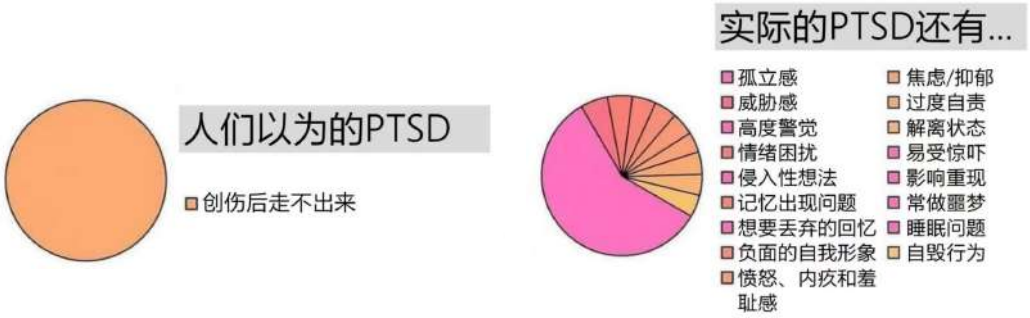
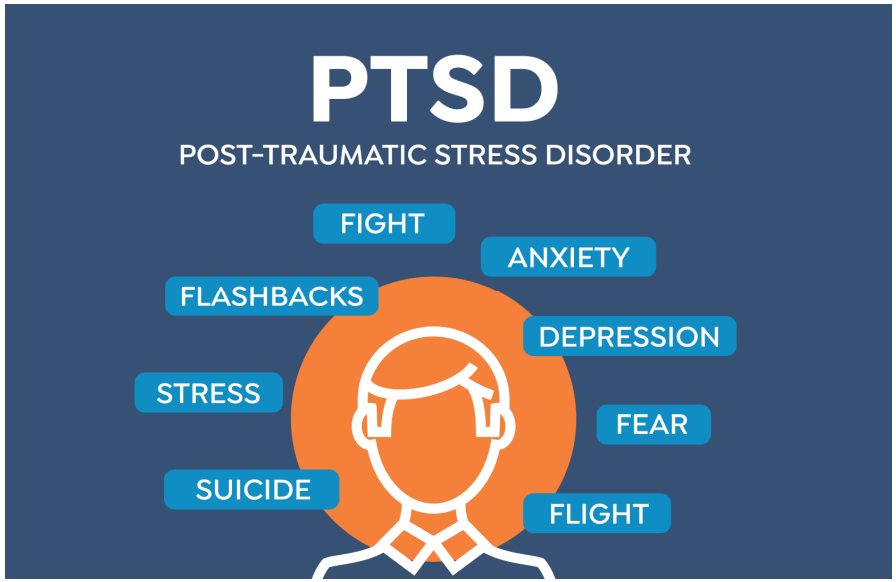
Decoding PTSD: From Discovery to Intervention

PTSD : Post-Traumatic Stress Disorder





What is the inner world of people with PTSD like ?

Decoding PTSD: From Discovery to Intervention

- Overview of PTSD: definition and causes, research models and paradigms——SJY
- Understanding PTSD: clinical manifestations and pathogenesis —— LT
- The Coping of PTSD: scientific intervention and research prospects—— LYG

Part 1:
Overview of PTSD: definition and causes, research models and paradigms

- Understanding PTSD: Definition and Causes
- Research Models and Experimental Paradigms of PTSD
- Behavioral Tests for Validating PTSD Models

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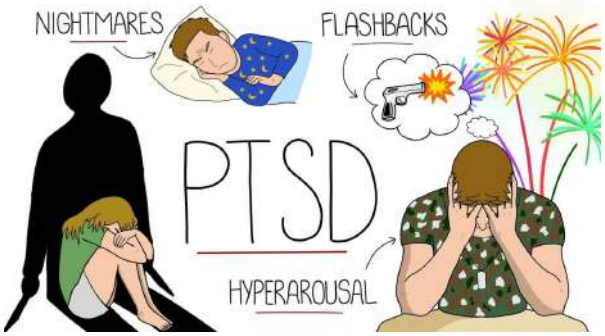
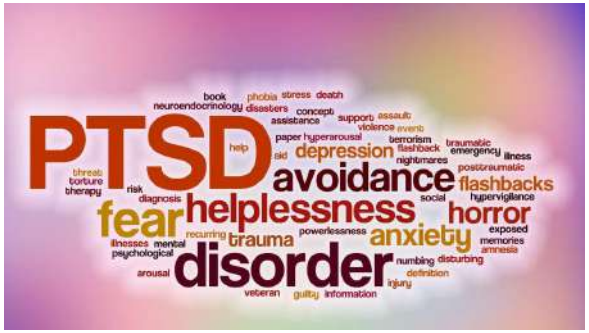
What is PTSD?

Post-Traumatic Stress Disorder (PTSD) is a mental disorder triggered by extreme psychological trauma events.

shell shock





Ressler, K.J., et al., *Nat Rev Neurol*,2022
Gersons B.P. and Carlier I.V., *Br J Psychiatry*,1992

How does PTSD occur?

(1) War and violent incidents: War / Terrorist attacks / Violent crimes

How does PTSD occur?

(2) Major accidents or disasters: Traffic accidents / Natural disasters / Industrial accidents

How does PTSD occur?

(3) Personal trauma experiences: Sexual assault / Domestic abuse / Serious medical accidents

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Research models of PTSD

(1) Rodent Models

C57BL/6

BALB/c

Rat

(2) Non-human Primate Models

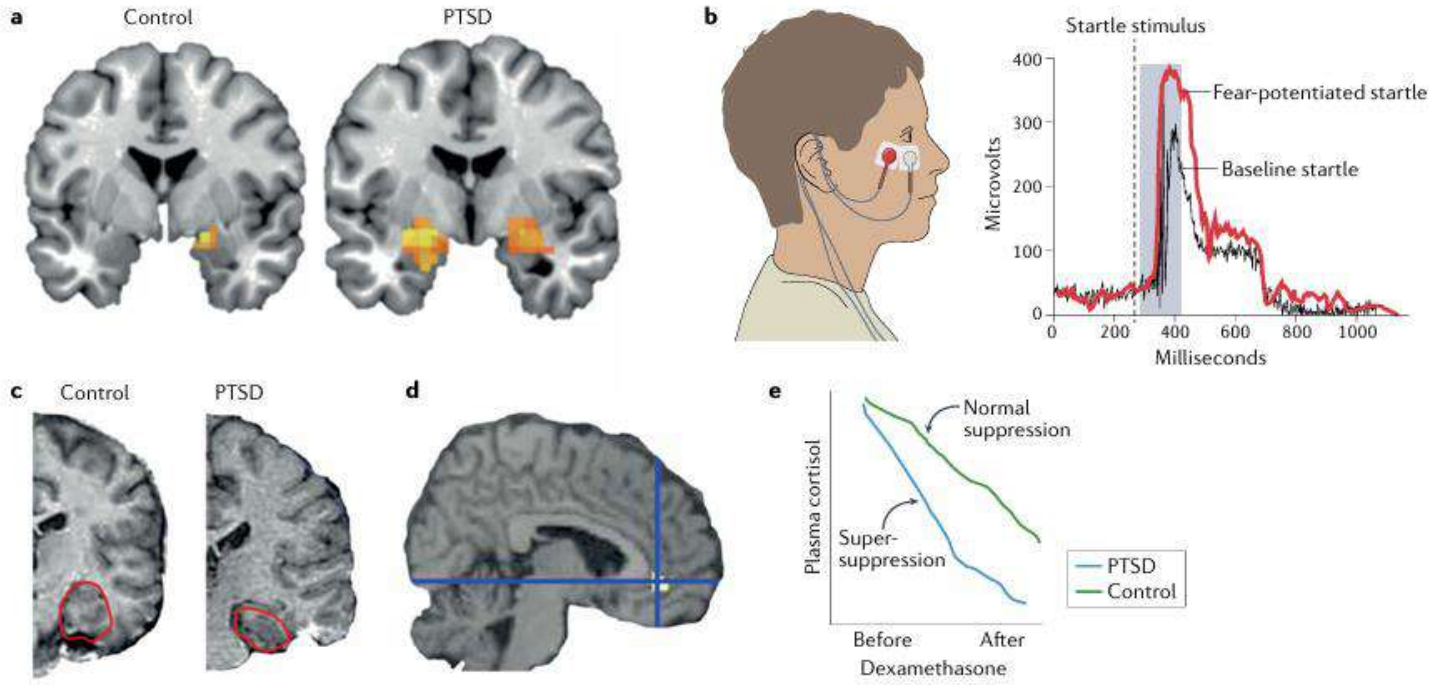
Rhesus macaque

Cynomolgus monkey

Yehuda R and LeDoux J., *Neuron*,2007
Kalin NH. and Shelton SE., *Ann N Y Acad Sci*,2003

Research models of PTSD

(3) Human Studies

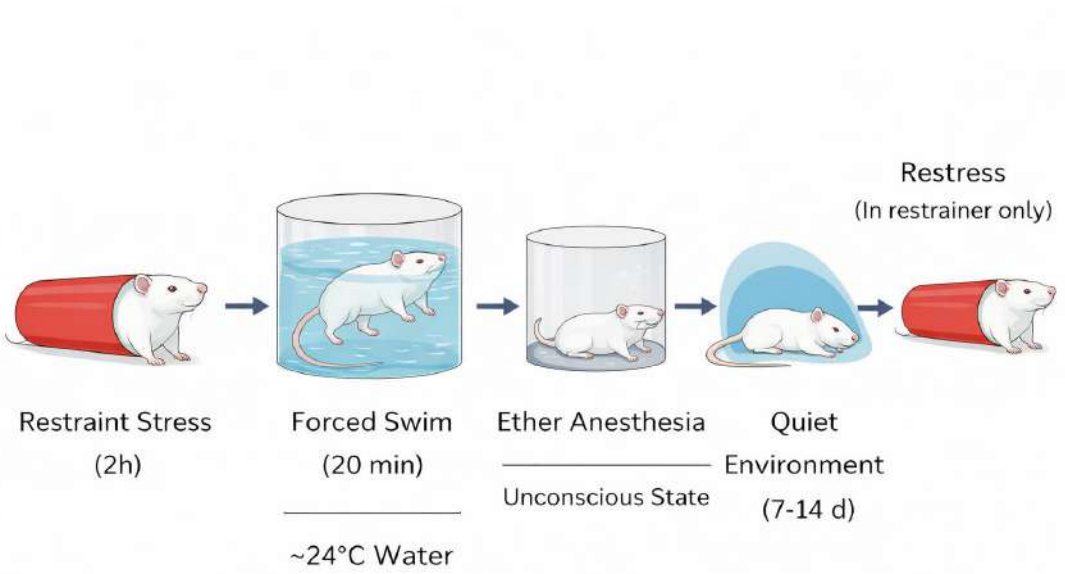


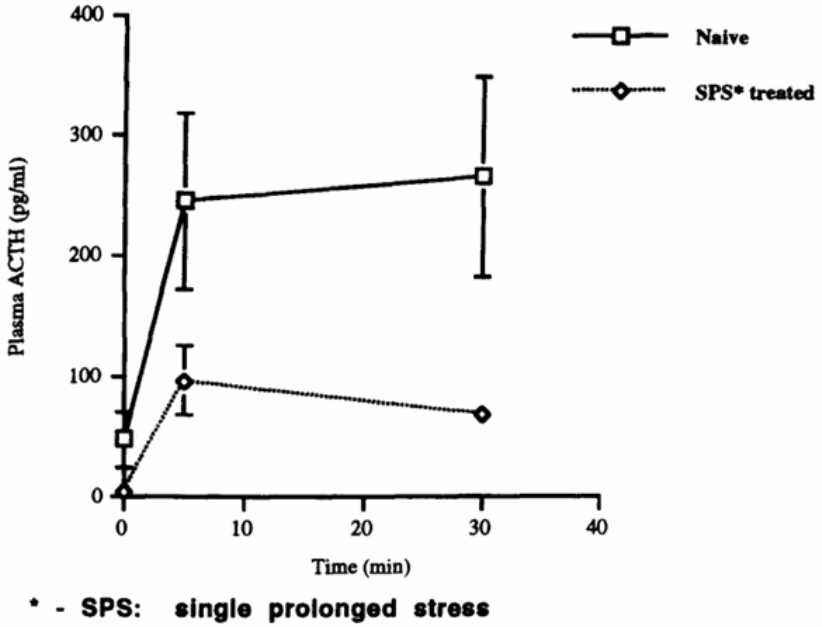
Fear-potentiated startle

Ressler, K.J., et al., *Nat Rev Neurol*,2022

Paradigms of PTSD: Physical stressors

Single Prolonged Stress (SPS)



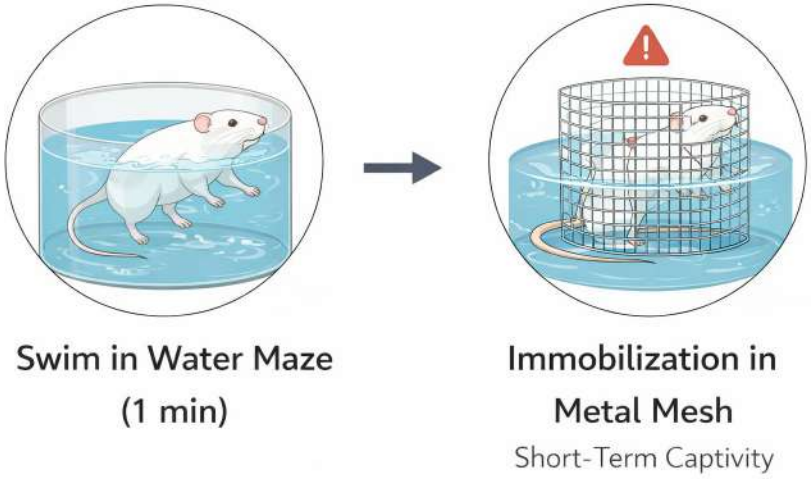


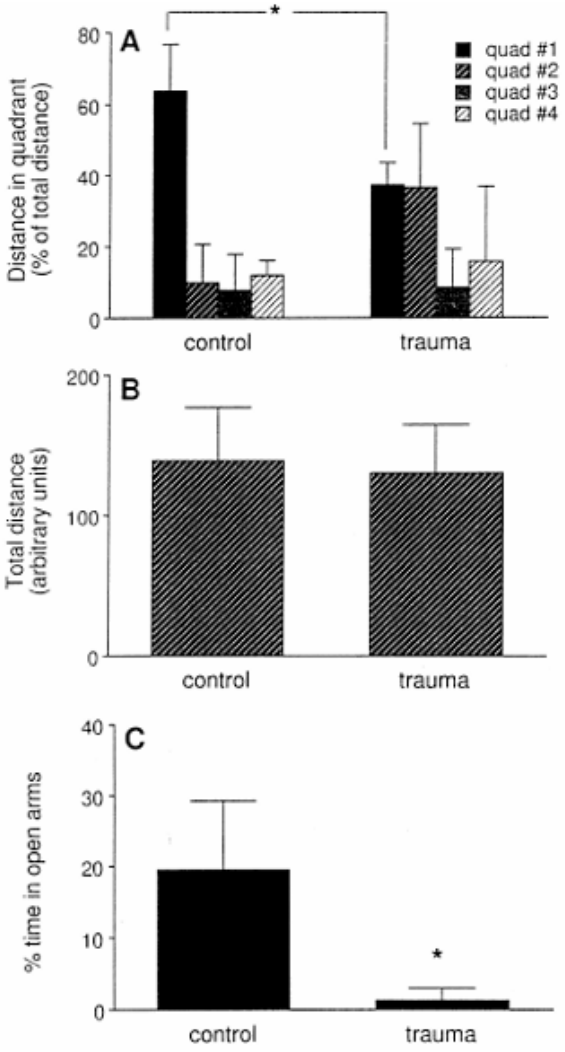
lower plasma ACTH

Liberzon I., et al., *Psychoneuroendocrinology*,1997

Paradigms of PTSD: Physical stressors

Under Water Trauma (UWT)



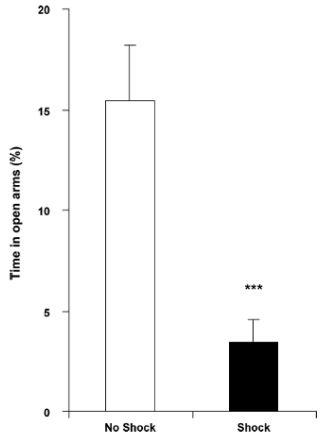


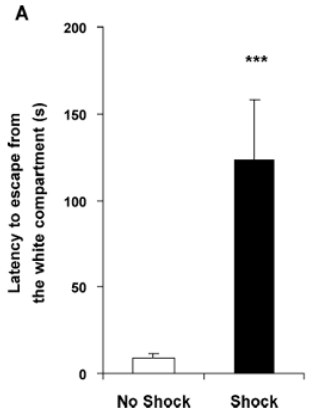
Loss of preference for the original platform quadrant indicates impaired spatial memory.

