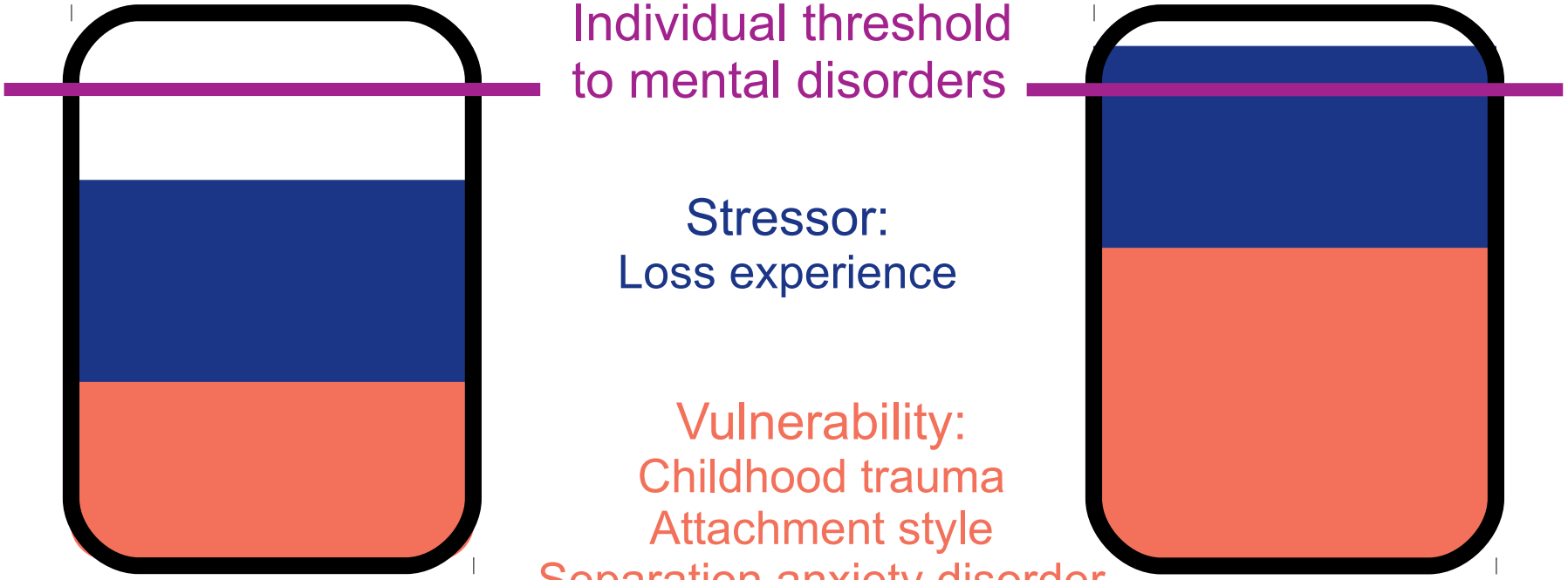


Vulnerability-stress model of mental disorders

Brain structure

“The brain is the source of behavior, but in turn it is modified by the behaviors it produces. This dynamic loop between brain structure and brain function is at the root of the neural basis of cognition, learning and plasticity.”

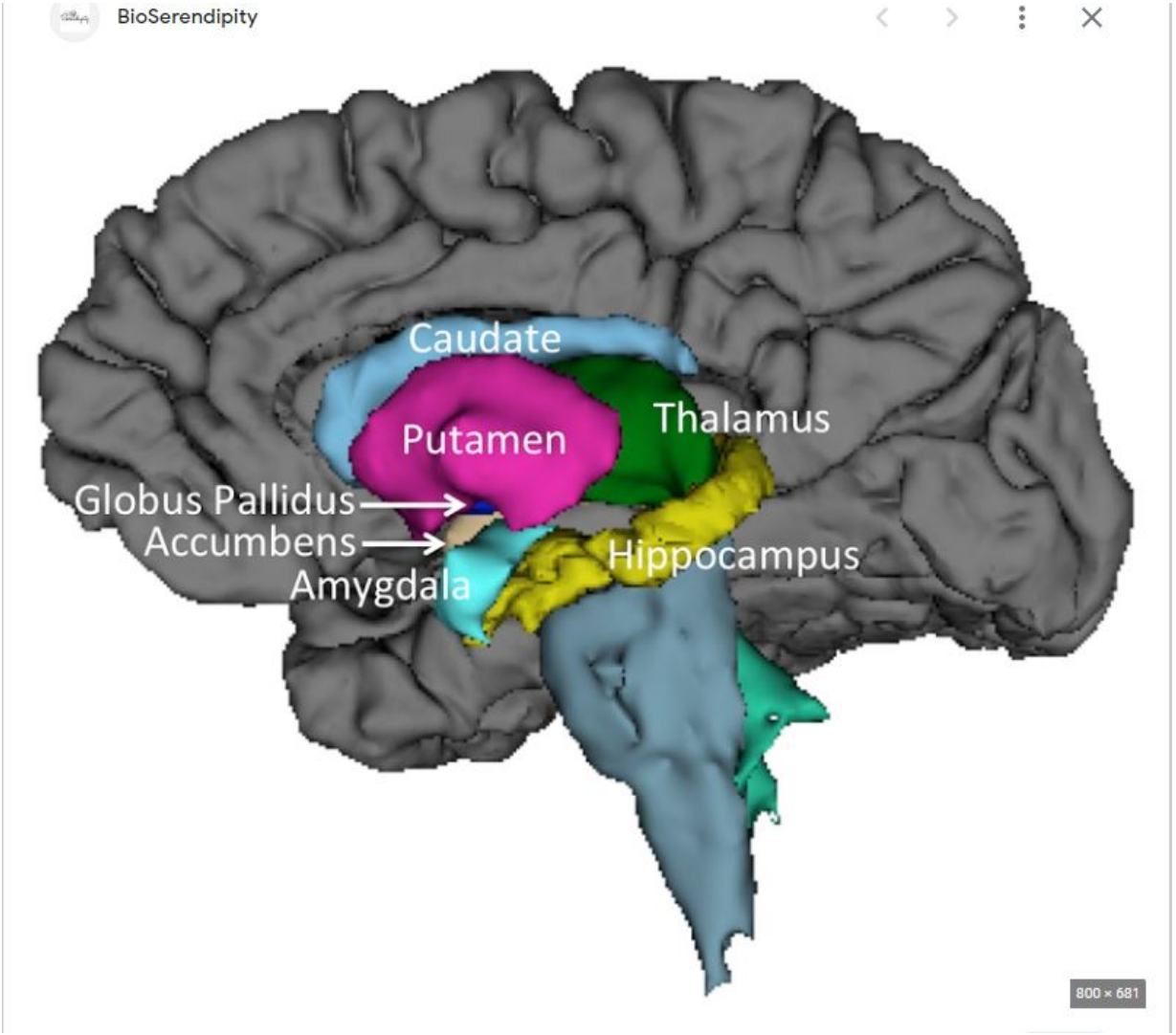
Zatorre et al., 2013, *Nature Neuroscience*

Limbic system

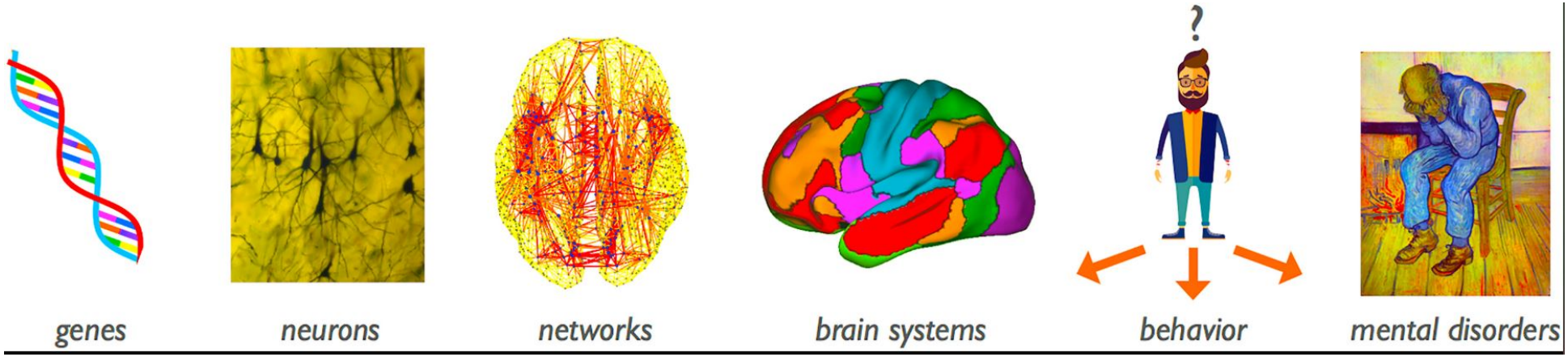
Limbic system ("visceral brain") as "a common denominator of a variety of viscerosomatic and emotional reactions" (MacLean, 1955).

