Atlas
Annual Thinking LAb on Fibromyalgia Syndrome

RUOLO DEL TRAUMA

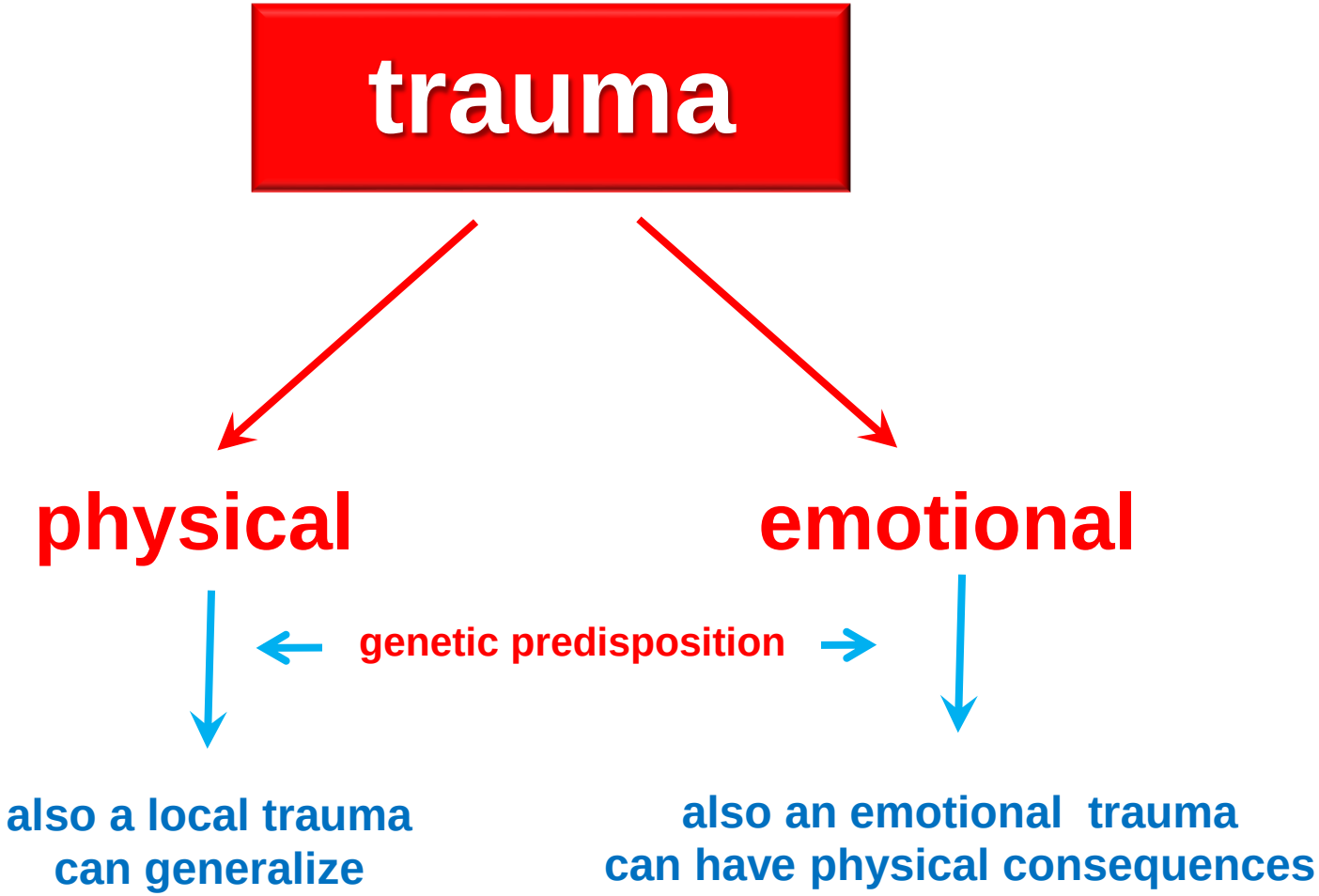
Prof. Riccardo Torta
Dipartimento di Neuroscienze – Università di Torino

Nhow Milano, 30 settembre - 1 ottobre 2022

What is a trauma?

Trauma is the response to a deeply distressing or disturbing event
that overwhelms an individual's ability to cope,

causes feelings of helplessness,
diminishes their sense of self
and their ability to feel a full range of emotions and experiences.