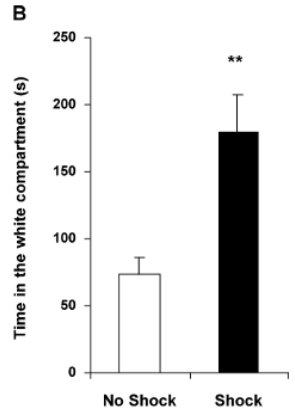
A period of anxiety that lasted for three weeks.

Richter-Levin G., *Psychiatry Res*,1998

Paradigms of PTSD: Physical stressors

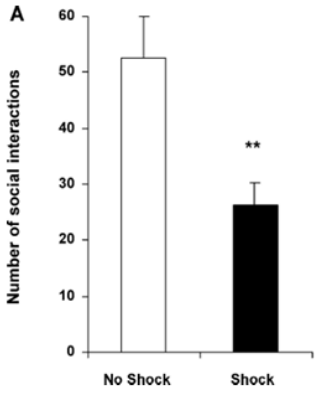


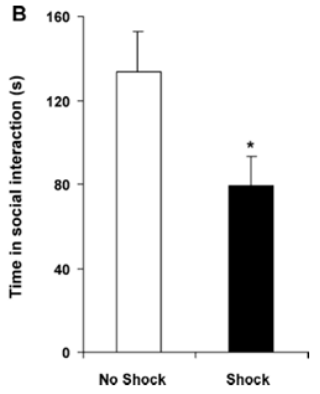


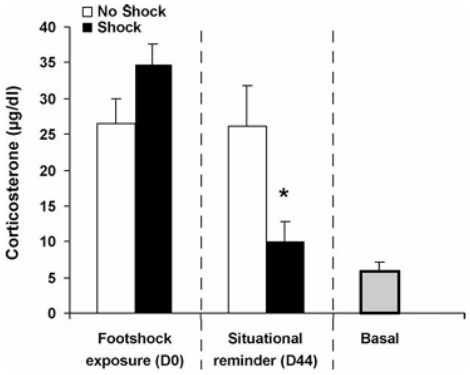


Increased anxiety levels

Trauma-related situational avoidance







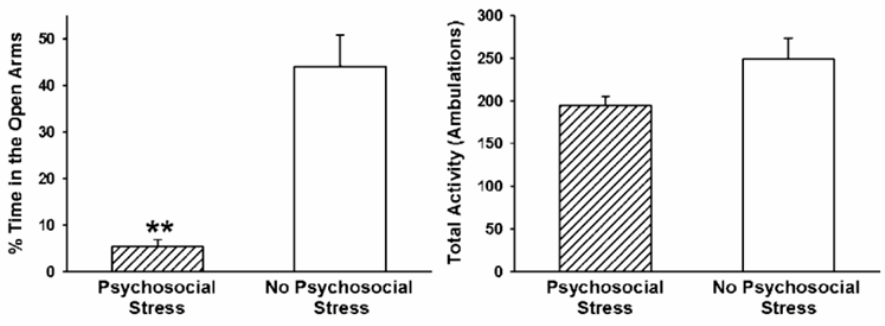
Social avoidance

Reduced cortisol levels

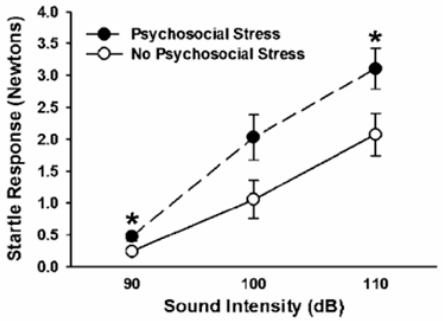
Bali, A. and Jaggi, A. S., *Life sciences*,2015

Paradigms of PTSD: Psychological stressors

Predator Stress (PS)



Increased anxiety levels

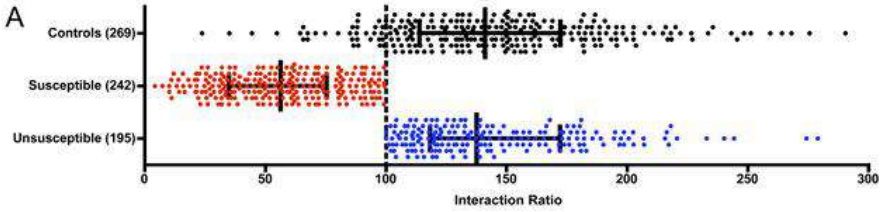


High-decibel startled reaction high

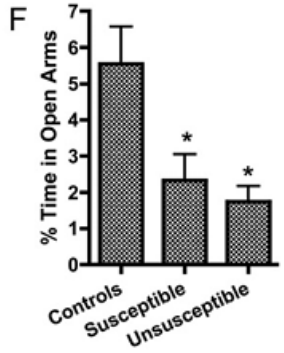
Zoladz P.R. and Diamond D.M., *Exp Neurol*,2016
Zoladz P.R. et al., *Stress*, 2008

Paradigms of PTSD: Psychological stressors

Social Defeat Stress (SDS)



Social avoidance



Increased anxiety levels

Krishnan V. et al., *Cell*, 2007

Part 1:
Overview of PTSD: definition and causes, research models and paradigms

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How to prove validity?

Restraint Struggle Test

Struggle frequency

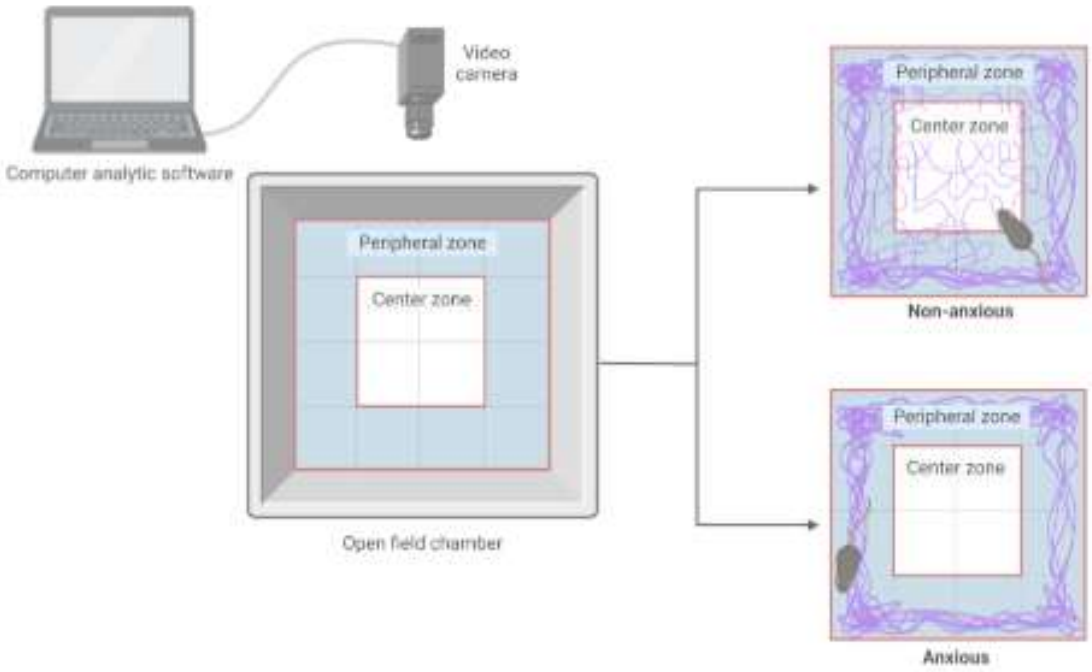
Struggle duration

Escape attempt behavior

Immobility time

How to prove validity?

Open Field Test



Crossing number

Rearing frequency

Time spent in center

Total distance traveled

Immobility time

How to prove validity?

Elevated Plus Maze Test

Open arm entries

Closed arm entries

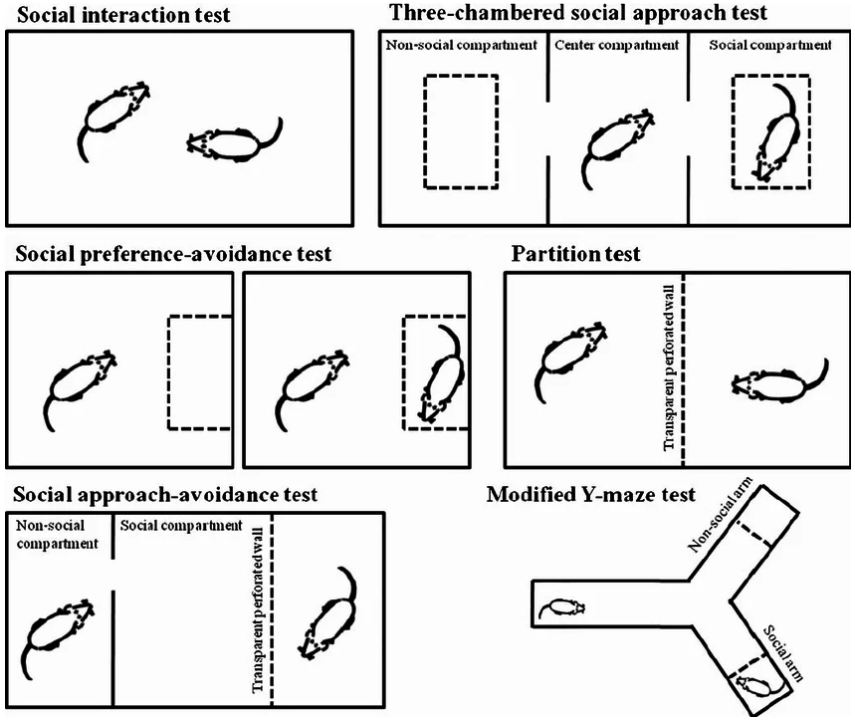
Time spent in open arms

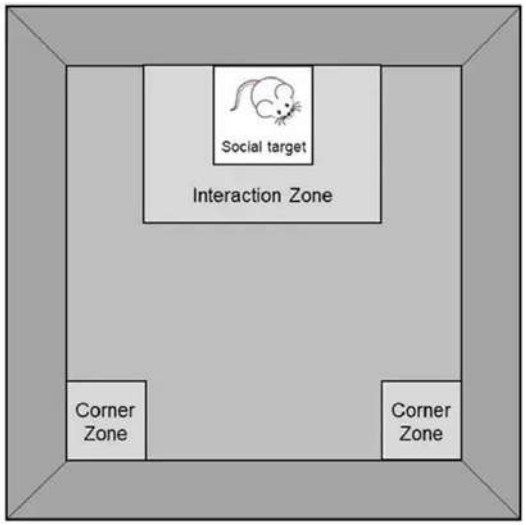
Time spent in closed arms

Total activity count

How to prove validity?

Social Interaction Test





Social interaction time

Approach frequency

Sniffing

Following

Avoidance

Take home message

- PTSD is a trauma-related mental disorder.
- Experimental paradigms simulate traumatic experiences through physical and psychological stress.
- Behavioral tests help validate PTSD models by measuring anxiety, avoidance, and stress-related behaviors.

Part 2 Understanding PTSD

- Core manifestations of PTSD and their biological basis.
- Biological mechanisms underlying the development and progression of PTSD.
- Common misconceptions

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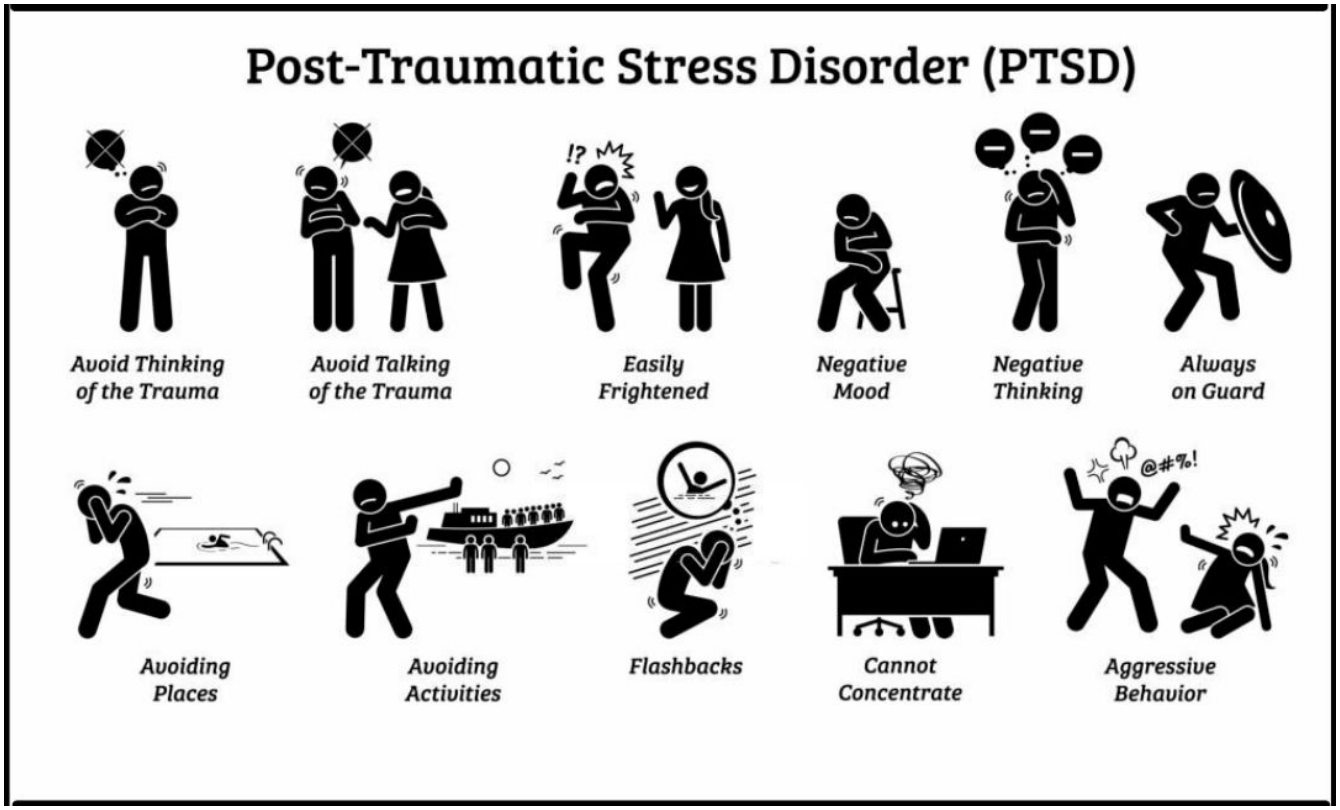
Common Clinical Manifestations of PTSD



1. Intrusive re-experience

Why are PTSD flashbacks intrusive?