Now controversial, but still in use as a term for brain regions involved in emotion processing.

Subcortical limbic structures



Brain structure - scale



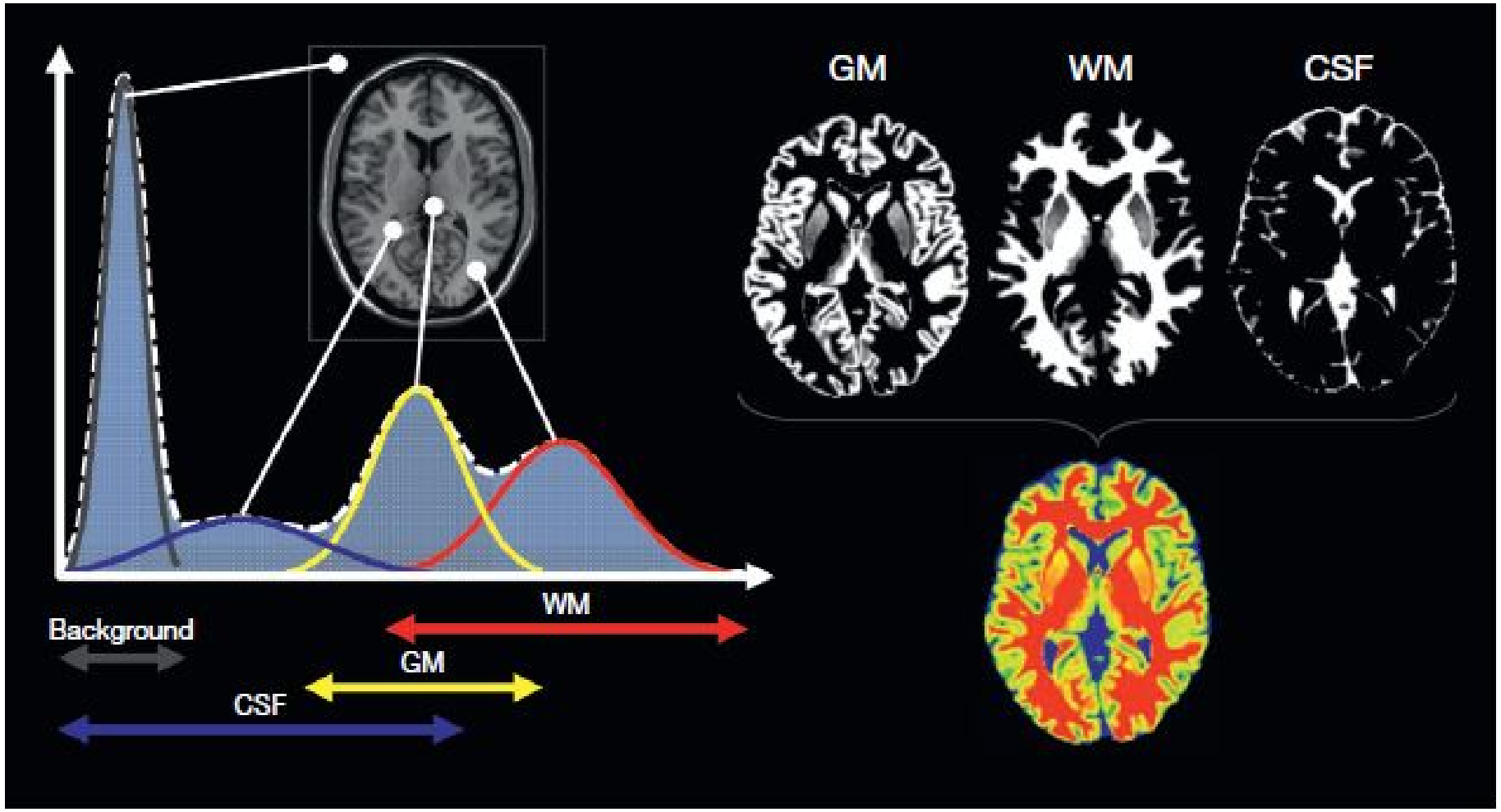
Microscopic

Macro-/ mesoscopic

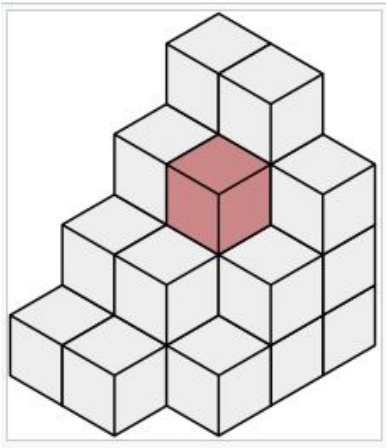
Image from: Van den Heuvel & Yeo (2017), Neuron

MRI tissue classification

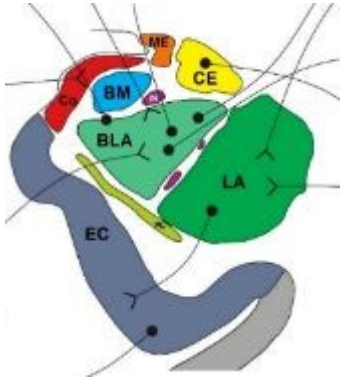
From Kurth, Luders & Gaser (2015), *Brain Mapping: An Encyclopedic Reference*