trauma
physical
emotional
genetic predisposition
also a local trauma
can generalize
also an emotional trauma
can have physical consequences

global prevalence of FMS among relatives of patients with FMS:
26% (male 14%; female 41%)

in a relative of a proband:
odds of FMS vs odds of RA = **8.5**

genetic predisposition to traumatic events consequences

gene-environmental interactions and epigenetic alterations

increased **incidence** of FMS
among **family members** of patients

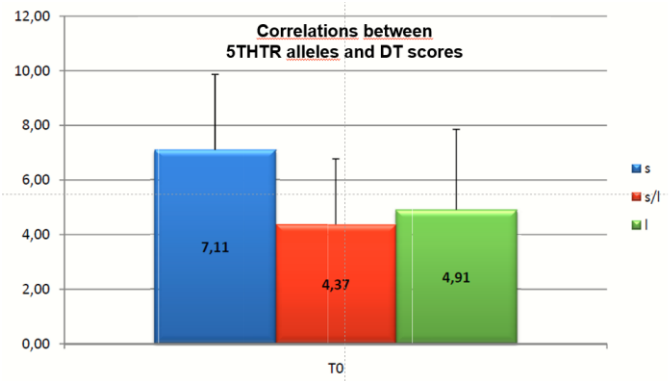
potential candidate genes found associated to FM are SLC64A4, TRPV2, MYT1L, and NRXN3

frequency of **s/s genotype** of 5HTTR:
31% FMS pts vs **16%** healthy controls

modification in **DR4 receptor gene** in FMS pts and low novelty seeking personality trait