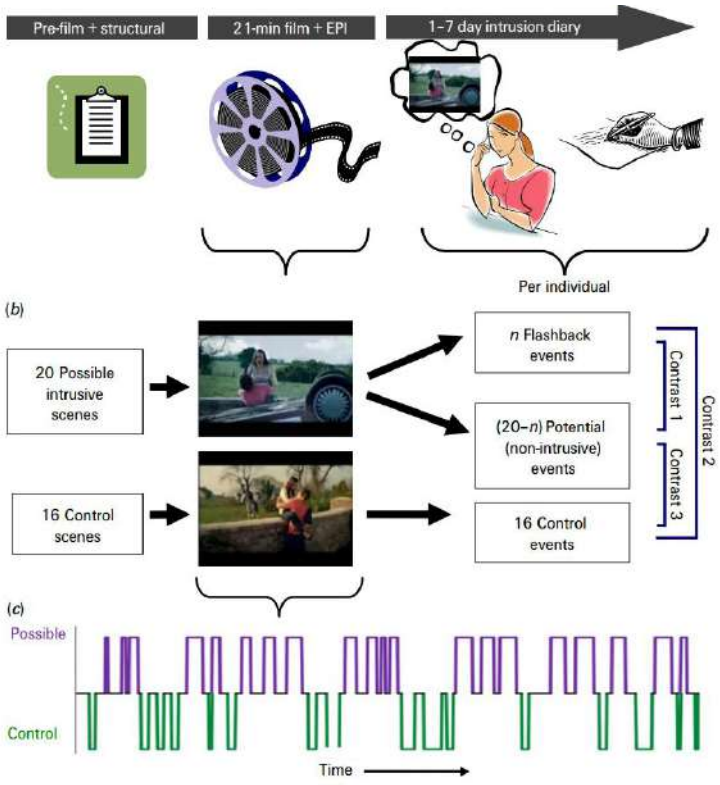
1. Randomness

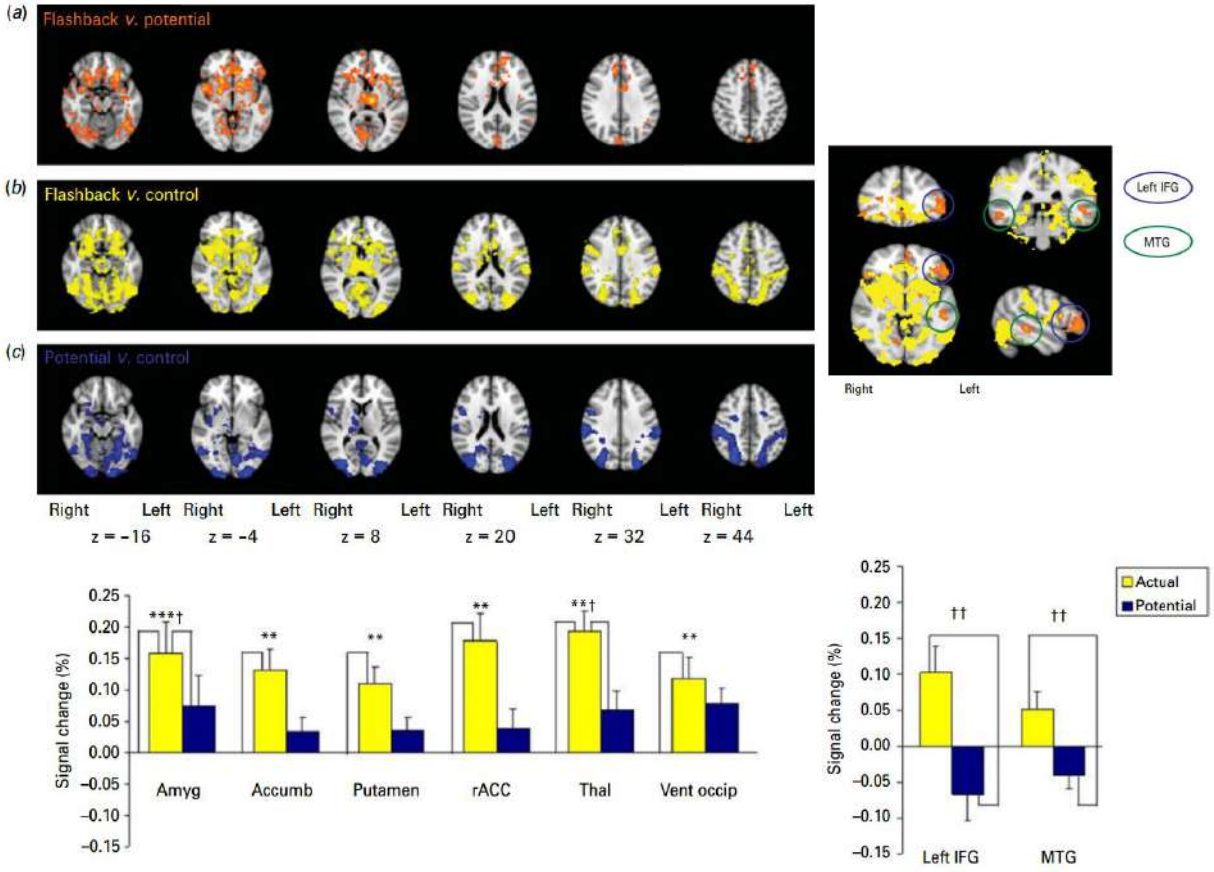
2. Episodes or Fragments

3. Vividness in sensation and perception

Ming Wang,et al.,*IJMHP*, 2019

Flashbacks are determined by the encoding process of the original traumatic event.





C. Bourne,et al., *Psychological Medicine* ,2013

2. Emotional Closure: Persistent Avoidance and Numbness

Characteristics of Emotional Closure

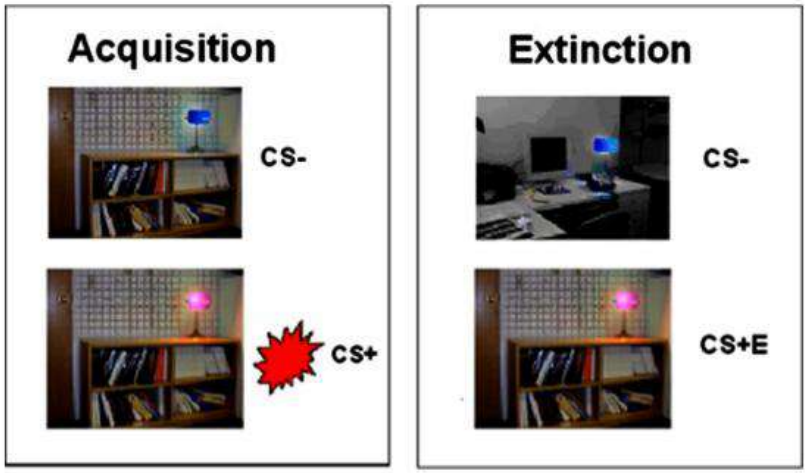
1. Continuous

2. active/passive

3. Memory dissociation

Le Doux JE,et al., *Mol Psychiatry*,2017

Avoidance symptoms correlate with the intensity of fear circuit activation.

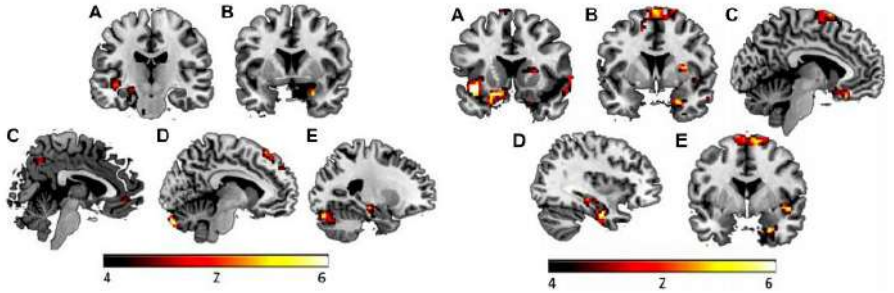


Acquisition

Table 1 | Correlations with CAPS avoidance symptoms.

Contrast map and brain region	Cluster size	MNI coordinates (*x*, *y*, *z*)	Analysis (*z*)
Fear acquisition			
CS+ > CS−			
Right hippocampus	**9**	**33, −27, −9**	**3.62**

Extinction



Insula→ The processing of emotions

Amygdala→ The processing of emotions

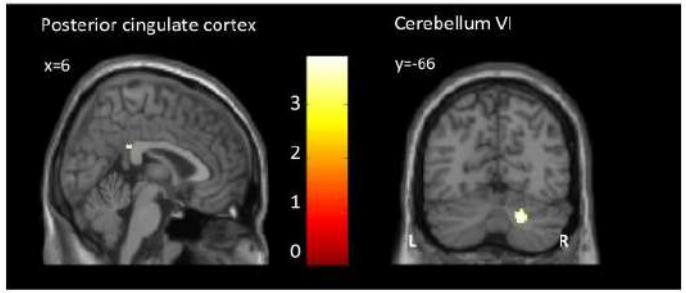
Hippocampus→ Scenario Memory

vmPFC、dmPFC→cognitive control

Sripada et al., *Frontiers in Human Neuroscience*,2013

3. Hyperarousal

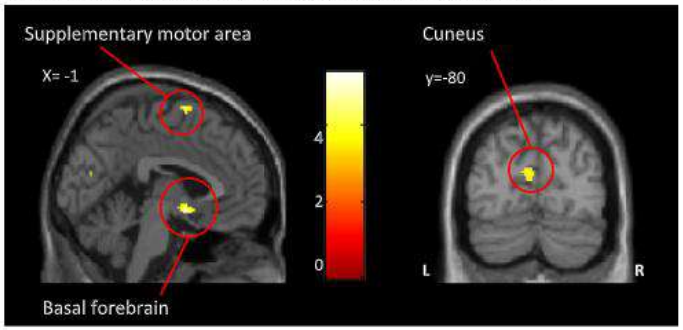
Subliminal Trauma>Neutral words in PTSD>Controls



Cerebellum VI :
rapid detection of trauma clues

Posterior cingulate cortex:
memory retrieval

Supraliminal Trauma>Neutral words within PTSD



Basal forebrain : cholinergic output

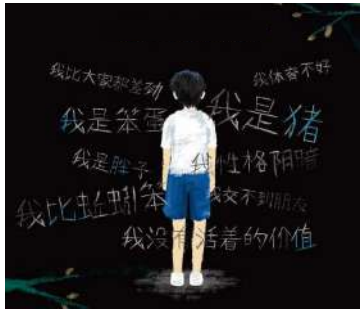
Supplementary motor area : rapid behavioral defense

Cuneus : visual processing and spatial memory

D. Rabellino et al., *Psychiatry Research: Neuroimaging* ,2016

4. Other Clinical Symptoms

Negative Perception



Comorbidity Characteristics

Atypical Symptoms

Sleep Disorders

Alcohol and Drug Abuse

Part 2 Understanding PTSD

- Core manifestations of PTSD and their biological basis.
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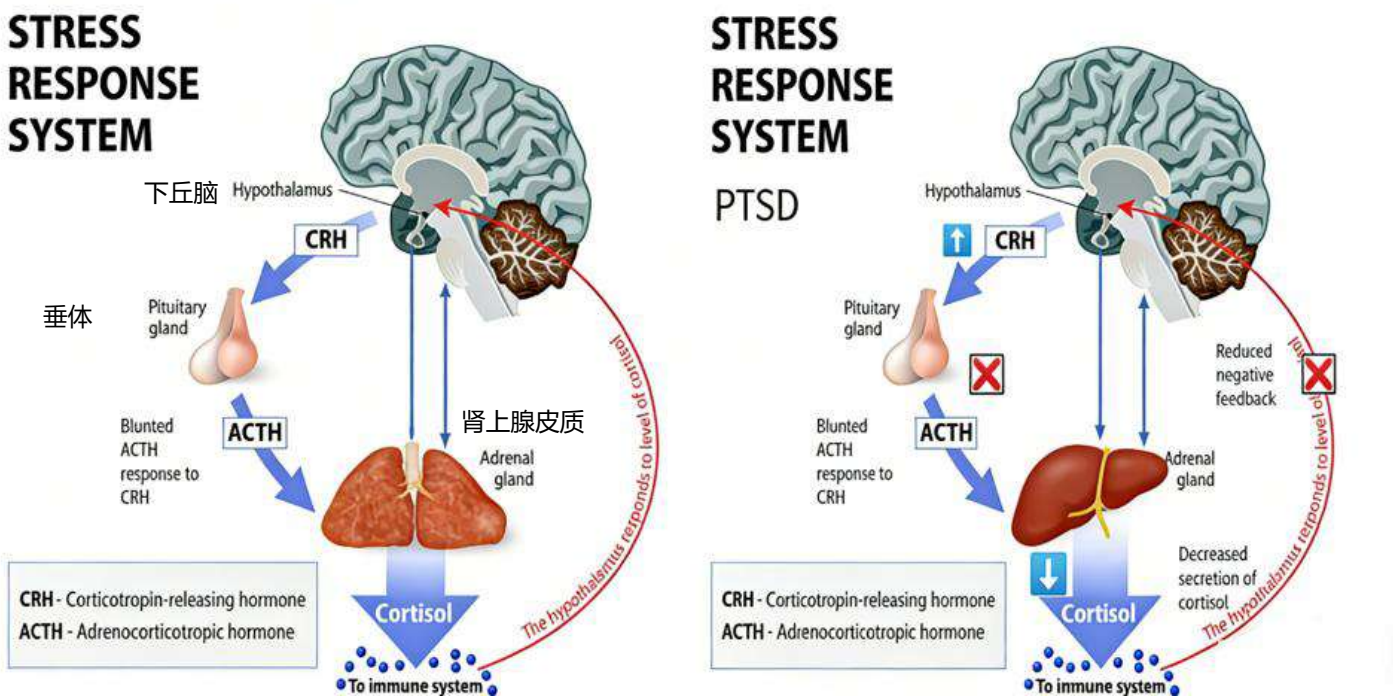
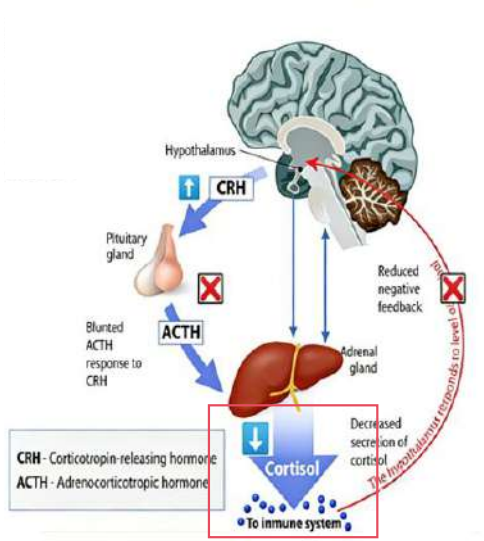
1. Hypothalamus-Pituitary-Adrenal (HPA) Axis——the core endocrine regulatory system of PTSD

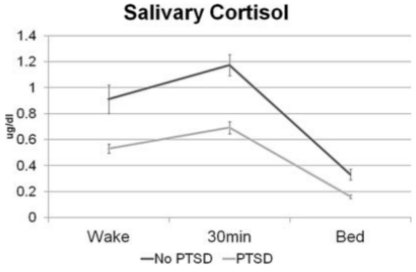


Sanil Rege,*Psych Scene Hub*,2024

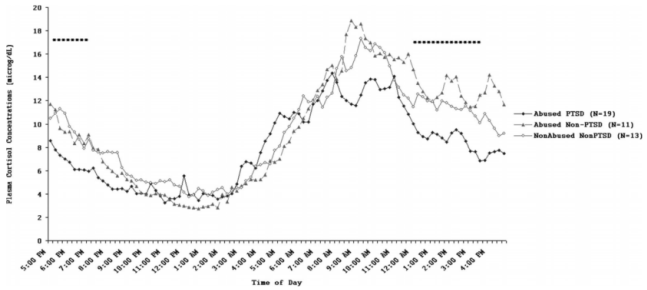
Abnormal cortisol secretion

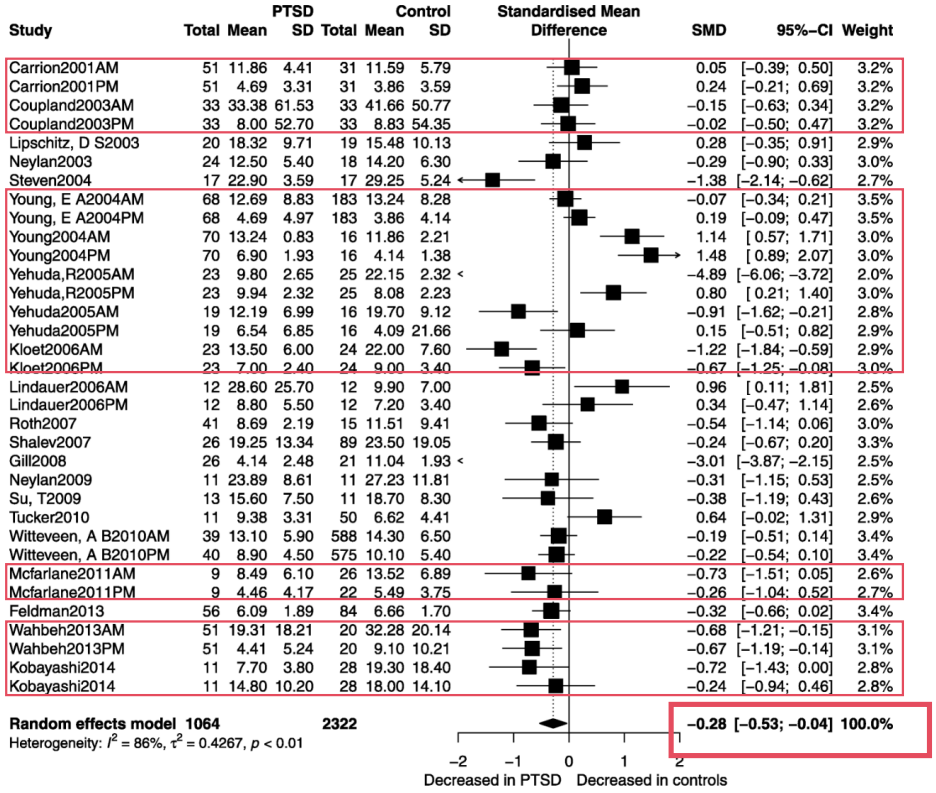


Veterans with PTSD



Women With Childhood Sexual Abuse-Related PTSD





Helane Wahbeh,Barry S. Oken, *Journal of Traumatic Stress,*2013
Douglas Bremner et al. *J Nerv Ment Dis*,2007
Pan et al. *BMC Psychiatry* ,2018