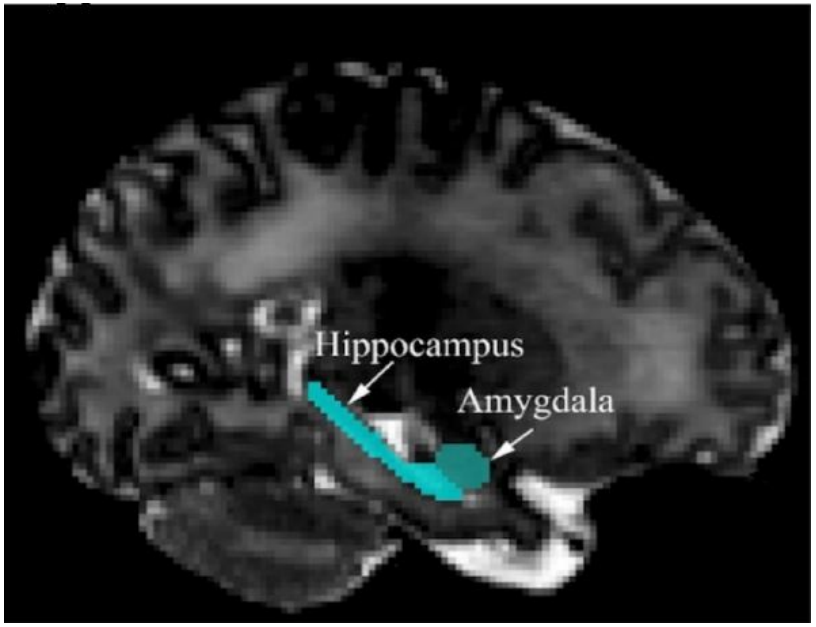


Voxel-based morphometry (VBM) versus cumulative volumetric measures



Nuclei of the amygdala





VBM

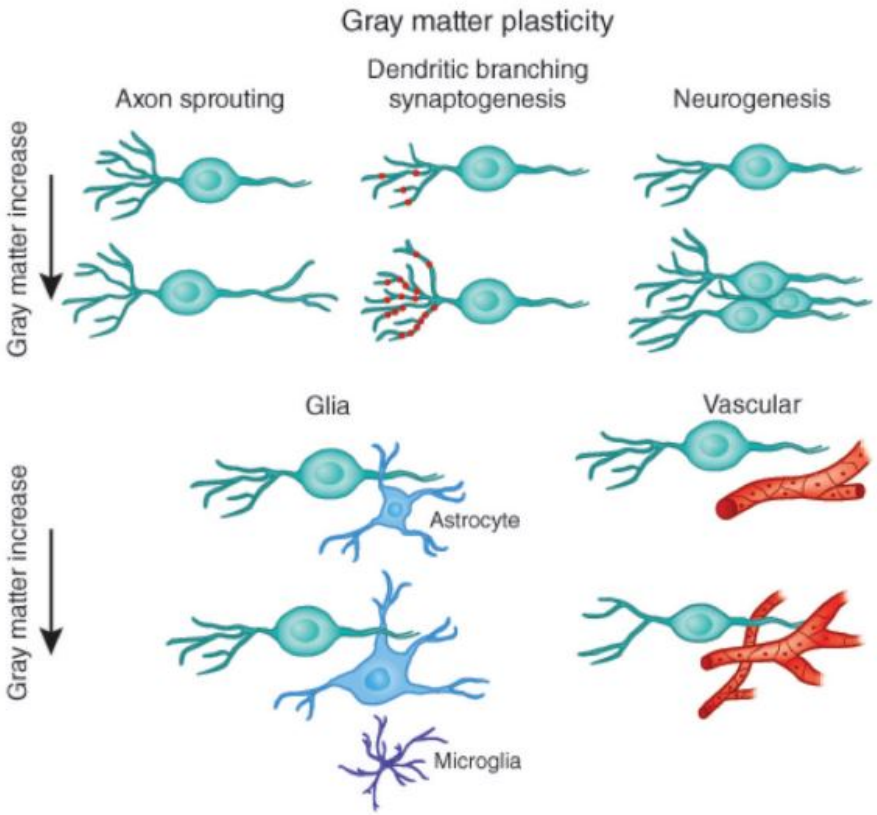
voxel-wise comparison of the local concentration of gray matter

voxel: 1 x 1 x 1 mm^3
contains ~ 100.000 neurons and
~ 400.000 glial cells

Segmentation (cumulative volumetric measure)

Right Amygdala e.g., 870 mm^3
Right Hippocampus e.g., 4000 mm^3

Structural plasticity

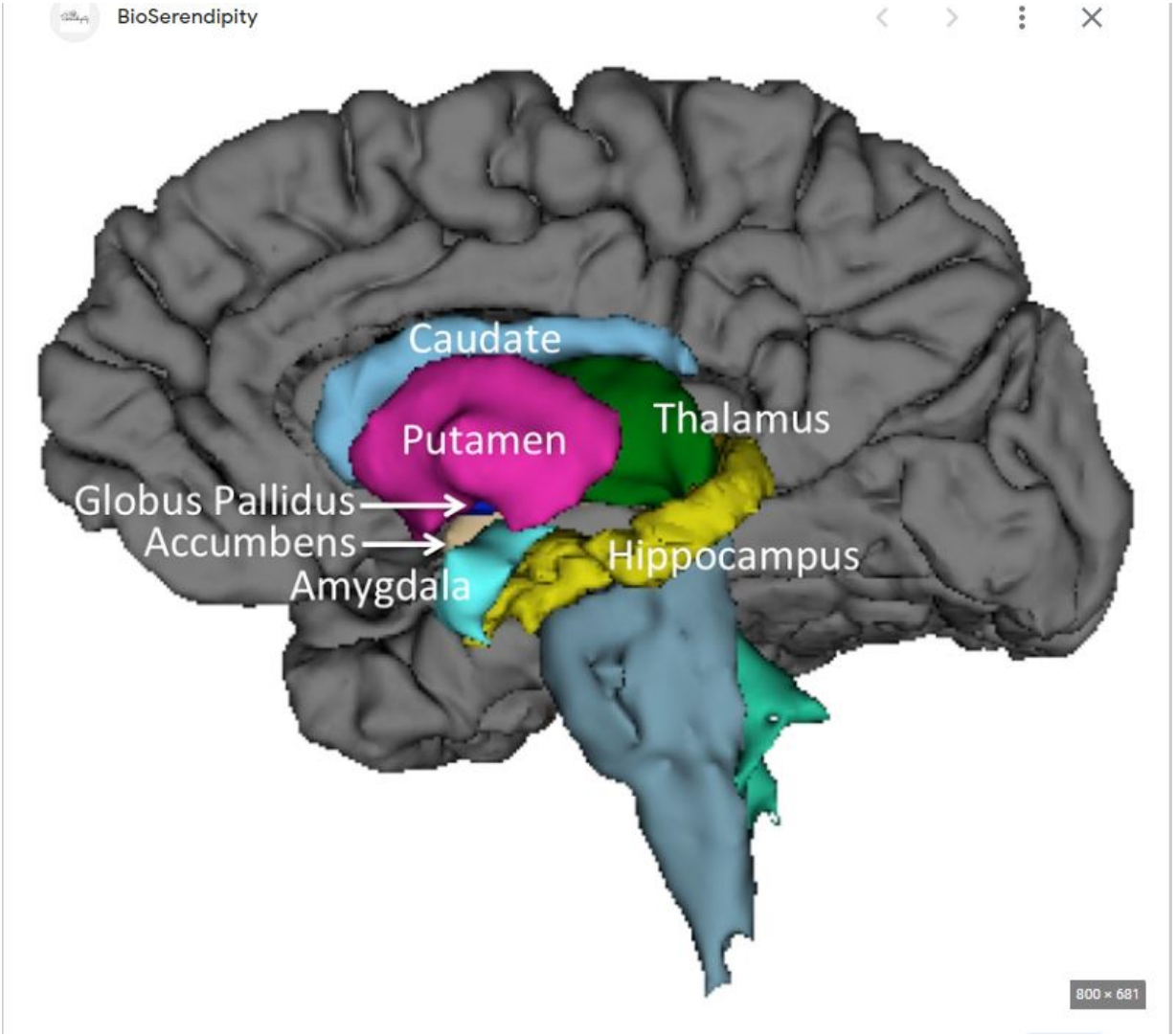


Larger volume
- Learning / memory ↑

Smaller volume
- Learning / memory ↓
- Neurotoxicity ↑
- Also possible: efficiency ↑

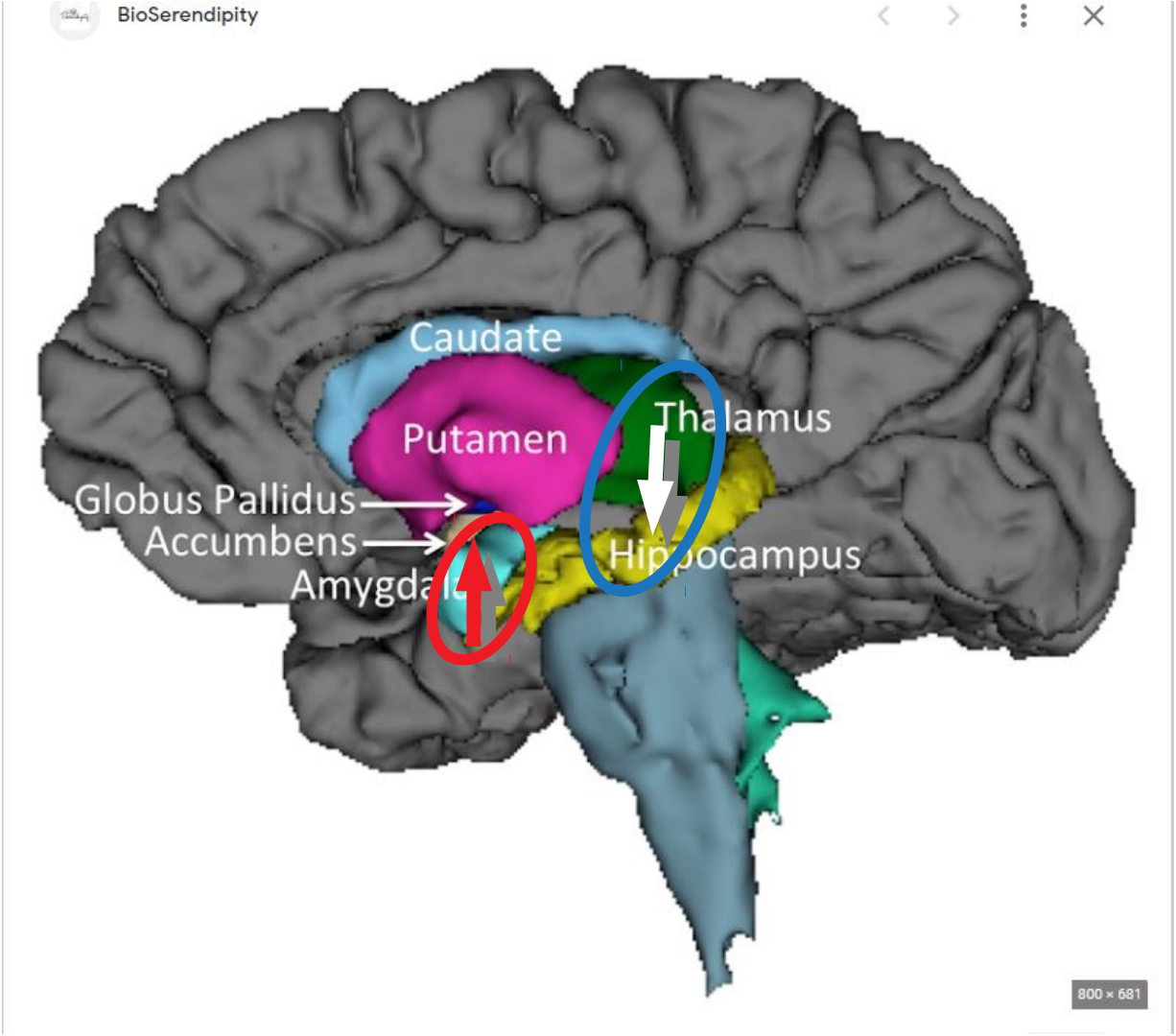
Zatorre et al., 2013, *Nature Neuroscience*