association between FMS and
COMT Val 158 Met haplotype

search of the genetic underpinnings

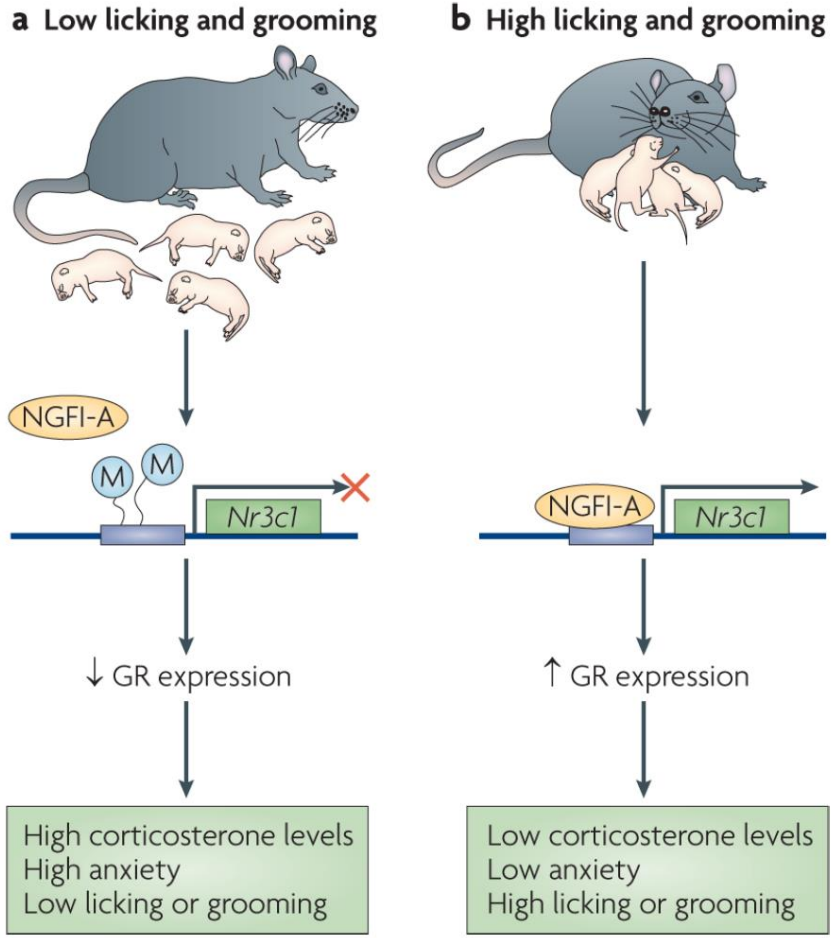


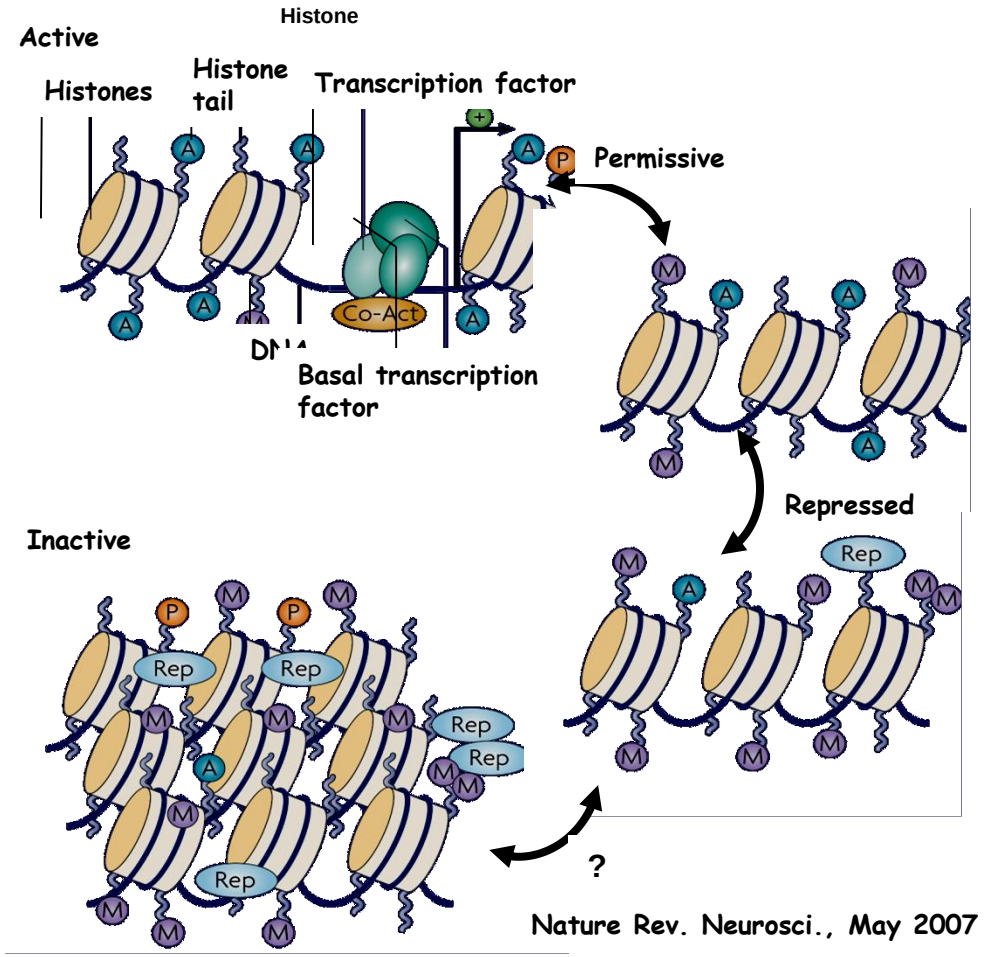
**the genetic factors identified to date do not fully explain the etiology of FM
but they influence the susceptibility for FM patients to traumatic events and symptoms relevance**

Buskila et al., 1996; Buskila et al., J 1997; Offenbacher et al., 1999; Arnold et al. 2004;
Zubieta et al. 2007; Torta et al., 2010; Ablin and Buskila, 2017; D'Agnelli et al., 2019

Epigenetic mechanisms of resilience

Epigenetics refers to stable changes in chromatin structure that underlie long-lasting alterations in gene expression and that are not associated with changes in DNA sequence





Abuse Leaves Its Mark on the Brain

Science,
February 2009

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The Epigenetics of Child Abuse

Nature Rev.,
April 2009

genetic susceptibility
(sensitivity to triggers)

triggering event

Physical trauma

traumatic/surgical event: 19-21%
train crash: 15%
whiplash: 10 – 20 %
post vehicle accident: 8%

«reactive FM»
(Greenfield et al., 1992)

Psychological trauma

catastrophicl event:
sexual / physical abuse
emotional neglect

trauma as trigger in rheumatologic disorder: Smythe, 1979

central sensitization neuroinflammation hypotesis

fibromyalgia

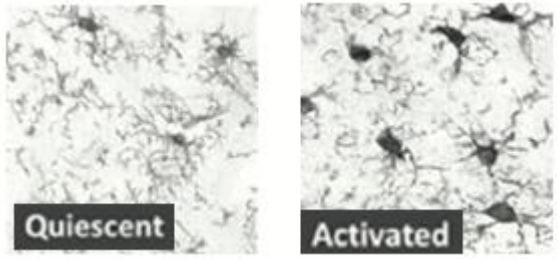
(Romeo et al., 2022; Yavne et al., 2018; Buskila,1997)

Physical trauma and pain generalization (1):

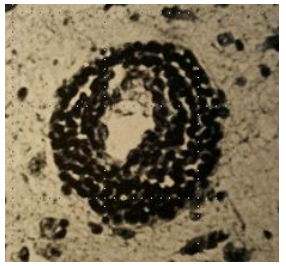
how may local injury metastasize into generalized hyperalgesia?

Spinal cord injury (SCI)

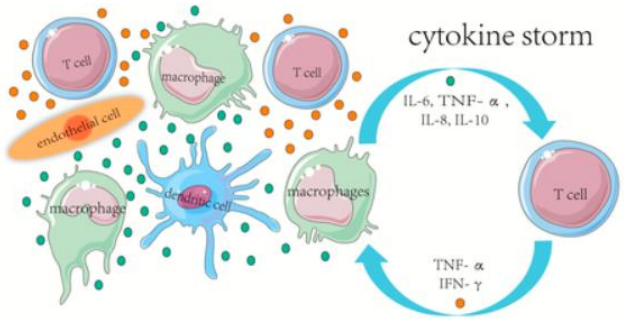
activation and proliferation of resident **microglia and astrocytes**



infiltration of circulating innate immune cells (neutrophils, monocytes and lymphocytes)



enhanced intraspinal synthesis and release of **cytokines,** chemokines and other vasoactive substances (e.g., histamine, complement proteins)



inflammation can persist **indefinitely** because self-repair is impaired,
immunity against CNS antigens develops
also for modification of cross-talk interaction between **CNS and Immune system**

(hypomethylated DNA pattern, in genes implicated in stress response, DNA repair, autonomic system response, and neuronal abnormalities)

D'Agnelli et al., 2019;Schwab et al., 2015

Psychological trauma and fibromyalgia:

Boisset-Pioro et al. Sexual and physical abuse in women with fibromyalgia syndrome. Arthritis Rheumatol 1995

authors	results	significance	trauma
Boisset-Pioro et al. (1995)	18 % FM pts vs. 4% ctr	P< 0.001	**physical abuse**
Walker et al. (1997)	33 % FM pts vs. 20% ctr	P < 0.01	**phys/sex assault**
Ciccone et al. (2005)	29 % FM pts vs. 11.3 ctr	P < 0.04	**rape**
Näring et al. (2007)	82 % FM pts vs. 61% ctr	P < 0.05	**trauma events**
Ablin et al. (2010)	24 % FM pts vs 11 % ctr	P < 0.05	**holocaust surv.**
Waller et al. (2015)	61 % FM pts vs 23 % ctr	P < 0.05	**phys/sex abuse**

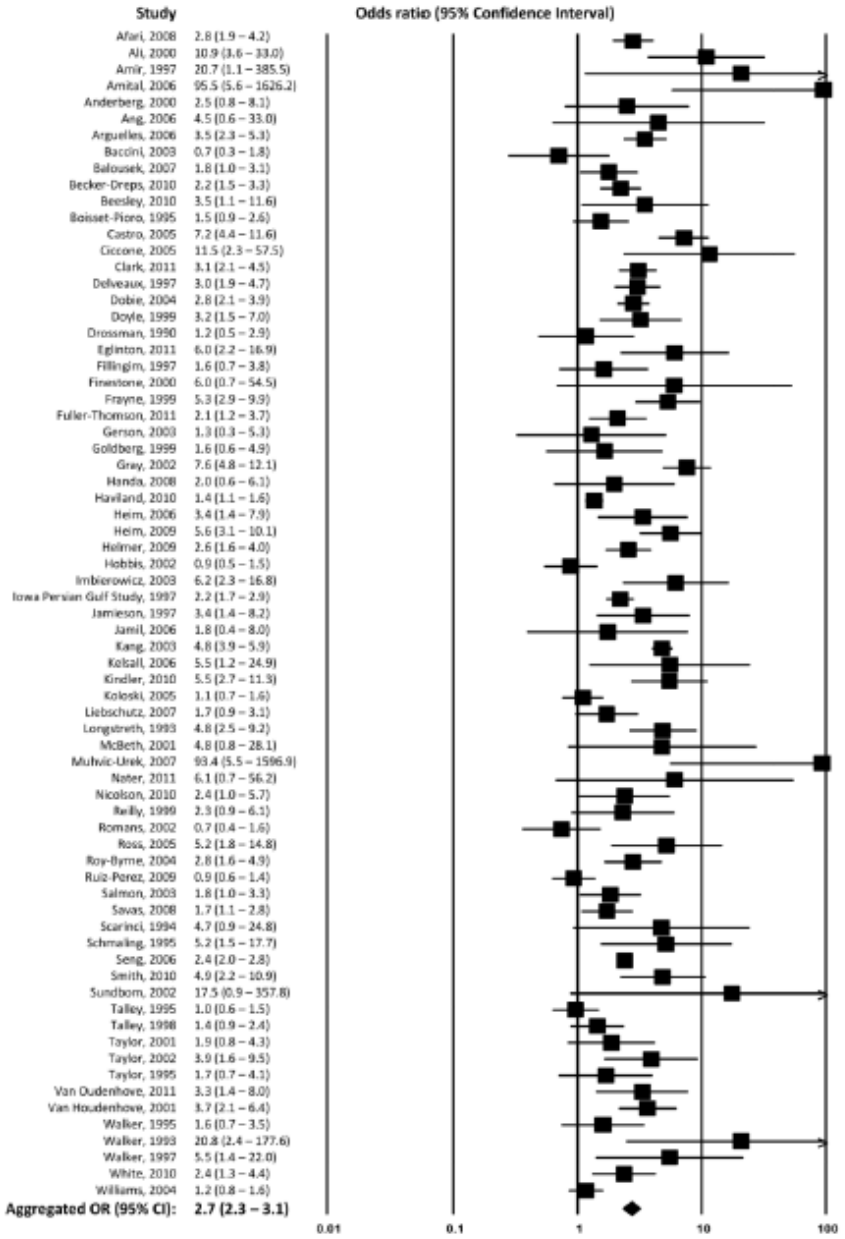
negative life events may affect brain modulatory circuits resulting in **central sensitization**

psychological distress, female gender augment the probability of chronic pain after trauma

the perception of trauma occasionally has greater influence than the trauma itself

depression and anxiety have a mediating negative effect

Yavne et al., 2018



Psychosom Med. 2014 January ; 76(1): 2–11

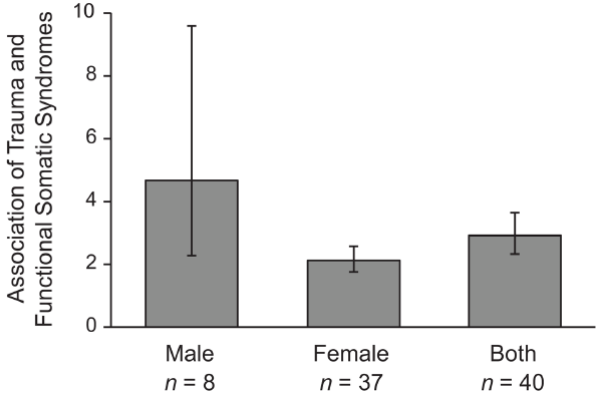
Psychological Trauma and Functional Somatic Syndromes: A Systematic Review and Meta-Analysis