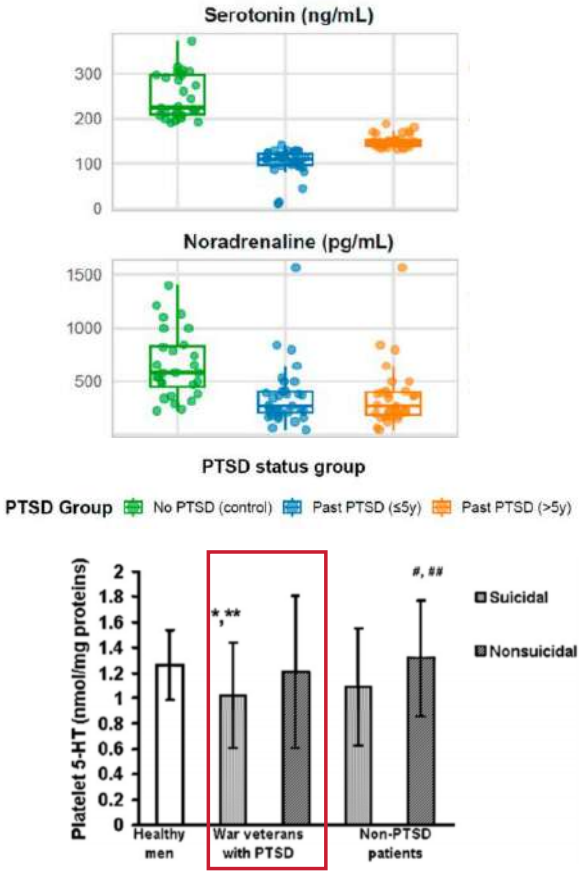
2. Monamine and Neurotransmitter Dysregulation

Serotonin（5-HT）

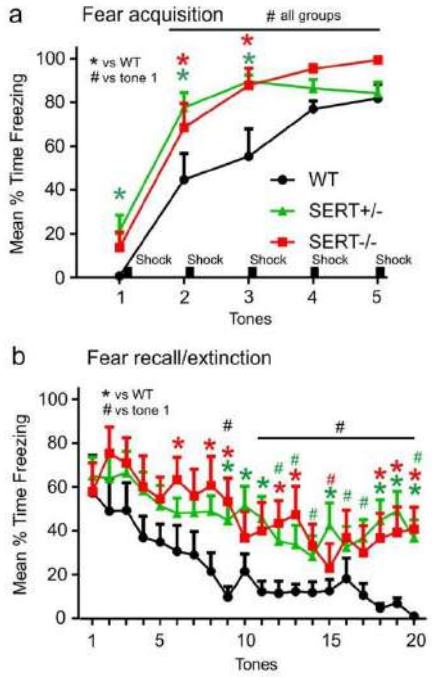
Noradrenaline（NE）

Dopamine（DA）

Distribution of biomarkers across PTSD status groups



PTSD-like manifestations in 5-HT-deficient mice

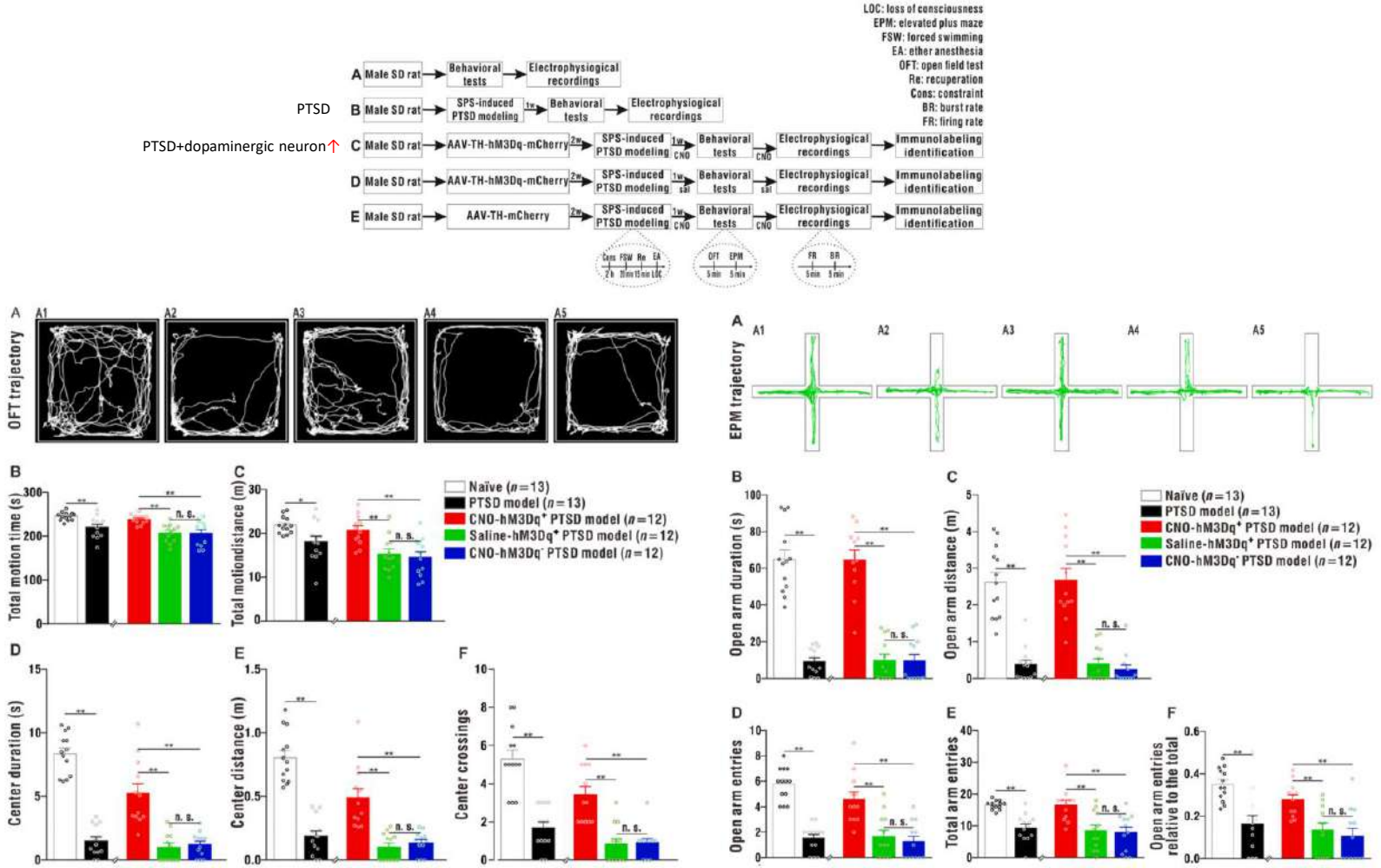


Johnson et al. ,*Translational Psychiatry* ,2019

Barbara Paraniak-Gieszczyk *,*Int. J. Mol. Sci.* ,2025

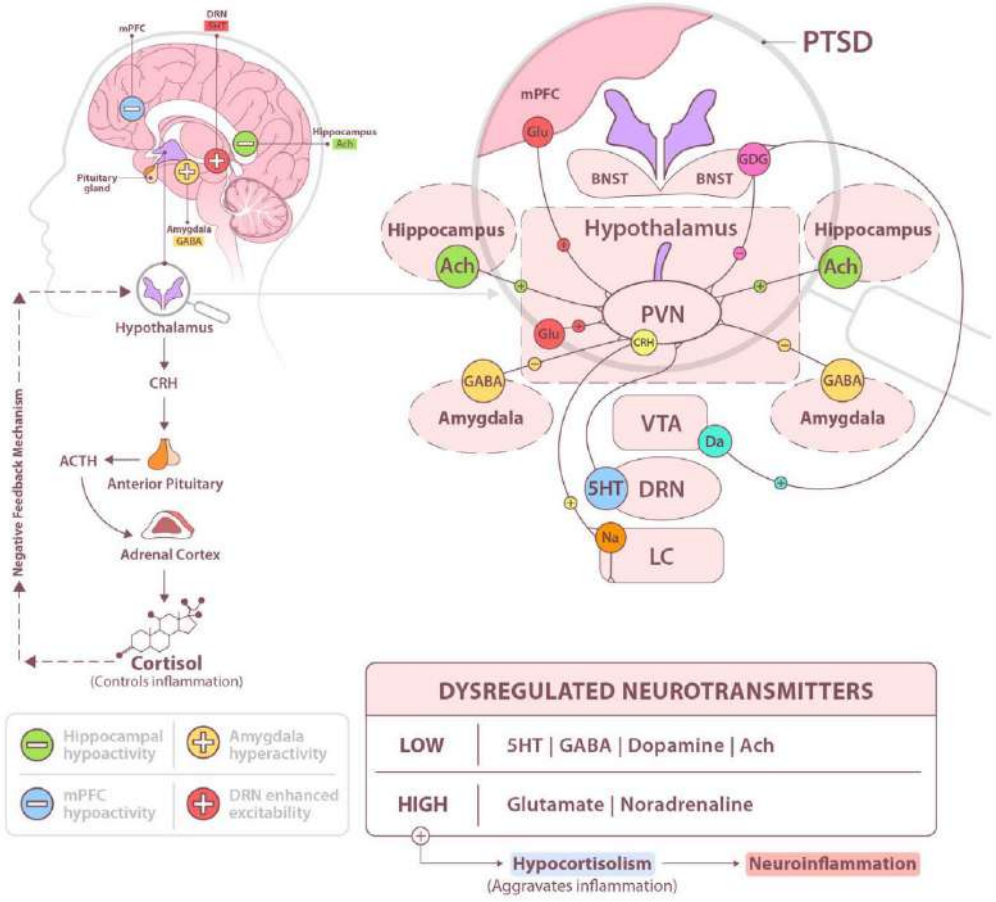
Z. Kovacic et al.,*Progress in Neuro-Psychopharmacology & Biological Psychiatry* ,2008

Activation of dopaminergic neurons improves anxiety-like behavior in rats with PTSD models.



P. Guan et al., *Neurochemistry International* ,2022

Neurohormonal regulation in relation to the hypothalamic–pituitary–adrenal (HPA) axis

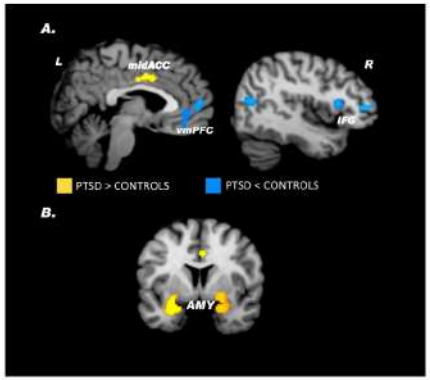


Anna Dorota Grzesi ´nska,*Int. J. Mol. Sci.*, 2025

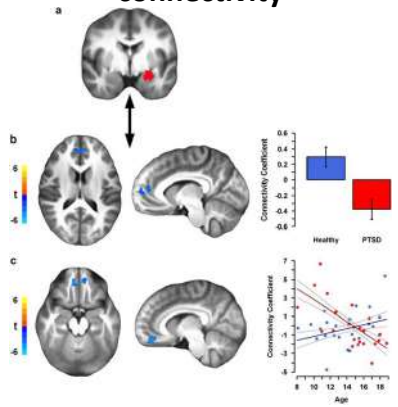
3. Abnormal brain region function

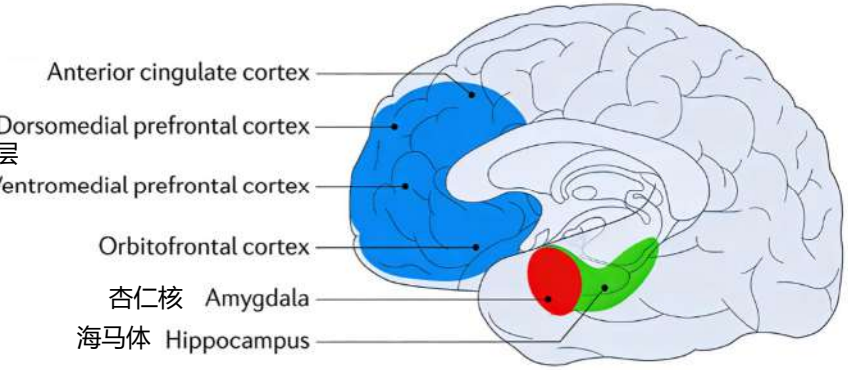
fMRI，functional magnetic resonance imaging