Subcortical limbic volumes



Altered volumes have been associated with psychogenic chronic stress exposure and mental disorders

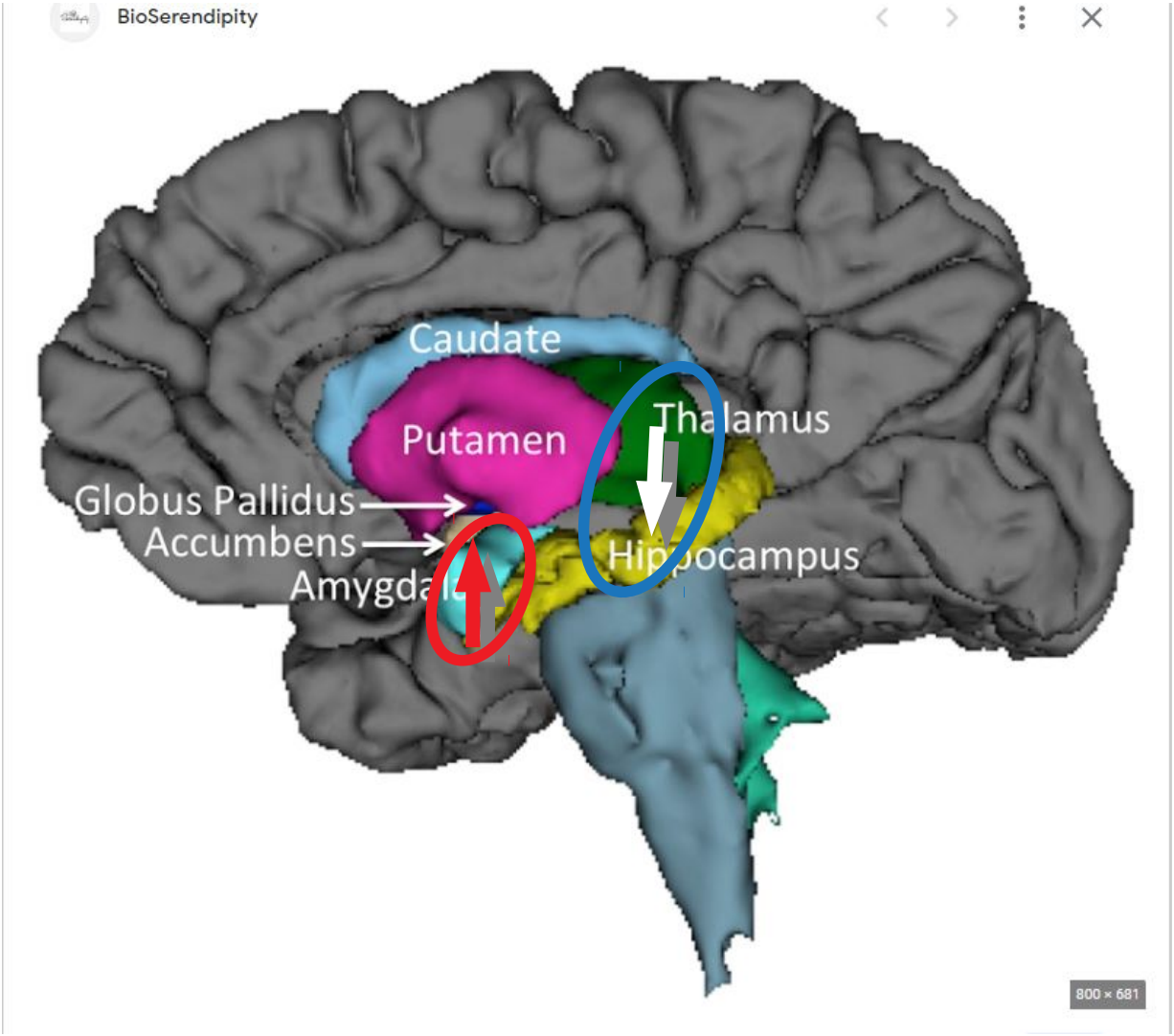
Subcortical volumes and stress exposure



Chronic stress exposure:

Amygdala ↑
Nucleus accumbens ↑
Hippocampus ↓
Thalamus ↓

Subcortical volumes and mental disorders

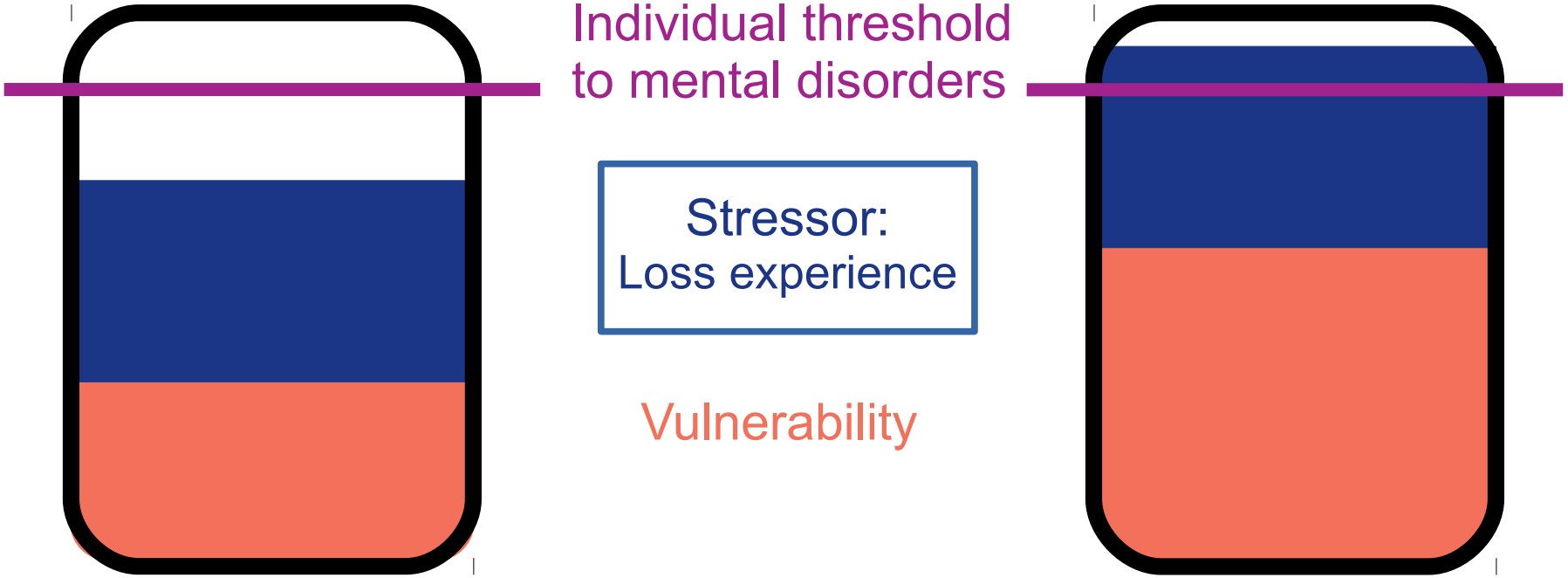


Anxiety and MDD:

Amygdala ↑
Nucleus accumbens ↑
Hippocampus ↓
Thalamus ↓

Loss of a loved one and subcortical limbic volumes in healthy and clinical populations

Vulnerability-stress model: Loss as a stressor



The number of affective loss experiences

Study 1: Healthy subjects, N= 32 (53% w), mean age [y]= 25±4, VBM of the whole brain
Study 2: Healthy subjects, N= 192 (50% w), mean age [y]= 24±3, VBM of the whole brain

Number of affective loss experiences in the previous 5 years:

No associations with subcortical limbic volumes in both studies

Dichotomous variable, a lower statistical threshold ($p<0.001$ uncorr., kmin=50 voxels):
Bilateral thalamic and right hippocampal local volumes: loss (5y) < no loss (5y)
only in the replication study.