Niloofar Afari, Ph.D.[1,2,3], Sandra M. Ahumada, B.A.[4], Lisa Johnson Wright, Ph.D.[5], Sheeva Mostoufi, M.S.[1,2], Golnaz Golnari, M.D.[3], Veronica Reis, Ph.D.[6], and Jessica Gundy Cuneo,

independent and aggregated association(s) of **reported trauma and FSSs for the 71 included studies**.

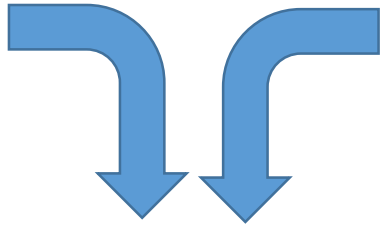
The aggregated random effects analysis revealed that individuals reporting exposure to trauma were

2.7 times more likely to have FSS
(OR (95% CI) = 2.7 (2.27 – 3.10)



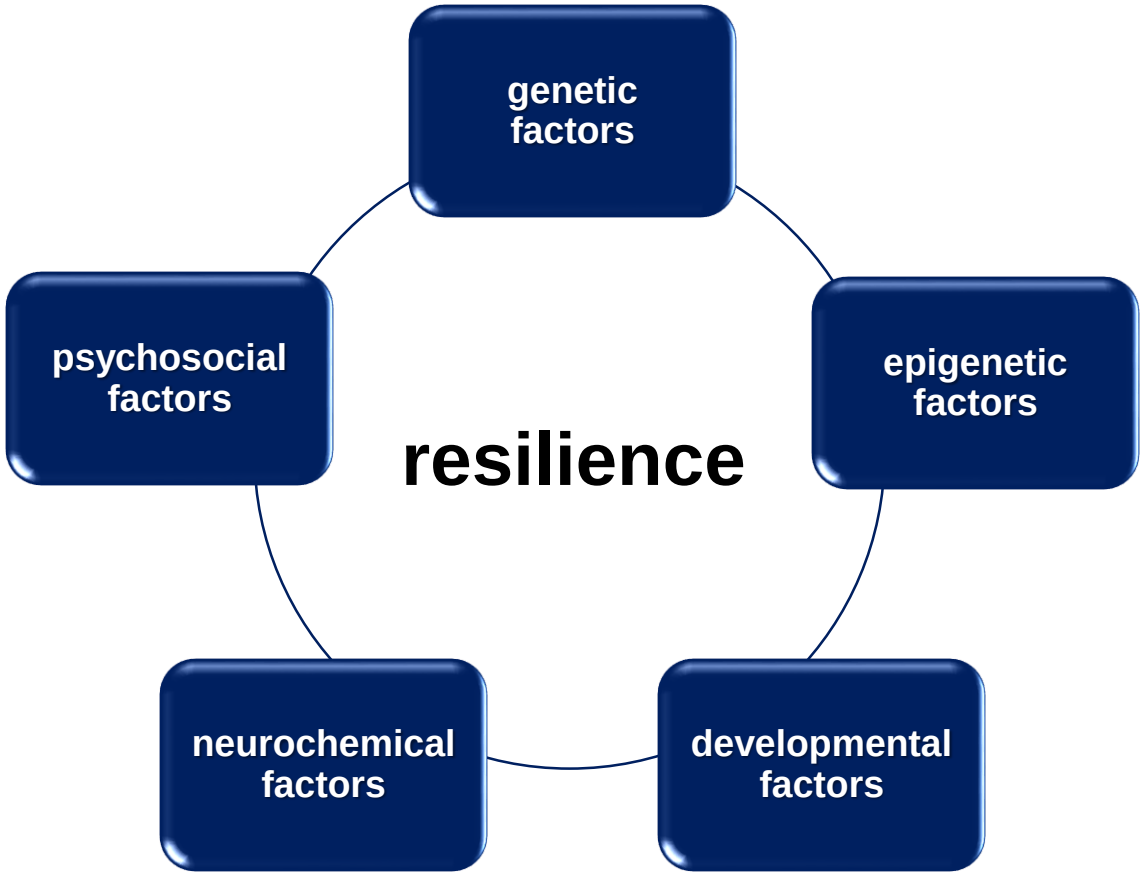
FSSs was more than twice for males than females

How to counteract trauma ?