Overactivation of the amygdala

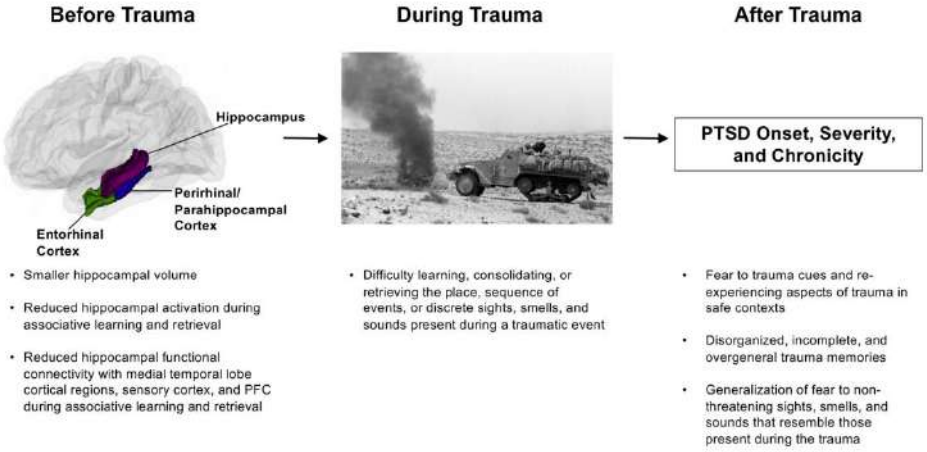


Decreased prefrontal-amygdala connectivity



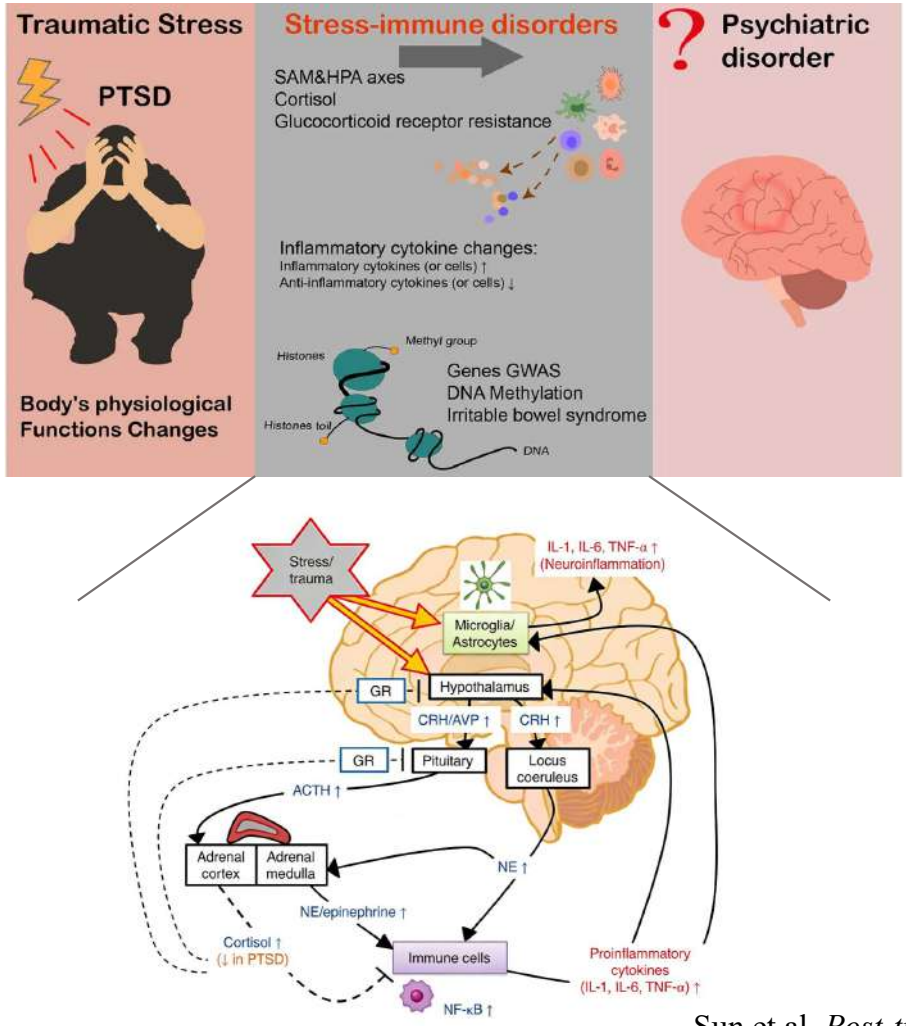


Hippocampal volume reduction



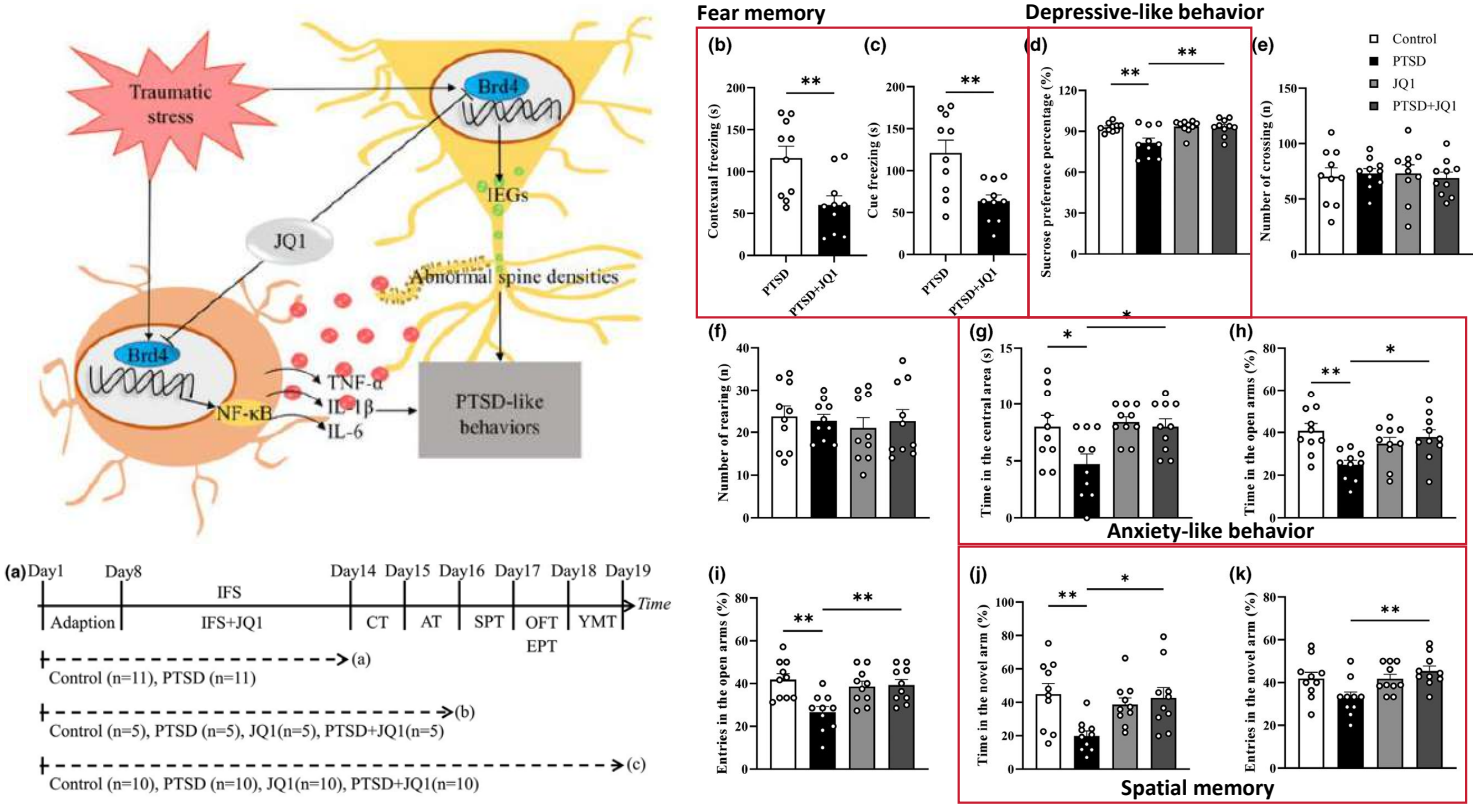
Vanessa M. Brown and Rajendra A. Morey, *Frontiers in Psychology*,2012
Hayes et al., *Biology of Mood & Anxiety Disorders*,2012
H.K. Lambert and K.A. McLaughlin, *Neuroscience and Biobehavioral Reviews*,2017

4. Neuroinflammation and immune activation



Sun et al.,*Post-traumatic Stress Disorder and Inflammation*,2021

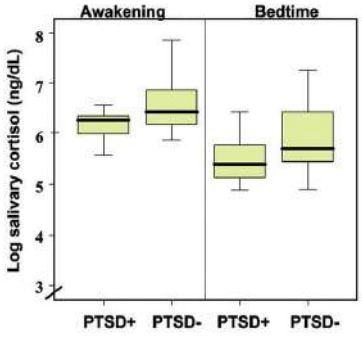
Modulation of Neuroinflammation Alleviates PTSD-Like Behavior and Fear Memory

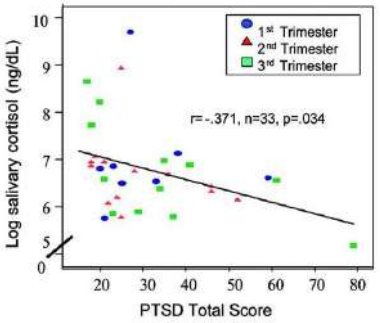


WANG et al., *Journal of Neurochemistry*,2021

5. Genetic susceptibility

Rachel Yehuda
PhD
Center for Affective Neuroscience
Friedman Brain Institute
Graduate School of Biomedical Sciences
Icahn School of Medicine at Mount Sinai
Psychiatry



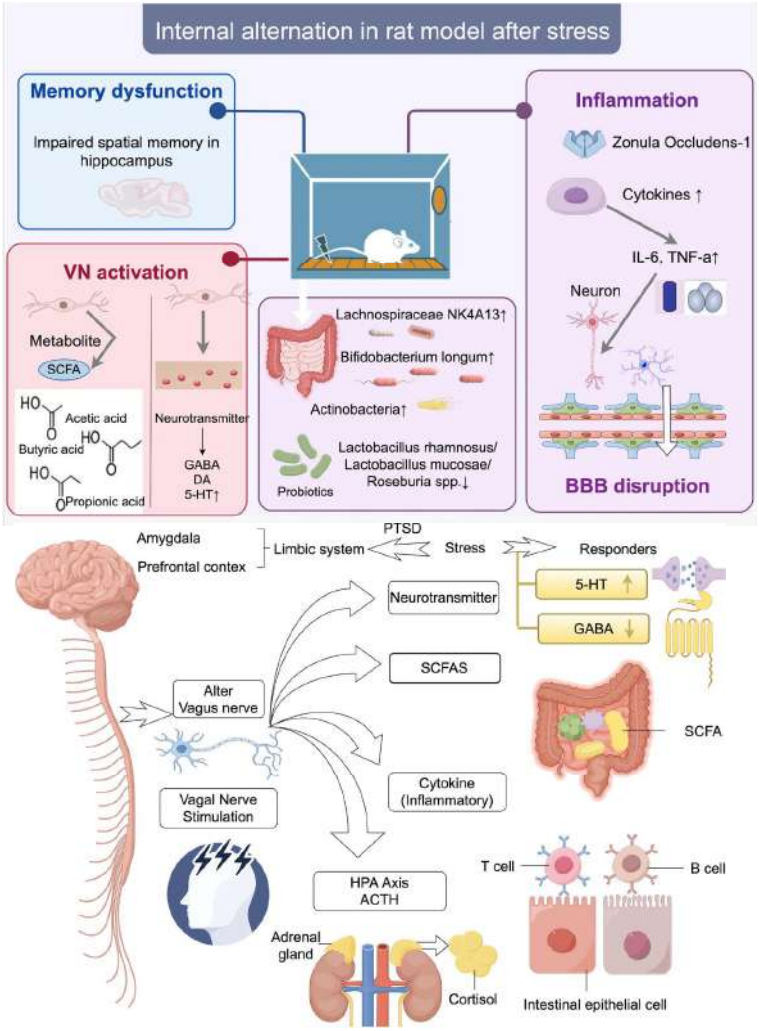


FKBP5:FK506-binding protein5 → HPA Axis

COMT:Catechol-O-methyltransferase → DA

BDNF:Brainderived neurotrophicfactor → Neurons

6. Intestinal flora imbalance



Yehuda et al., *J Clin Endocrinol Metab*,2005
Pan et al., *Frontiers in Pharmacology*,2025

Part 2 Understanding PTSD

- Core manifestations of PTSD and their biological basis.
- Biological mechanisms underlying the development and progression of PTSD.
- Common misconceptions

Only those who have experienced major traumatic events develop PTSD.

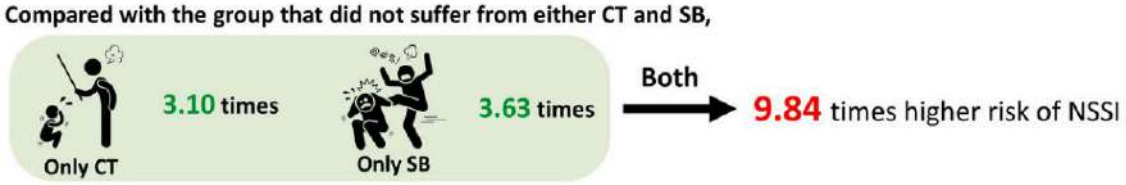
The prevalence of everyday trauma is higher






Trauma is a one-time event.

Chronic/repetitive trauma leads to more severe PTSD

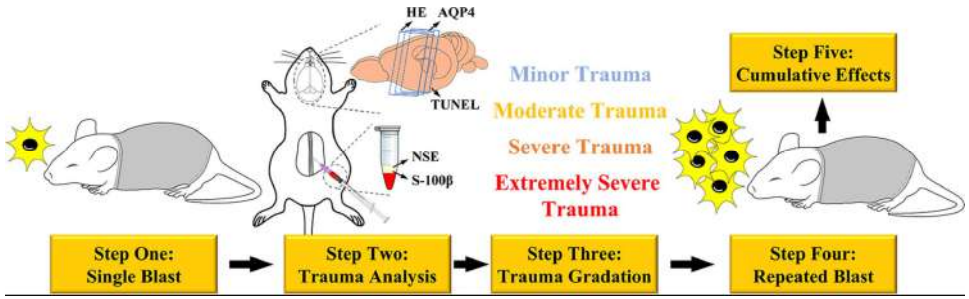


CT = childhood trauma

- **CT :** Emotional abuse > Emotional neglect > Sexual abuse

SB = school bullying

- **SB :** Verbal bullying > Cyberbullying



Trauma severity: 69%↑

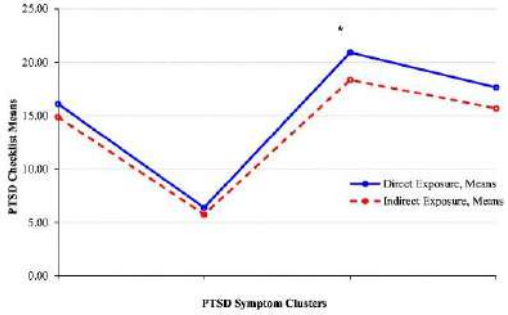
Y. Jin et al., *Child Abuse & Neglect* ,2026

X. Huang, B. Xia, L. Chang et al.,*Theoretical and Applied Mechanics Letters* ,2024

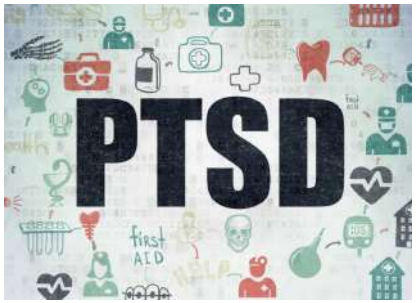
The trauma must have been inflicted directly upon you.

Direct and indirect exposure

Four Types of Trauma Exposure （DSM-5-TR）



Elizabeth G. Szogi & Karen A. Sullivan,*Psychol. Inj. and Law* ,2018



YES

TRAUMA

NO

Independent, yet compatible

PTSD = Depression

PTSD cannot be cured.

Intervenable, manageable, clinically curable

RCT: Concurrent Treatment of Posttraumatic Stress Disorder and Alcohol Use Disorder in Women

POPULATION

90 Women

Women with posttraumatic stress disorder (PTSD) and moderate-to-severe alcohol use disorder

Mean age, 44.7 y

INTERVENTION

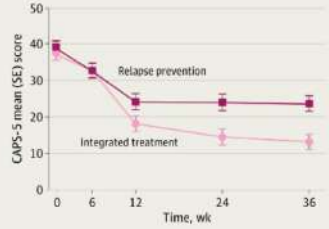
90 Patients randomized
All patients received 12 individual sessions of their assigned treatment program

45 Integrated treatment
Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE)

45 Relapse prevention
Treatment guided by the Project MATCH Cognitive-Behavioral Coping Skills Therapy Manual

FINDINGS

Compared with relapse prevention, integrated treatment significantly reduced PTSD; alcohol use also decreased in both groups, but with no significant between-group difference



Alcohol use
Integrated intervention: 144.41 (95% CI, 104.66-184.15) g/wk at baseline, 92.65 (95% CI, 48.81-136.48) g/wk at 9-mo
Relapse prevention: 133.45 (95% CI, 93.71-173.19) g/wk at baseline; 77.80 (95% CI, 31.65-123.95) g/wk at 9-mo

SETTINGS / LOCATIONS

3 Addiction services in Sweden

PRIMARY OUTCOME

Change from baseline to 9 mo in PTSD symptom severity, measured by the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5; range, 0-80; higher scores indicate greater severity) and weekly alcohol use, measured by Timeline Followback self-report (g/wk)

Persson A, Axén Å, Capusan AJ, Magnusson Å, Helig M. Concurrent treatment of posttraumatic stress disorder and alcohol use disorder in women: a randomized clinical trial. *JAMA Netw Open*. 2025;8(7):e2521087. doi:10.1001/jamanetworkopen.2025.21087

Take-home Message

1. PTSD comprises three core symptom clusters, which are associated with specific biological and pathological bases.
2. PTSD results from the interaction of multiple factors, mechanisms, and targets.
3. Scientifically correcting common misconceptions about PTSD is a crucial foundation for understanding and treating the condition.