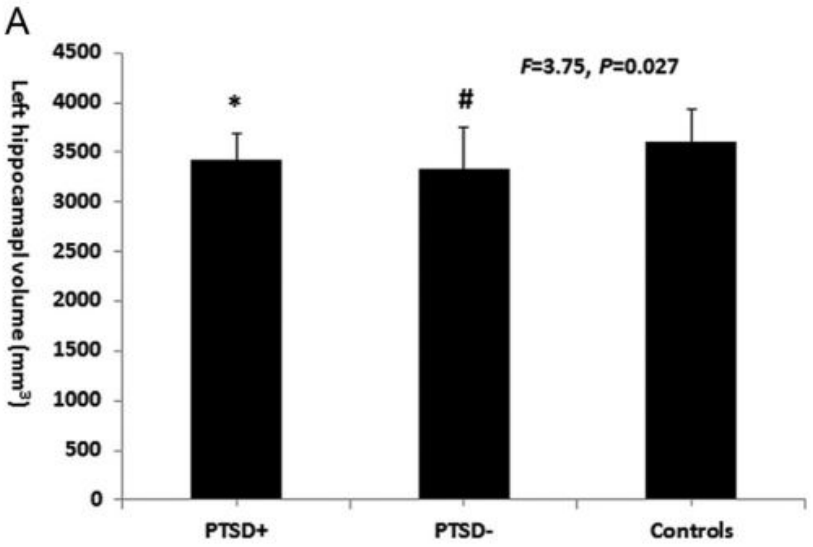
Benetti et al. (2010), *Human Brain Mapping*; Acosta et al. (2018), *Neuroscience*

Parents with and without PTSD after child loss

N=107 [PTSD+ = 57, PTSD- = 11, control group = 39], mean age [y] = 57±6/ 58±7/ 59±6, cumulative volumetric measure (Freesurfer) of hippocampus and amygdala

Loss of the only child:

Left hippocampal volumes: (PTSD+ / PTSD-) < control
No significant differences for right hippocampal volumes or amygdalar volumes
No significant correlations for either subcortical volume and time since loss



post hoc:
PTSD+ < control: p= 0.033
PTSD- < control: p= 0.021
PTSD+ vs PTSD-: p= 0.309

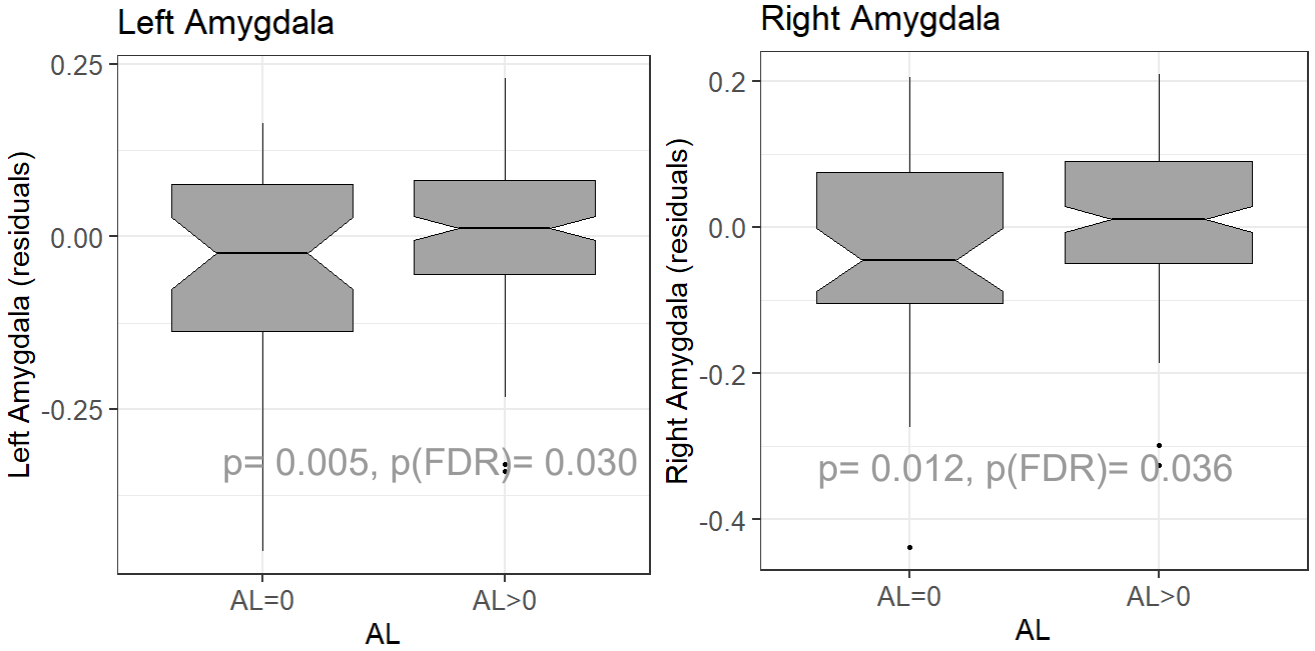
Luo et al. (2016), *Journal of Affective Disorders*

Healthy subjects and lifelong affective loss experiences

Healthy subjects, N= 196 (50% w), mean age [y]= 24± 3, [(AL=0) = 42 / loss (AL>0)= 154], cumulative volumetric measure (label-fusion-based segmentation) of hippocampus, amygdala, thalamus, basal ganglia (nucleus accumbens, putamen, caudate), whole brain VBM analysis

Lifelong affective loss experiences:

Bilateral amygdalar volumes: loss > no loss

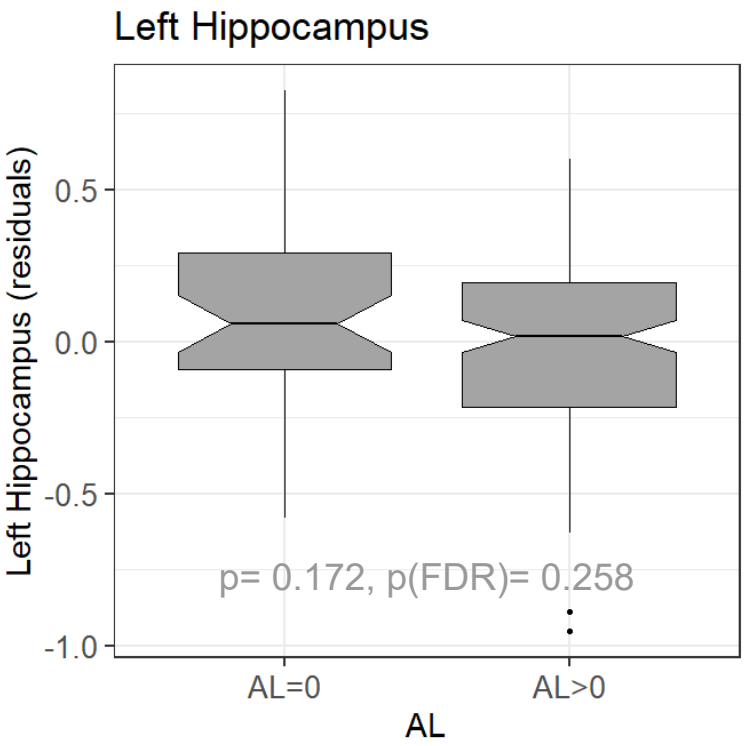


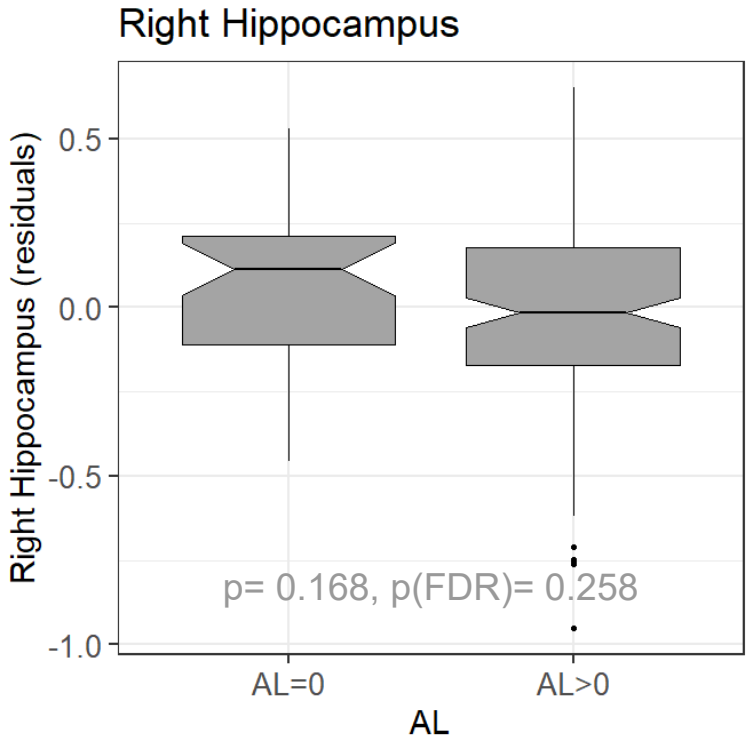
Independent of time of occurrence (childhood/ adolescence, adulthood) and type of loss

Acosta et al. (2021), *J Neurosci Res*

Healthy subjects and lifelong affective loss experiences

No significant differences in hippocampal volumes in the main analyses.





After controlling for the total number of losses:

Right hippocampal volume: **loss < no loss** (p= 0.030),

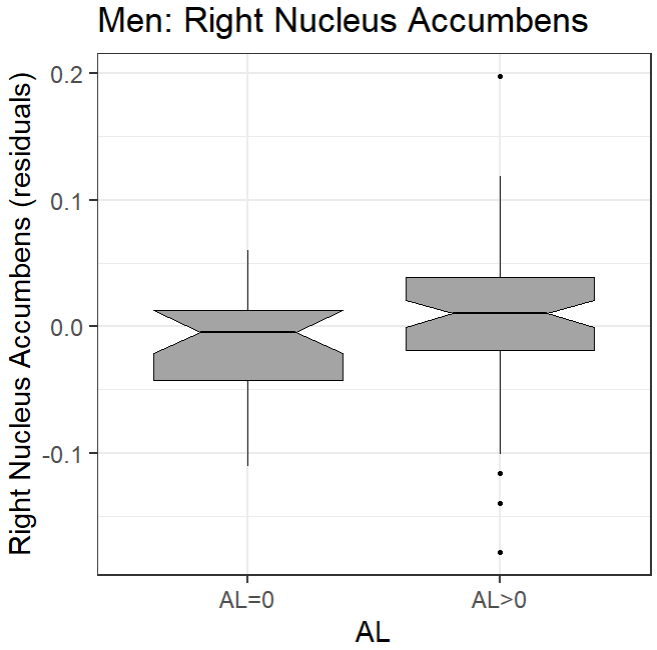
Left hippocampal volume: loss of a close friend/relative < no loss (p=0.033)

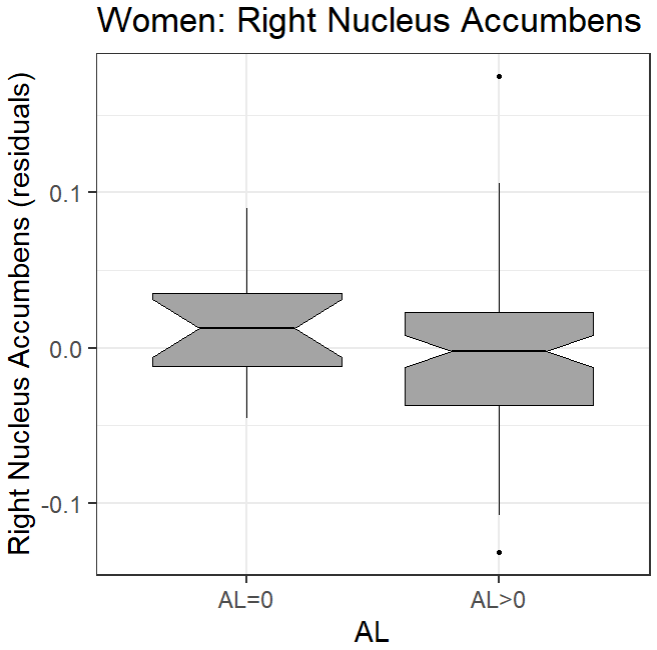
loss of a first-degree relative/spouse < no loss (p=0.053)

Healthy subjects and lifelong affective loss experiences

- **Right thalamic local volumes (temporal, visual, parietal):**
  loss < no loss (p<0.001 uncorr., VBM analysis)
  No significant differences for thalamic volumes in the segmentation analyses

- **Basal ganglia:** significant sex-differences for the right nucleus accumbens
  In men, but not in women:
  Right nucleus accumbens volume: loss > no loss (p<0.05)





AL x sex: p= 0.035

Summary

No significant effects on subcortical volumes for the number of affective loss experiences in the previous 5 years.

Significant associations of lifelong affective loss experiences with subcortical limbic volumes:

- Larger amygdalar volumes
- Smaller right hippocampal volumes
- Smaller left hippocampal volumes for the loss of the only child and the loss of a close friend / relative
- Smaller thalamic local volumes
- Larger nucleus accumbens volumes in men

Summary

No significant effects on subcortical volumes for the number of affective loss experiences in the previous 5 years

Significant associations of lifelong affective loss experiences with subcortical limbic volumes:

- Larger amygdalar volumes

also observed in MDD and anxiety disorders

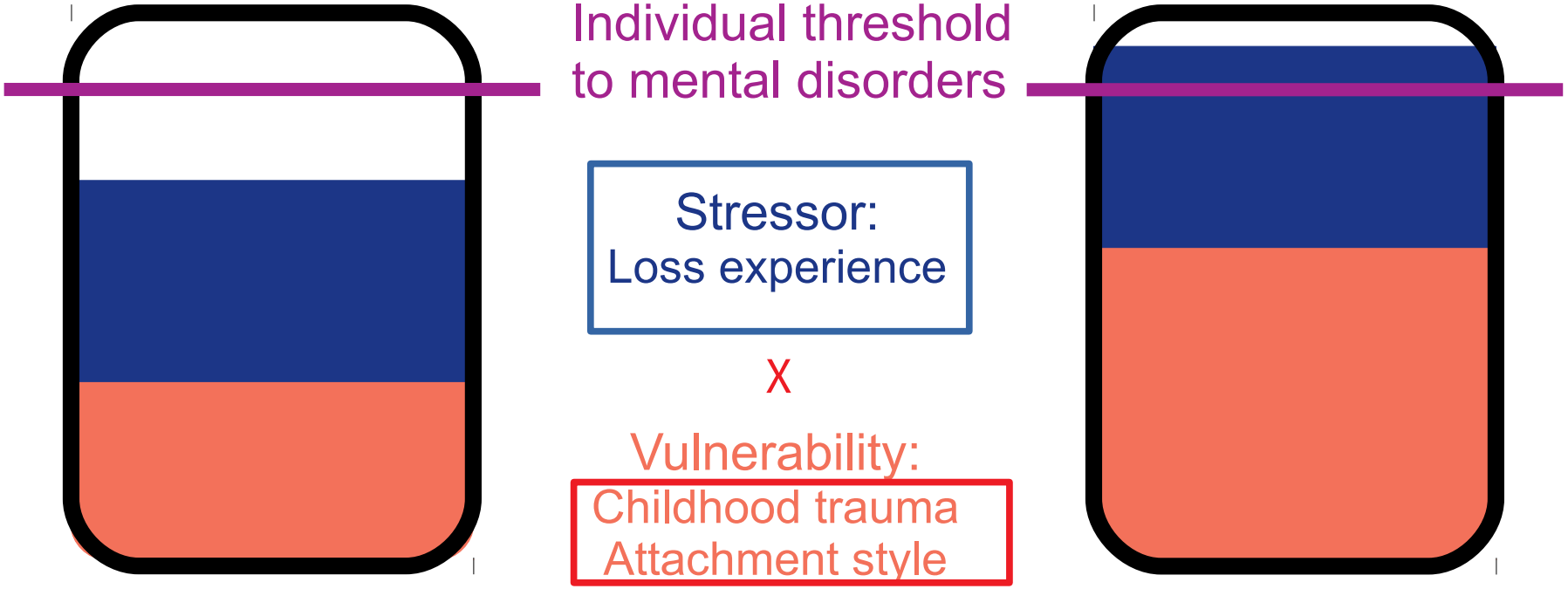
- Smaller right hippocampal volumes
- Smaller left hippocampal volumes for the loss of the only child and the loss of a close friend / relative

also observed in MDD, anxiety disorders, bipolar disorder and schizophrenia spectrum disorders