resilience  **reappraisal**

 **trauma consequences**

adaptive capacity that helps to overcome difficulties



stress habituation

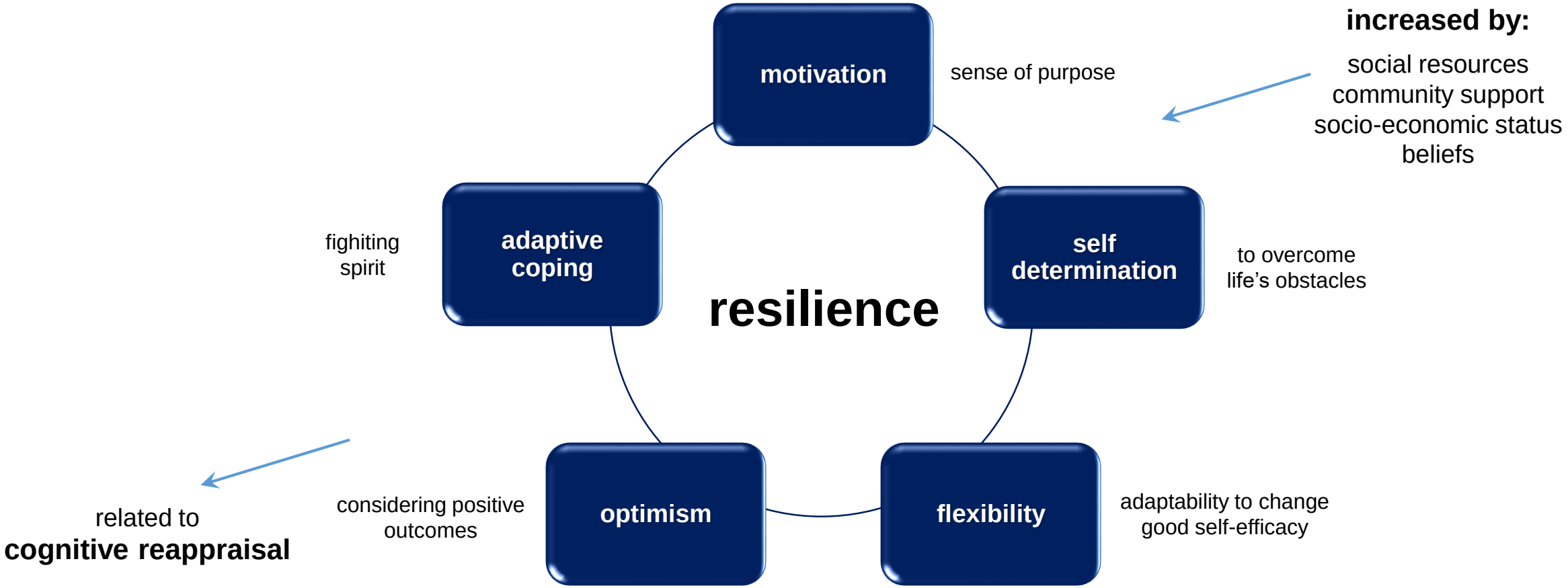
60-80% of people respond to a PTE with resilience

post-traumatic growth

new meanings to events
modifying priorities

negative correlation between resilience and FM severity

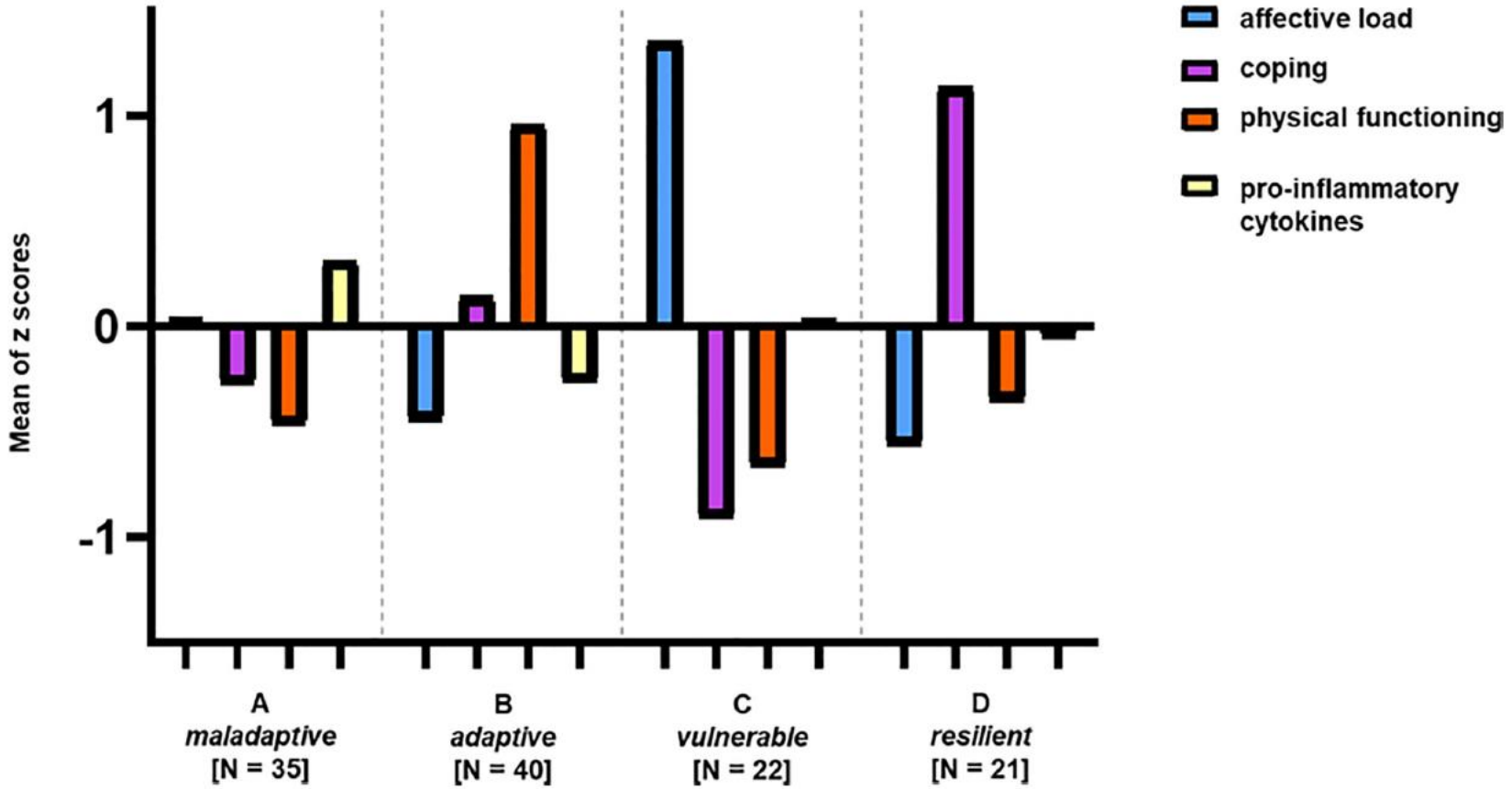
personal resources most salient for resilience