The Coping of PTSD: scientific intervention and research prospects

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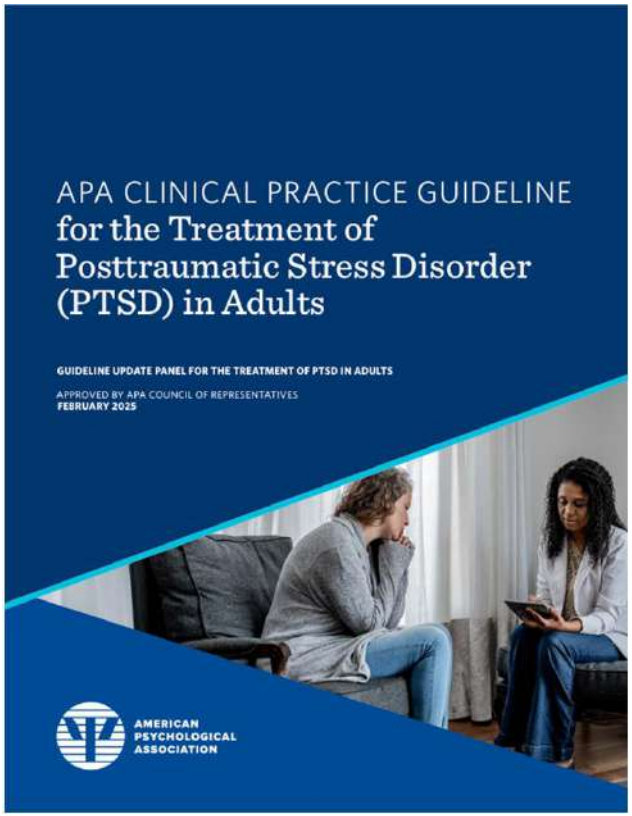
The Coping of PTSD: scientific intervention and research prospects

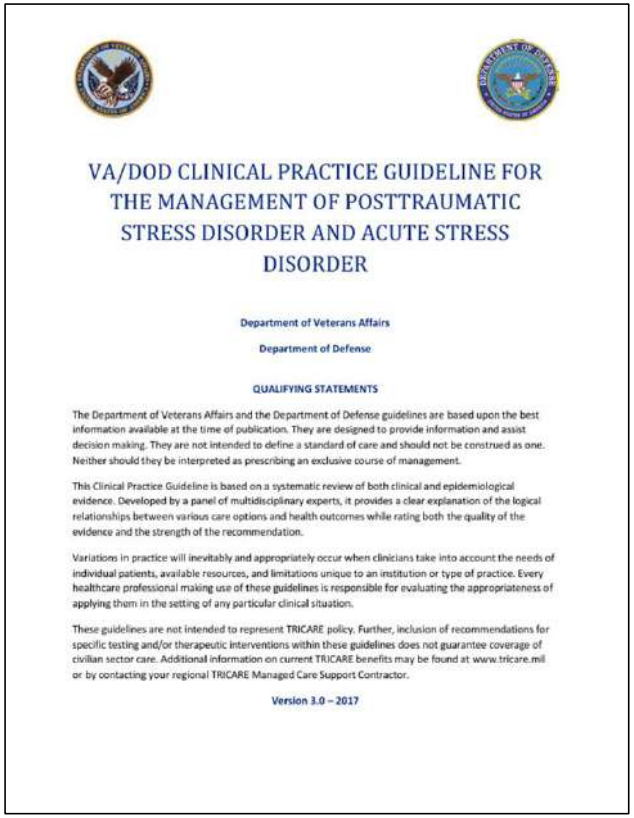
1. Common psychotherapy
2. Implications from fear conditioning
3. Pharmacotherapy
4. Other promising intervention
5. Challenges and prospects

1. Common psychotherapy

APA guidelines



VA/DoD guideline



VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF POSTTRAUMATIC STRESS DISORDER AND ACUTE STRESS DISORDER

Department of Veterans Affairs

Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 3.0 – 2017

Psychotherapy recommended by APA and VA/DoD :

A. Prolonged Exposure (PE)
B. Cognitive Processing Therapy (CPT)

A. Prolonged Exposure (PE)

Theoretical Basis :

Emotional processing theory. Traumatic memories form a pathological "fear structure" in the brain.

Treatment Goal :

To modify the pathological fear structure by activating it and introducing new, incompatible information (e.g., "I am safe now")

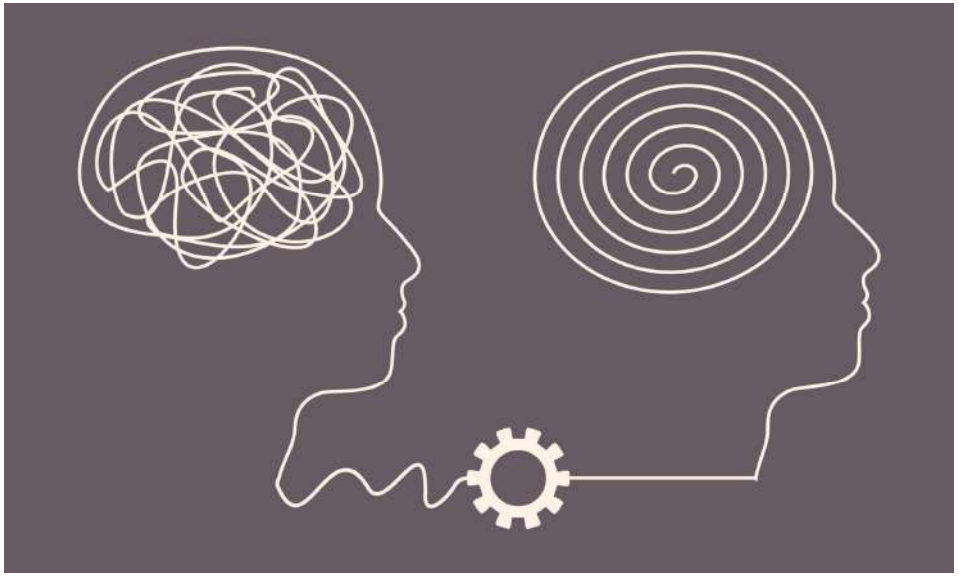
PE includes:

Psychoeducation about PTSD and common reactions to trauma
Breathing retraining
Vivo exposure/Imaginal exposure

B. Cognitive Processing Therapy (CPT)

Theoretical Basis :

Social cognitive theory. Patients form extreme, unrealistic negative beliefs in an attempt to make sense of the event



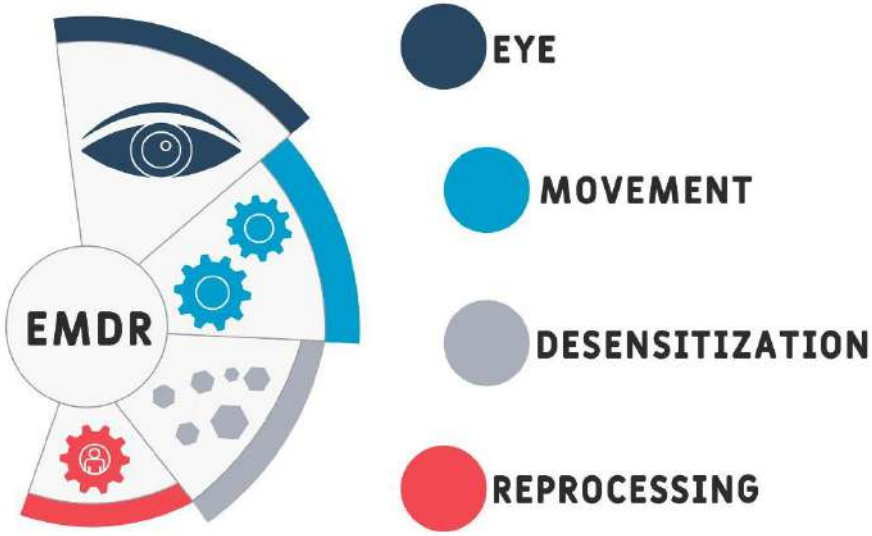
Treatment Goal :

Identify maladaptive cognitions
Replace them with more balanced, realistic beliefs

CPT includes:

Psychoeducation about the cognitive model
CT skill

C. Eye Movement Desensitization Reprocessing (EMDR)



Theoretical Basis :

The Adaptive Information Processing model. The memory was not adequately processed.

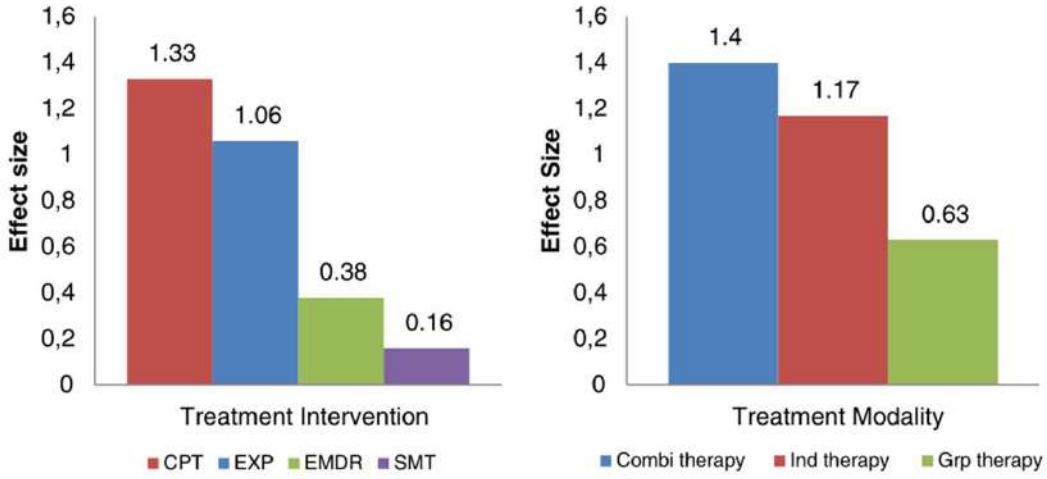
Treatment Goal :

Change the way that the memory is stored
Reducing and eliminating the problematic symptoms.

Theoretical Basis :

Focus on the trauma memory while simultaneously experiencing bilateral stimulation: eye movements and other forms of rhythmic left-right (bilateral) stimulation (e.g., tones or taps).

The efficacy of recommended treatments



1. CPT and PE are more effective than EMDR and SMT
2. Combination Therapy and Individual Therapy are more effective than Group Therapy

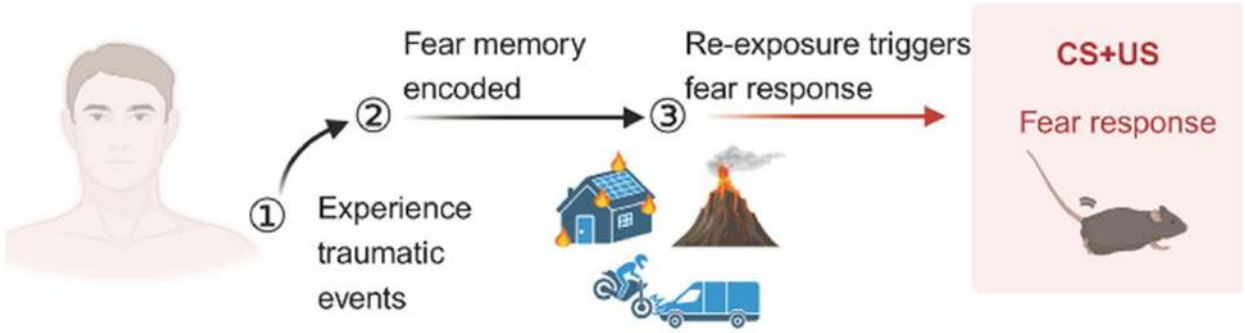
Haagen, J. F. G. *et al. Clinical Psychology Review* **40**, 184–194 (2015)

The Coping of PTSD: scientific intervention and research prospects

1. Recommended psychotherapy
2. **Implications from fear conditioning**

Pavlovian conditioning/Classical conditioning

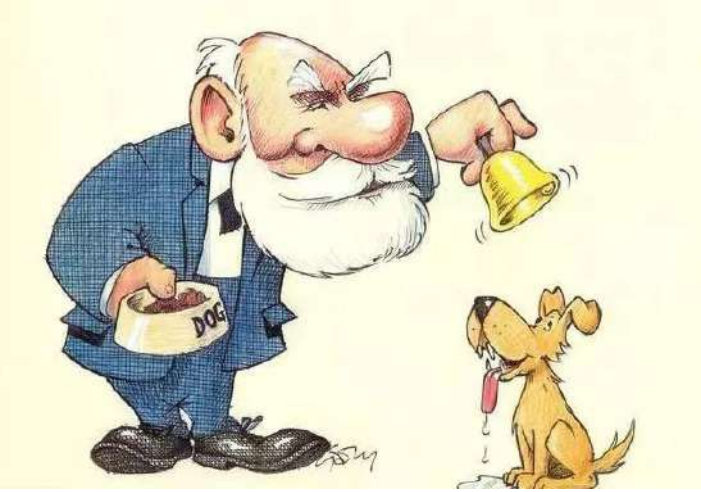
Fear conditioning in PTSD



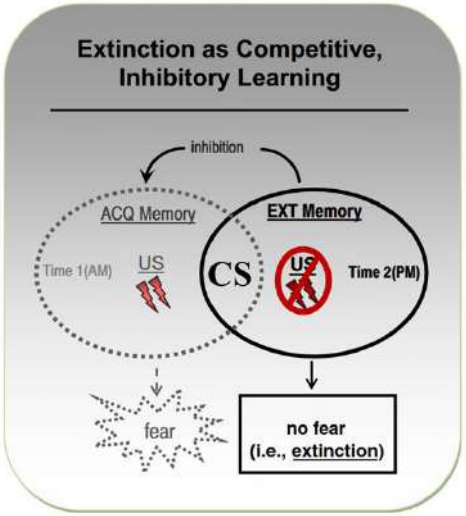
Chen, J. *et al. Neurosci. Bull.* **41**, 1054–1084 (2025)

How Fear Memory is Updated?

1.*Memory Extinction (消退)*



Extinction refers to the gradual weakening of a CR



new CS-no US memory
VS
original CS-US memory

Limits:

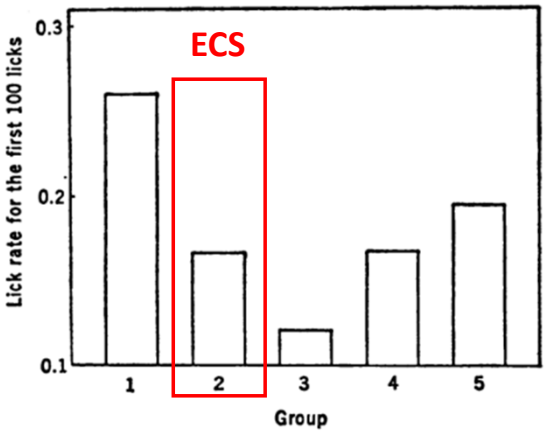
- ☐ **Spontaneous recovery**
- ☐ **Context renewal**

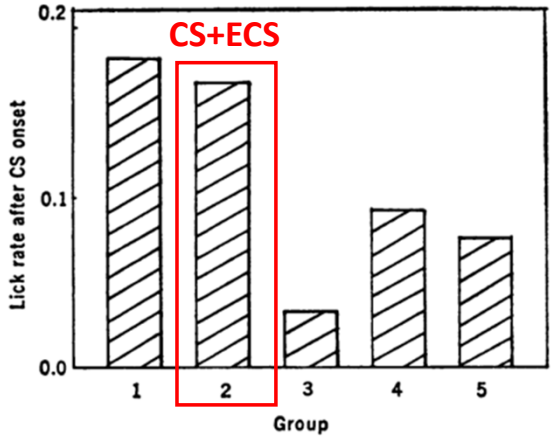
Can we "erase" memory?

Lissek, S. *et al. International Journal of Psychophysiology* **98**, 594–605 (2015)

How Fear Memory is Updated?