- Smaller thalamic local volumes
- Larger nucleus accumbens volumes in men

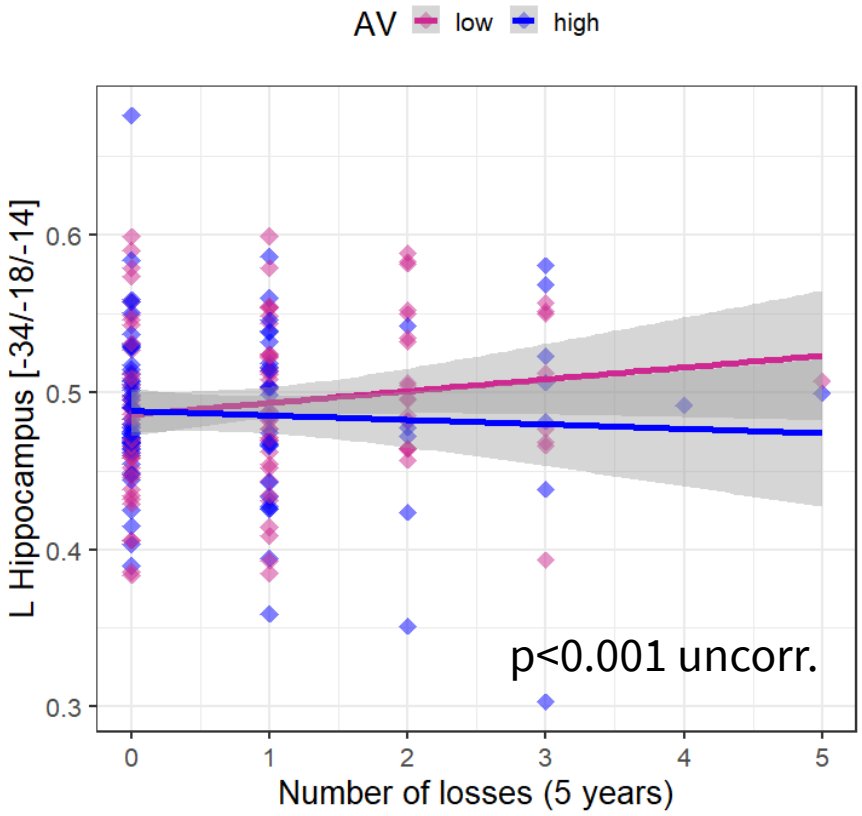
Loss of a loved one and subcortical limbic volumes – moderation by adult attachment style and childhood trauma

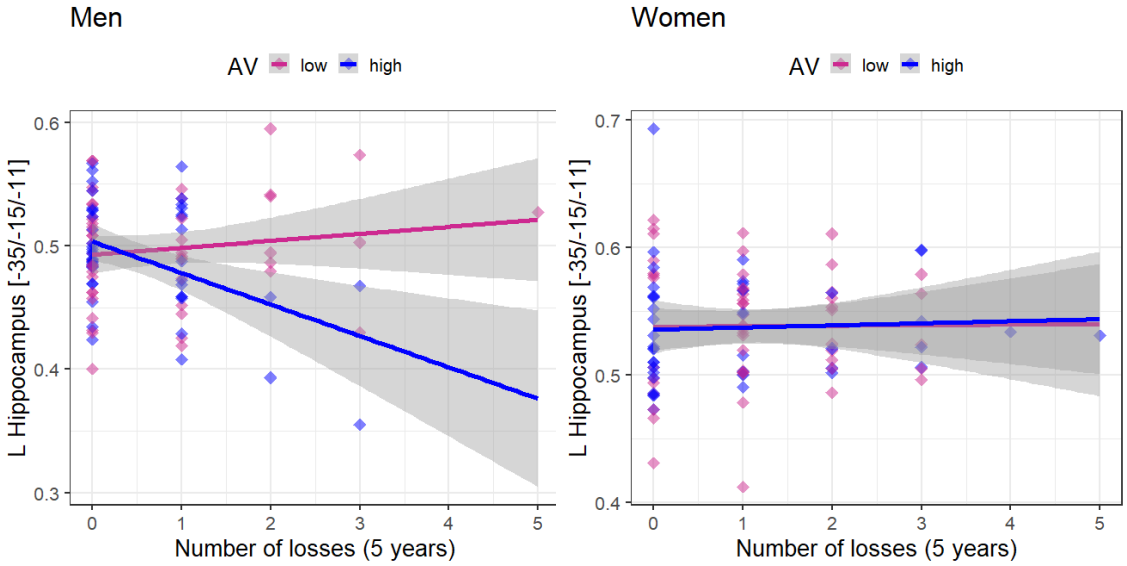
Vulnerability-stress model: Stressor x vulnerability



Number of affective loss experiences and adult attachment style (AAS)

Number of loss experiences (previous 5 years) X avoidance (AAS):





p<0.001 uncorr.

Benetti et al. (2010), *Human Brain Mapping*; Acosta et al. (2018), *Neuroscience*

Number of affective loss experiences and adult attachment style (AAS)

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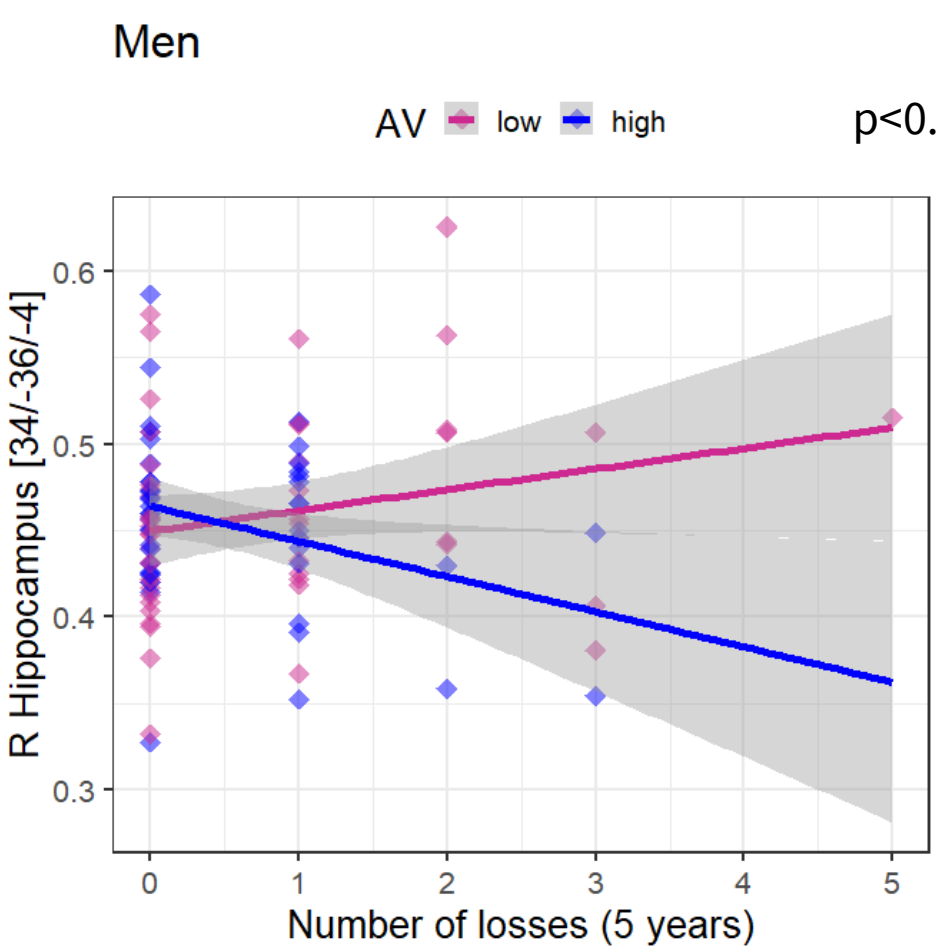
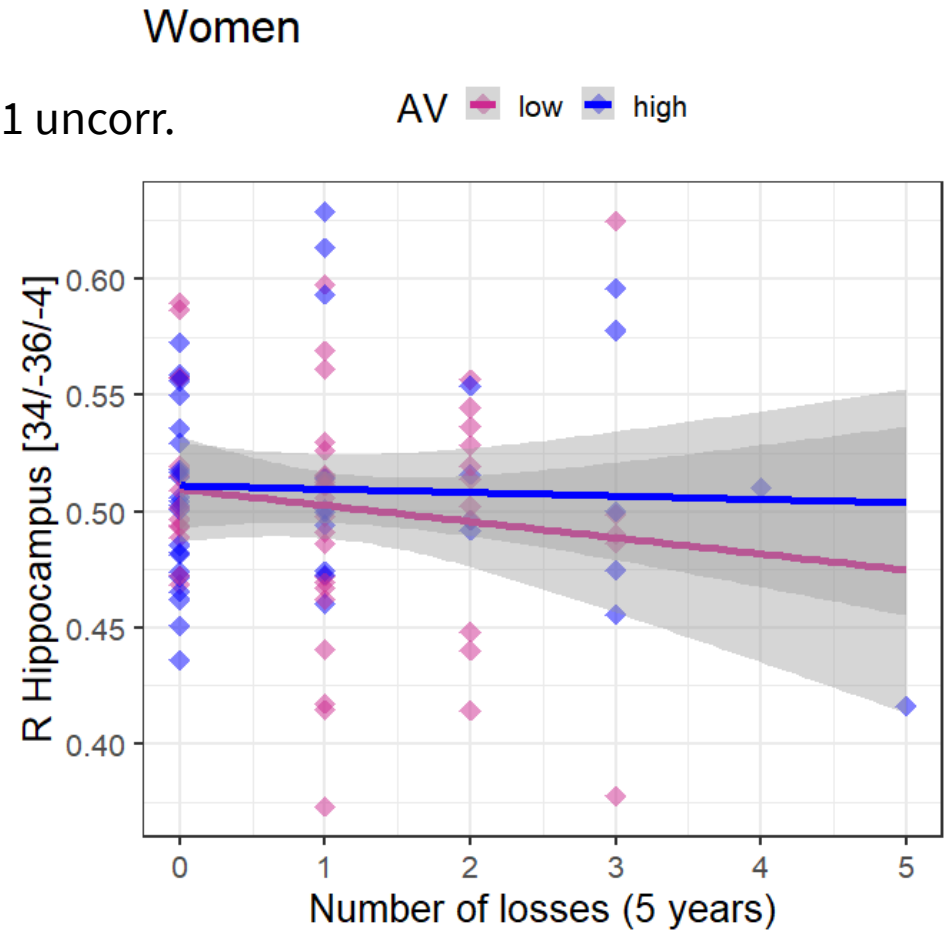