Clustering fibromyalgia patients: A combination of psychosocial and somatic factors leads to resilient coping in a subgroup of fibromyalgia patients

Alexandra Braun[1]*, Dimitar Evdokimov[1], Johanna Frank[1], Paul Pauli[2], Nurcan Üçeyler[1], Claudia Sommer[1]

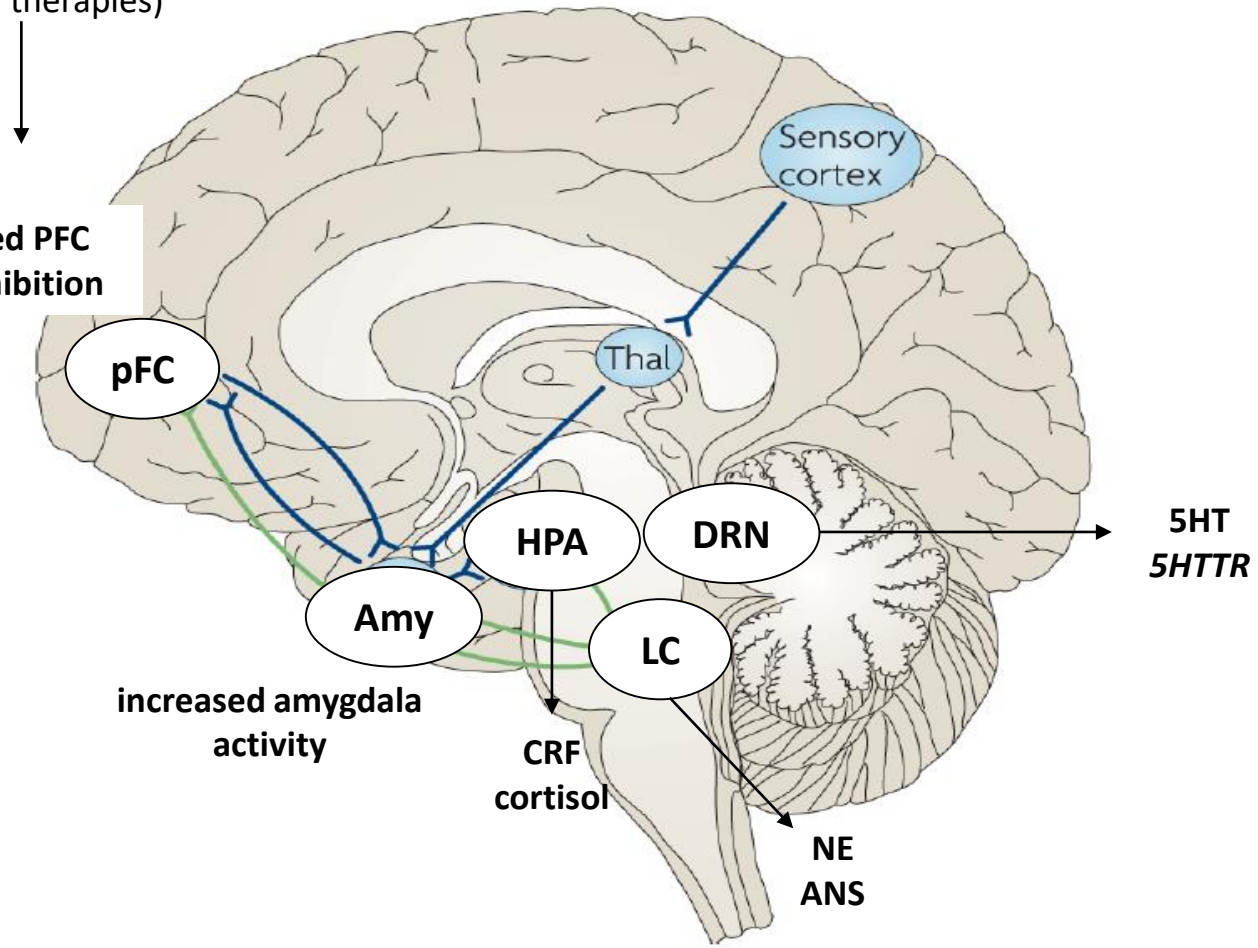
PLOS ONE 15 (12) 2020



Neurobiology of resilience

Cognitive reappraisal

more adaptive coping strategies
(eg. CBT therapies)



pFC increases inhibition of emotional **Amy** activity

HPA adaptation to stressfull events (CRF,cortisol)

LC activation of noradrenergic responce of ANS

DRN modulation of vulnerability (trough 5HTTr)

Hanssen et al., 2017

patients with PTSD showed **hypoconnectivity** within neural networks involved in emotional downregulation

maltreatment exposure induces greater **activation in left amygdala** and reduced activation in cognitive control regions (frontal gyrus, anterior cingulate cortex)

psychotherapies (eg CBT)
experiences
personal training
mind-body interventions

normalization of connectivity in regions associated with cognitive control and memory.

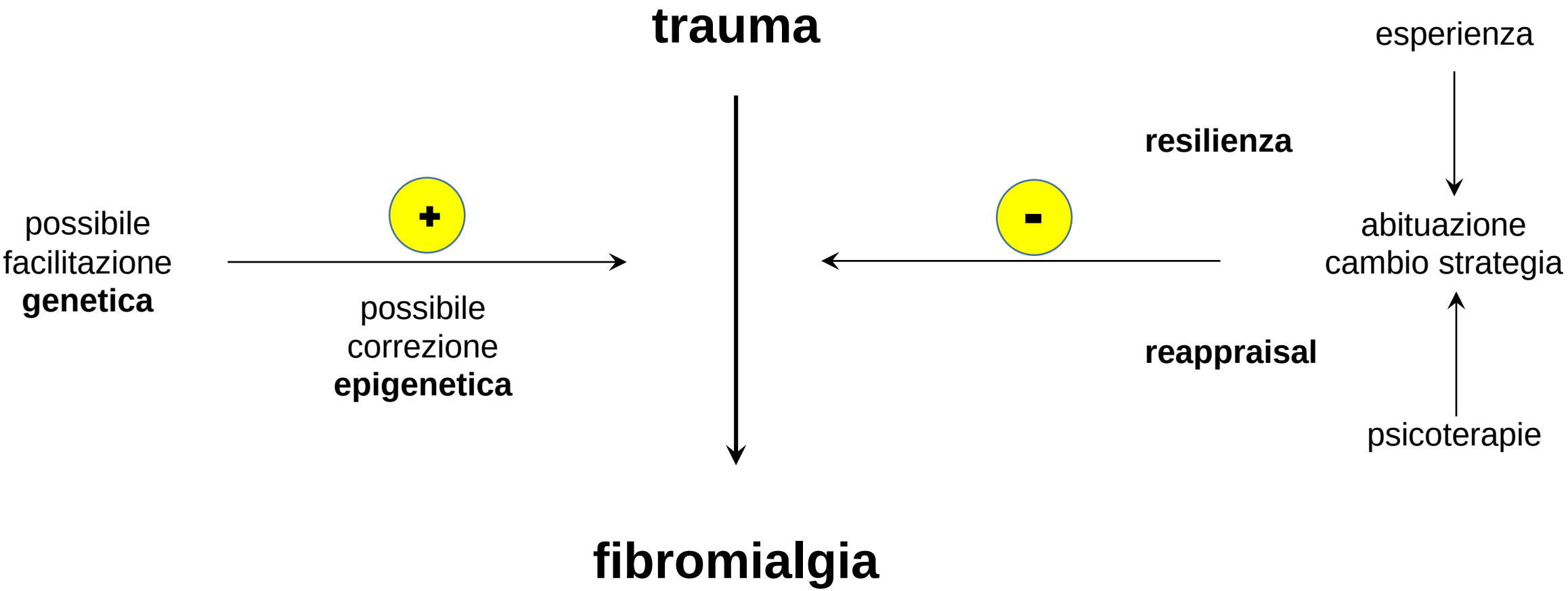
activation in cognitive areas such as the prefrontal cortex (PFC)

(re)appraisal

the ability to change one's cognitive and emotional points of view of life, modifying its emotional consequence

alters stress perception of the emotions

Schlumpf et al., 2019; Cisler et al., 2016;Littrel, 2009;


trauma
esperienza
resilienza
possibile
facilitazione
genetica
+
-
abituazione
cambio strategia
possibile
correzione
epigenetica
reappraisal
psicoterapie
fibromialgia