2. *Memory Reconsolidation(再巩固)*





ECS: interference memory

CS: induce memory retrieval

Group1: ECS interference memories soon after fear-conditioning

Group2: ECS interference memories 24h after fear-conditioning

Traditional view:

Memories are static and unchangeable

Correction:

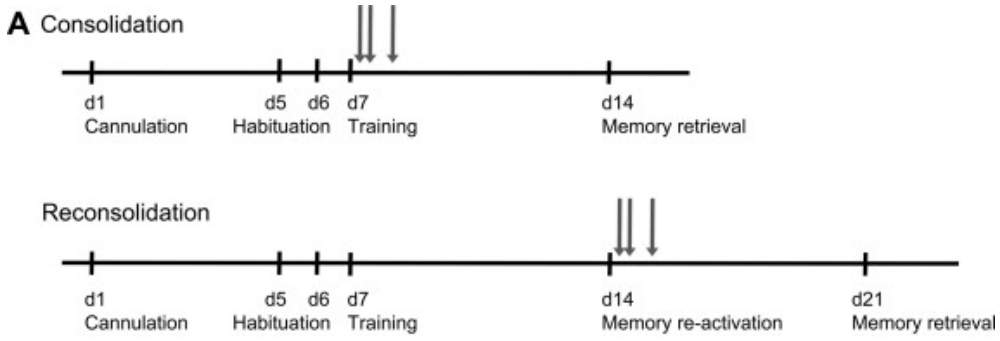
- Memories are dynamic and can be modified
- Memories become more vulnerable and destabilized when retrieval

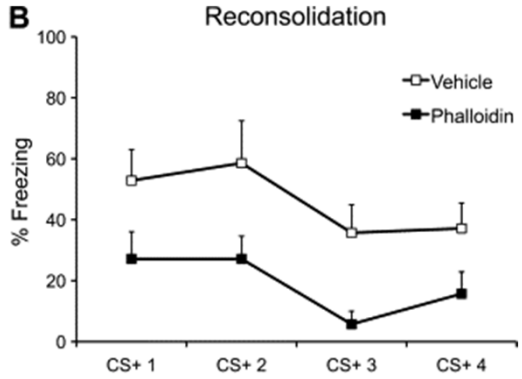
Reconsolidation is a dynamic process that updates retrieved memories with new protein synthesis

Misanin, J. R. *et al. Science* **160**, 554–555 (1968)

How Fear Memory is Updated?

2. *Memory Reconsolidation*





Reconsolidation occurs during memory retrieval, stabilizing recalled memories in a time-sensitive manner

In Reconsolidation window(0.5 and 6 h post-retrieval), it is possible to “erase” memory

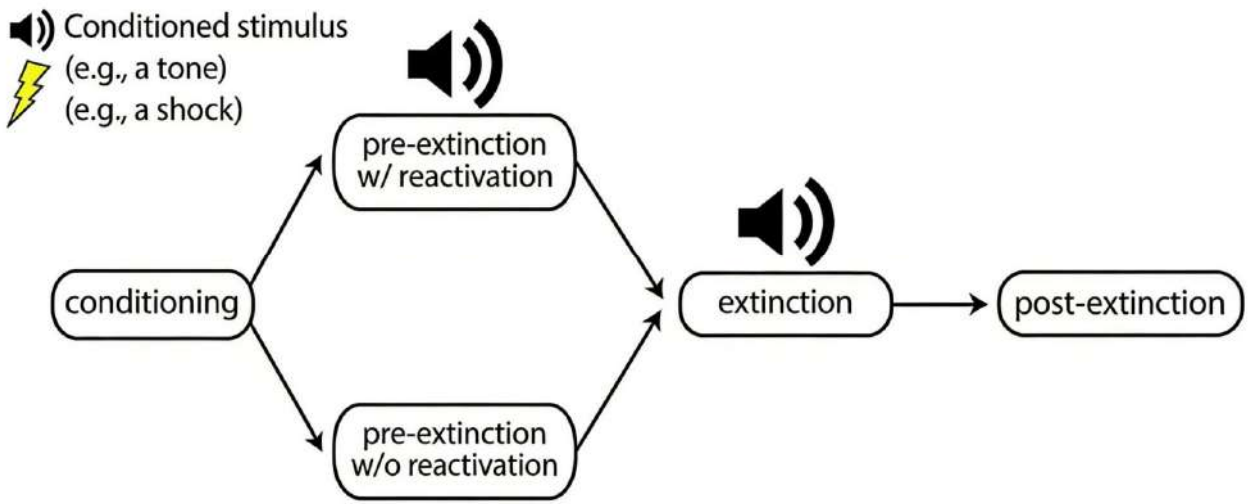
Rehberg, K. *et al. Neurobiology of Learning and Memory* **94**, 117–126 (2010)

How can we use memory reconsolidation to alleviate fear memory in PTSD?

Pharmacological/Optogenetic blockade

Behavioral Therapy Based on Reconsolidation:

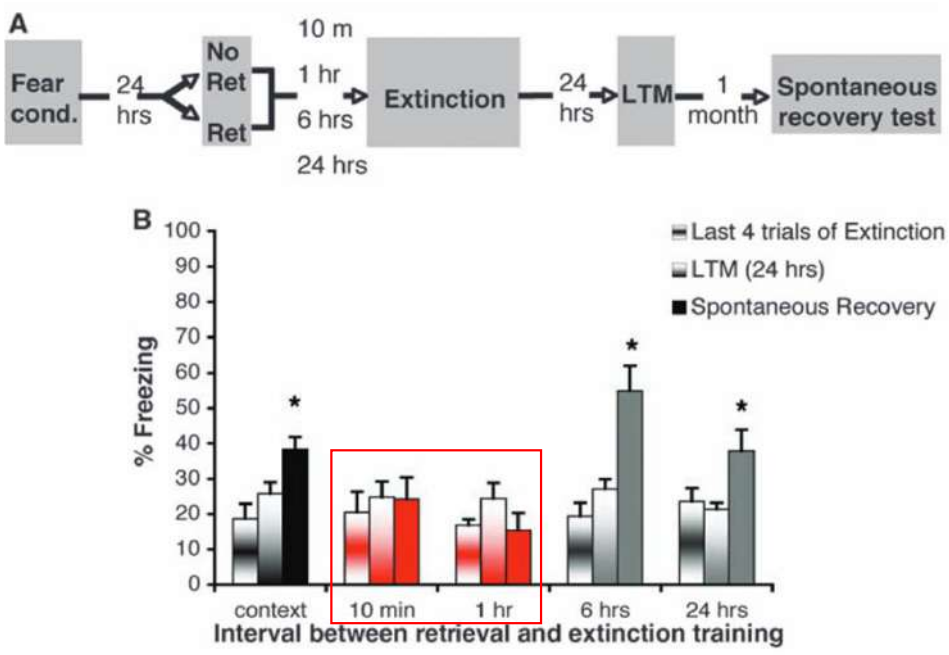
- Post-retrieval extinction (PRE) protocol

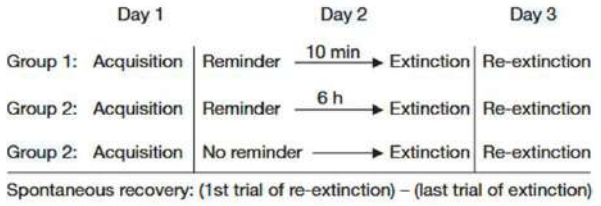


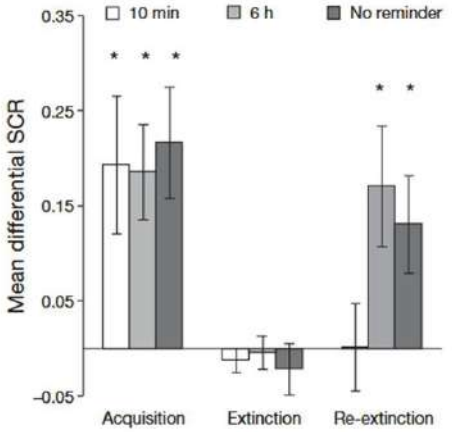
Dunsmoor, J. E. *et al. Neuron* **88**, 47–63 (2015)

Several factors contribute to the efficacy PRE

Factor 1. Interval between retrieval and extinction training







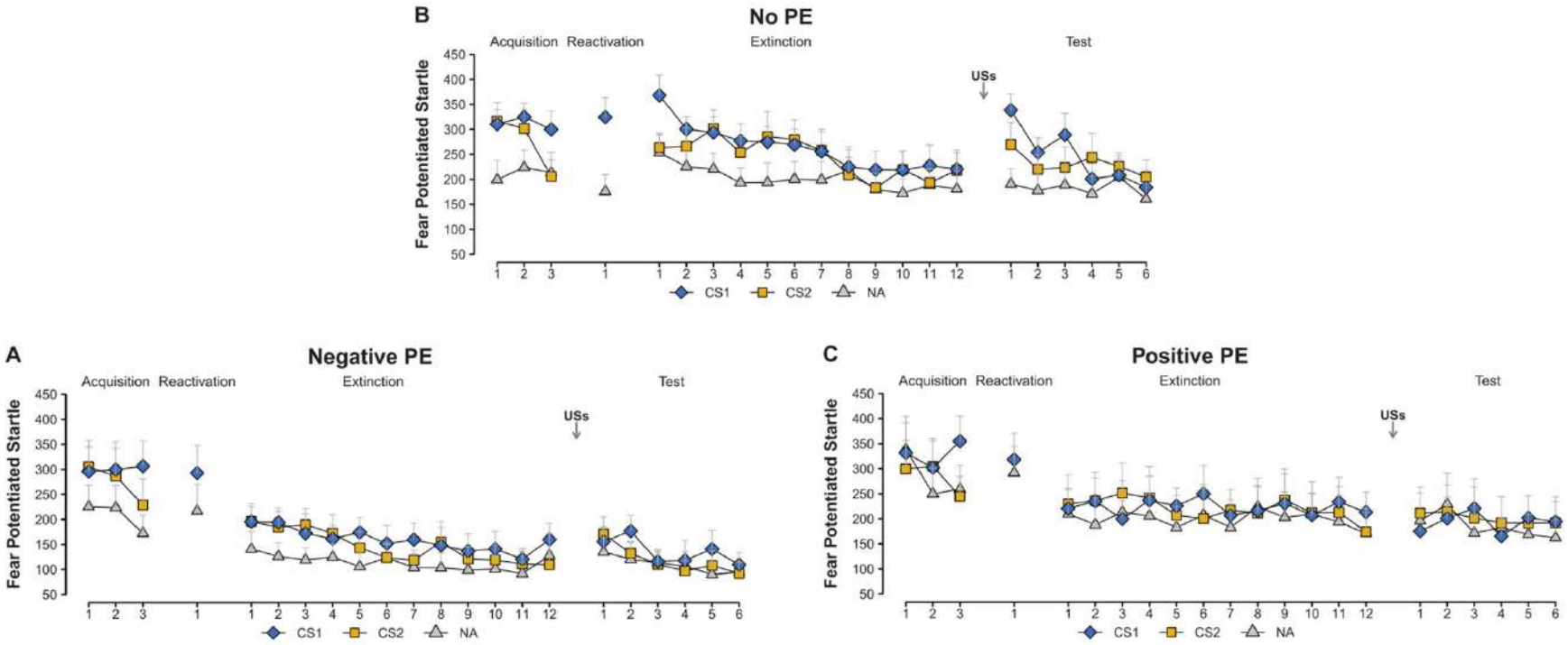
In humans, reactivating fear memories 10 min, before extinction produces a durable reduction in fear that can last at least a year

Monfils, M.-H. *et al. Science* **324**, 951–955 (2009)

Schiller, D. *et al. Nature* **463**, 49–53 (2010)

Several factors contribute to the efficacy PRE

Factor 2. Discrepancy between the original learning context and the reactivated context

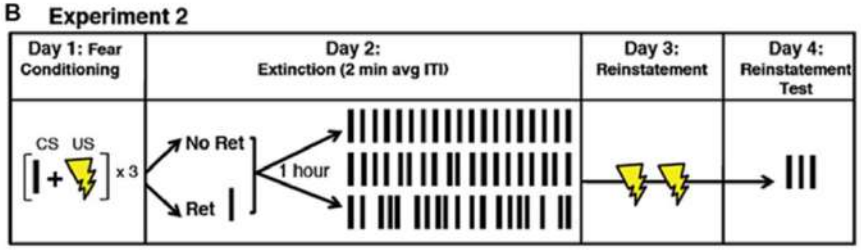


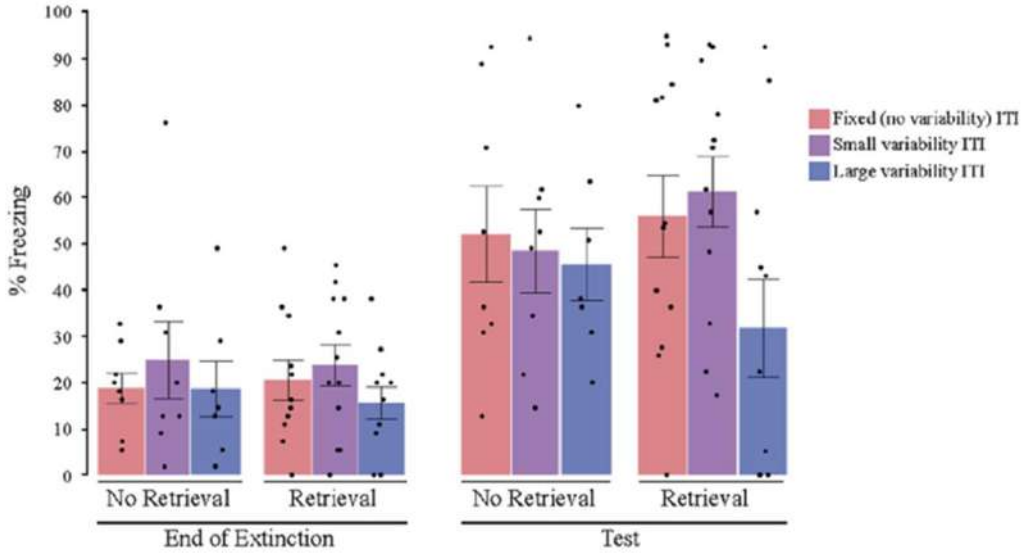
Multiple PEs (predict errors) is more effective than single-PE

Sevenster, D. *et al. Science* **339**, 830–833 (2013)

Several factors contribute to the efficacy PRE

Factor 3. Inter-trial intervals (ITIs) during the extinction





The unpredictability of interval length is vital

Auchter, A. *et al. Front. Behav. Neurosci.* **11**, (2017)

Post-retrieval extinction (PRE) protocol is a promising alternative to the standard ET strategy

Standard ET (Exposure therapy)

Add retrieval before extinction:

1. time window
2. degree of PE
3. inter-trial intervals (ITIs)

Post-retrieval extinction (PRE) protocol

The Coping of PTSD: scientific intervention and research prospects

1. Recommended psychotherapy
2. Implications from fear conditioning
3. **Pharmacotherapy**

3. Pharmacotherapy

3.1. FDA-Approved Drugs for PTSD

Serotonin (5-HT)

First-line treatments

SSRIs: Paroxetine 帕罗西汀

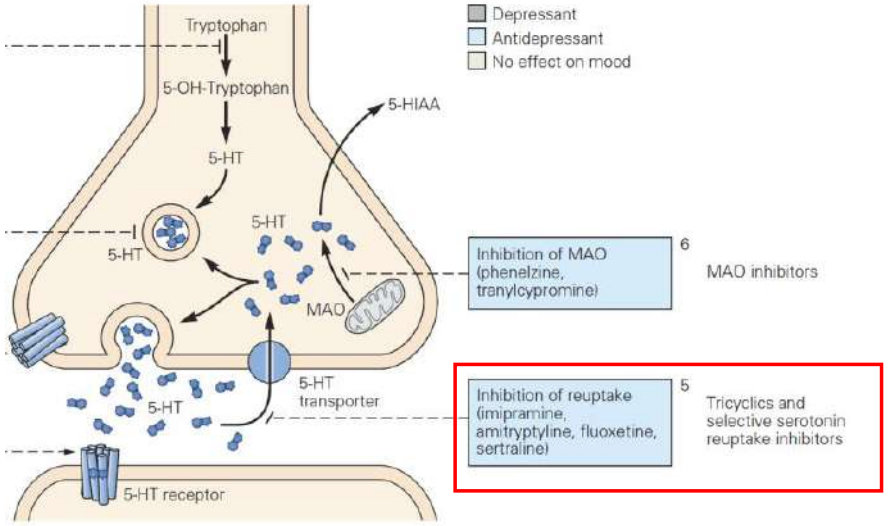
Sertraline 舍曲林

If failed

Antidepressants

SNRI: Venlafaxine 文拉法辛

SARI: Nefazodone 奈法唑酮

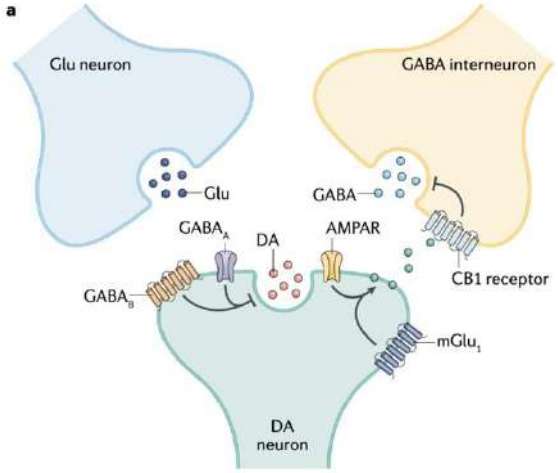


- ✓ Increase serotonin availability in the synaptic cleft
- ✓ Enhances serotoninergic neurotransmission