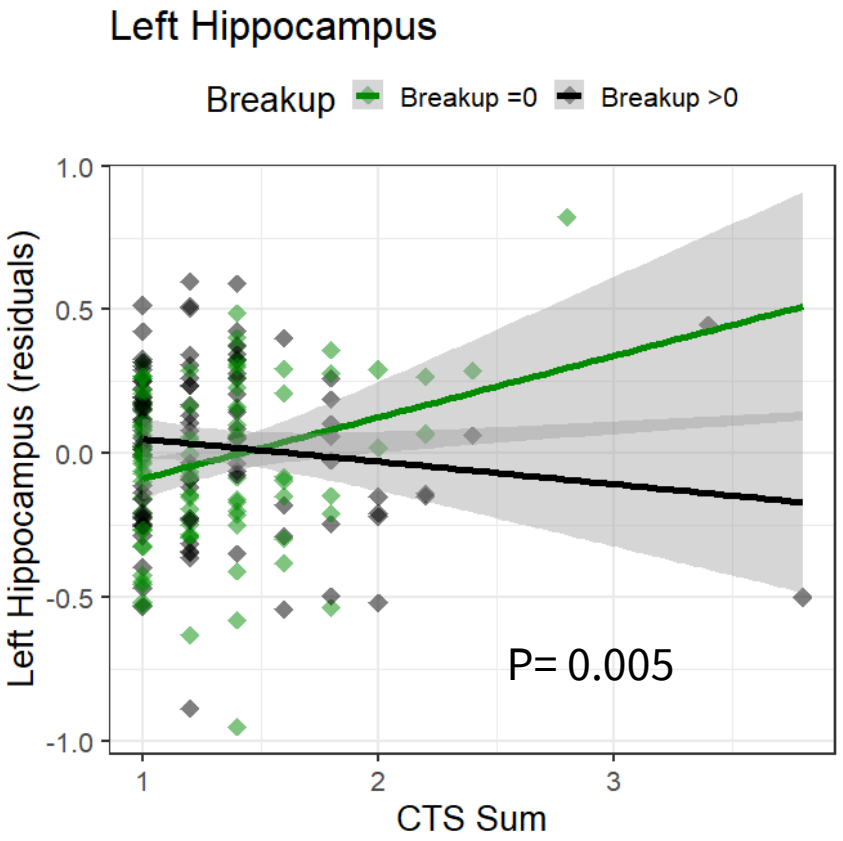
p<0.001 uncorr.

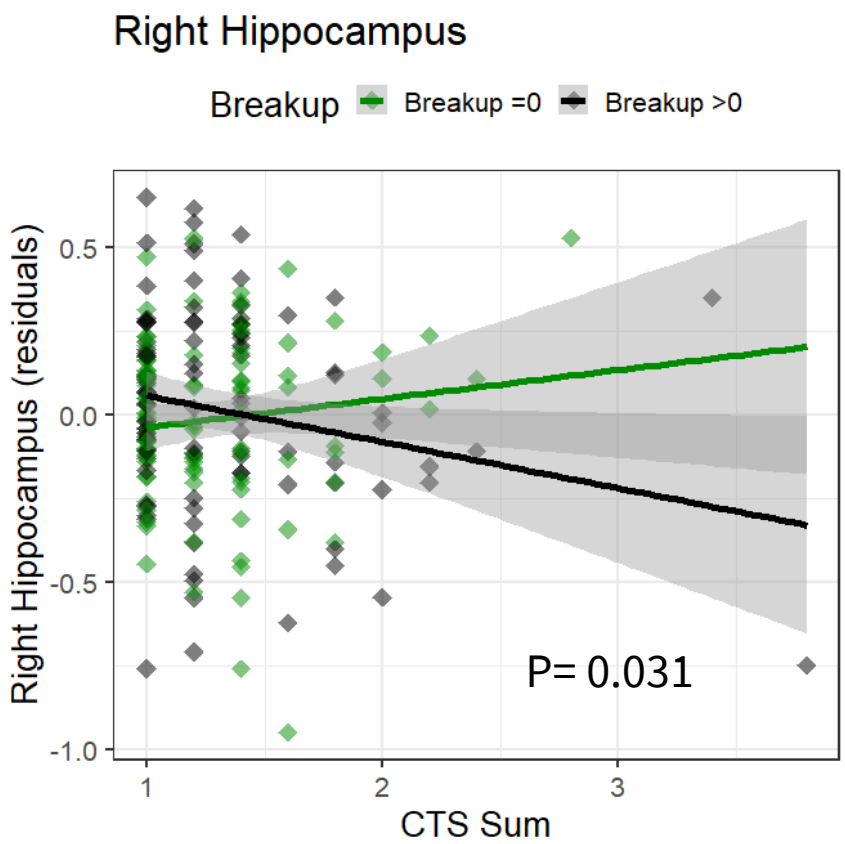


Loss and childhood trauma

Healthy subjects, N= 196 (50%w), mean age [y] = 24±3, Childhood Trauma Screener (CTS), cumulative volumetric measure (label-fusion-based segmentation)

Relationship breakup x childhood trauma: bilateral hippocampi





Acosta et al., 2022, *Zeitschrift für Psychosomatische Medizin und Psychotherapie*

Summary

A higher number of affective loss experiences in the previous 5 years was associated with smaller hippocampal volumes in men high in avoidance compared to men low in avoidance or to women.

In association with breakup compared to no breakup bilateral hippocampal volumes were smaller in persons with higher childhood trauma.

Conclusion

In association with retrospectively recalled affective loss experiences subcortical limbic volume alterations have been observed that resemble those observed after chronic stress exposure and in mental disorders.

The subcortical volume alterations might constitute a higher vulnerability to develop a mental disorder.

The data support the notion that an avoidant attachment style in men and childhood trauma act as vulnerability factors in the face of affective loss experiences.

Thank you for your attention