3. Pharmacotherapy

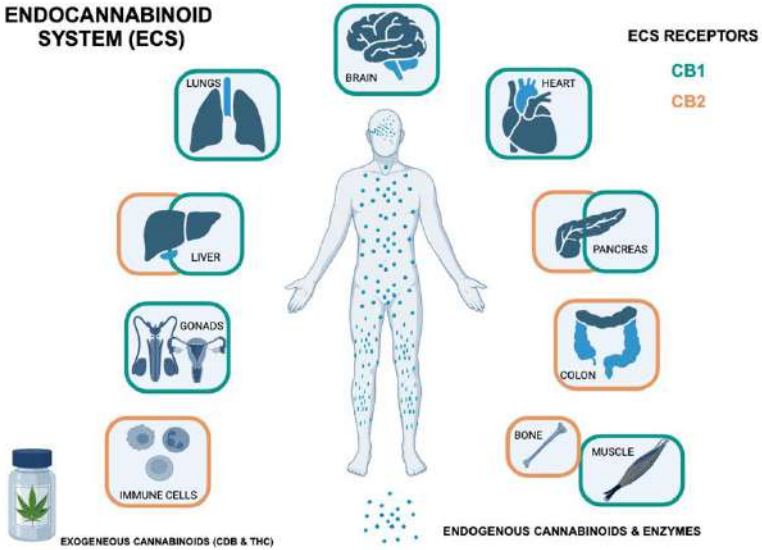
3.2 Novel Drugs under Clinical Trials

New targets: Glutamate, NMDA receptors, endogenous cannabinoid system, adrenaline system



Glutamatergic Antagonists

Riluzole



CB2 agonists

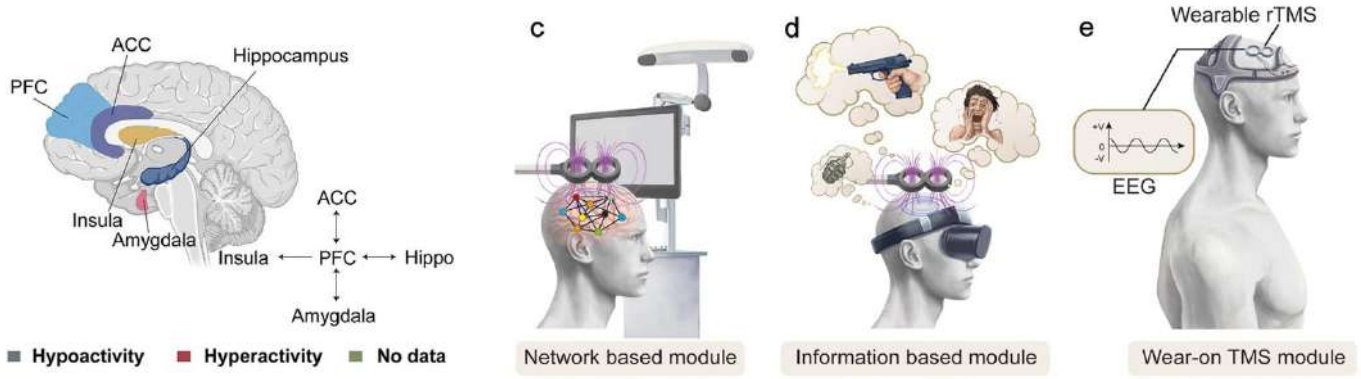
Cannabidiol

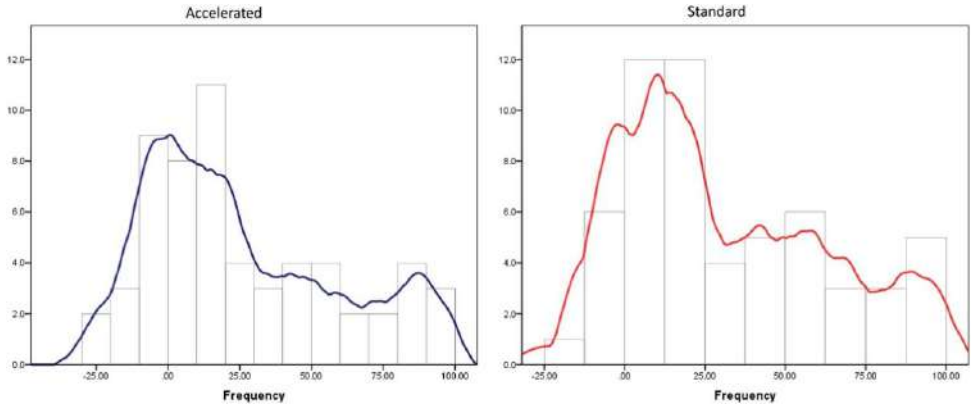
The Coping of PTSD: scientific intervention and research prospects

1. Recommended psychotherapy
2. Implications from fear conditioning
3. Pharmacotherapy
4. **Other promising intervention**

4. Other promising intervention

4.1 repetitive Transcranial magnetic stimulation (rTMS)





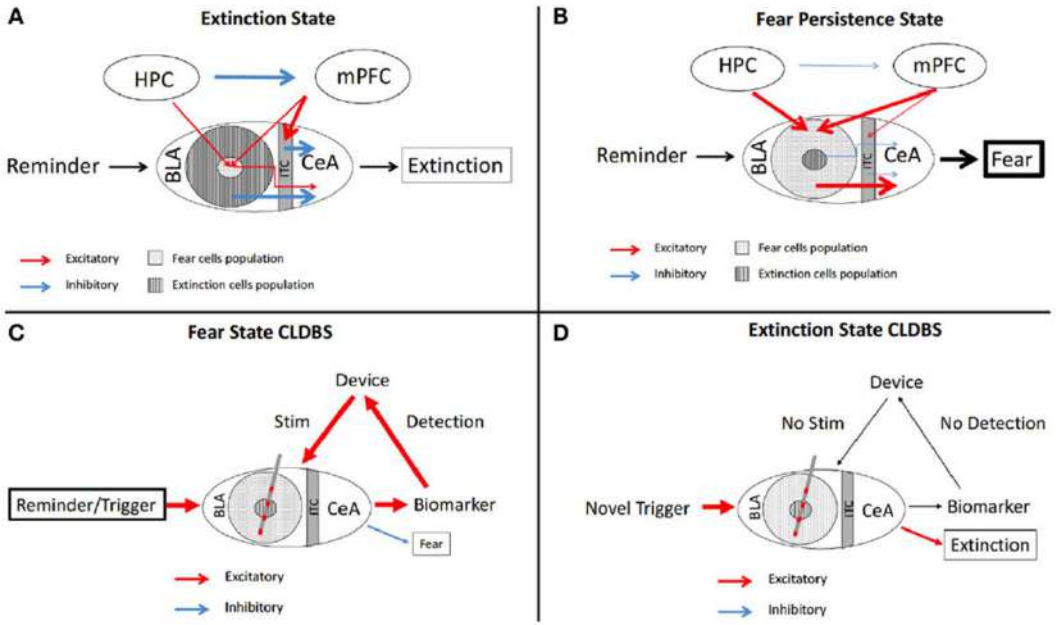
Neural circuit-based brain stimulation

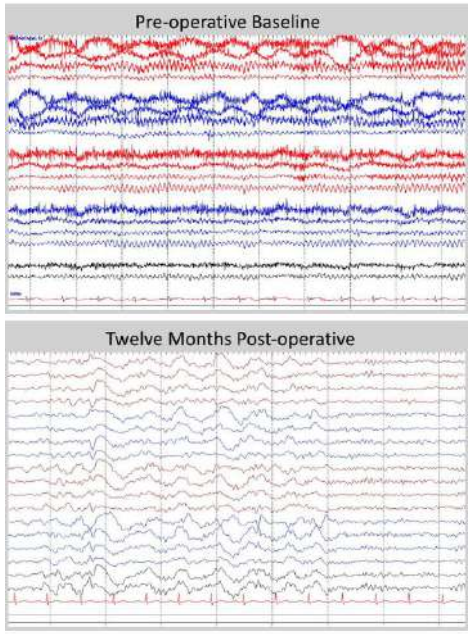
- ✓ Enhanced neuroplasticity
- ✓ Normalizing network connectivity
- ✓ Reduces neuroinflammation

Yuan, T.-F. *et al. Fundamental Research* **5**, 2432–2441 (2025)

4. Other promising intervention

4.2 Closed loop deep brain stimulation (CLDBS)





Bina, R. W. *et al. Front. Neurosci.* **12**, 300 (2018)

The Coping of PTSD: scientific intervention and research prospects

1. Recommended psychotherapy
2. Implications from fear conditioning
3. Pharmacotherapy
4. Other promising intervention
5. **Challenges and prospects**

5. Challenges and prospects

5.1 Identify and classify all biomarker

Biological markers, or biomarkers, are broadly defined as objective indications of the medical state of the person observed

Substance (molecular or histological)

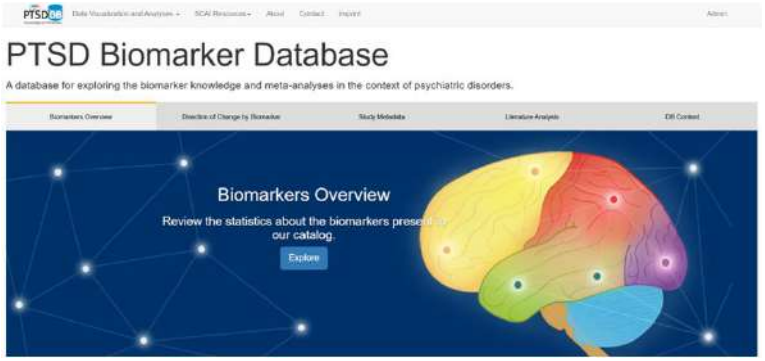
e.g., Methylation changes in the SLC6A4 genes

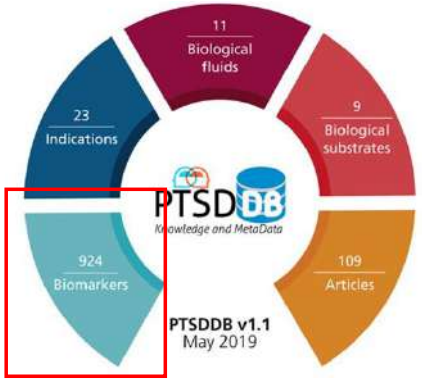
Response (physiological)

e.g., Heart rate variability (HRV)

Structure changes (radiographic)

e.g., Volume in anterior cingulate cortex (ACC)





PTSD Biomarker Database:
https://ptsd.scai.fraunhofer.de/

5. Challenges and prospects

5.2 Comorbidity(共病)

Table 3. Lifetime Comorbidity With PTSD*

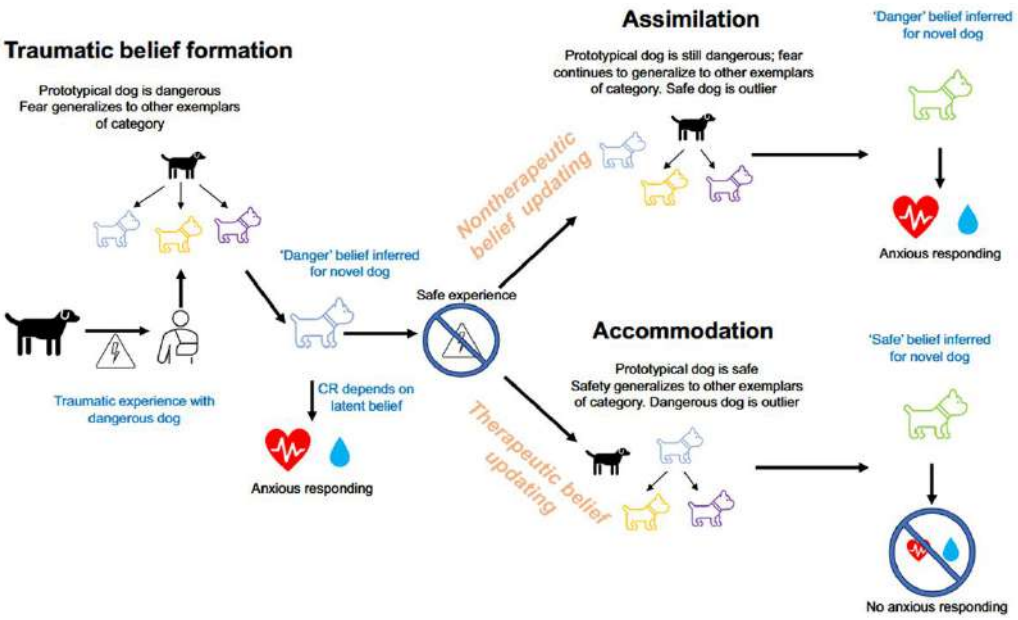
Comorbid Disorders	% of Subjects With PTSD (n=111)	% of Subjects Without PTSD (n=690)	OR (95% CI)
Any anxiety	55.0	26.1	3.46 (2.29-5.21)
Panic disorder	7.2	2.3	3.27 (1.37-7.84)
Agoraphobia	11.7	2.0	6.40 (2.92-14.03)
Simple phobia	36.0	16.1	2.94 (1.90-4.55)
Social phobia	26.1	13.0	2.36 (1.46-3.80)
GAD	4.5	0.7	6.46 (1.84-22.70)
Major depression	43.2	13.3	4.95 (3.21-7.65)
Alcohol A/D	21.6	8.1	3.12 (1.84-5.30)
Marijuana A/D	7.2	2.2	3.49 (1.45-8.45)
Cocaine A/D	3.6	2.0	1.80 (0.58-5.59)
Any illicit drug A/D	13.5	4.8	3.11 (1.63-5.94)
Any disorder	73.0	38.3	4.36 (2.79-6.81)

Breslau, N. *Arch Gen Psychiatry* **54**, 81 (1997)

- **Challenges for diagnosis**
- **Therapeutic regimen**

5. Challenges and prospects

5.3 Computational neuroscience



Biases in latent-state and model-based learning

↓

Behavioral and neurocircuitry findings in PTSD

Cisler, J. M. *et al. Trends in Neurosciences* **47**, 150–162 (2024)

Take-home massages for Part.3

1. **Recommended psychotherapy**
   - **CPT and PE is strongly recommended psychotherapy, the efficacy of EMDR for PTSD is a controversial subject among researchers**

2. **Implications from fear conditioning**
   - **Post-retrieval extinction (PRE) protocol based on Reconsolidation is a promising alternative to the standard ET strategy**

3. **Pharmacotherapy**
   - **Sertraline and paroxetine are the first-line treatments.**
   - **Fluoxetine and venlafaxine are prescribed as off-label medications.**
   - **If failed, antidepressants such as nefazodone, imipramine, and phenelzine were prescribed**

4. **Other promising intervention**
   - **Closed loop deep brain stimulation (CLDBS)**
   - **Repetitive Transcranial magnetic stimulation (rTMS)**

5. **Challenges and prospects**
   - **Identify and classify all biomarker**
   - **Comorbidity as a challenge for diagnosis and treatment**
   - **Computational neuroscience offers a new perspective of PTSD**