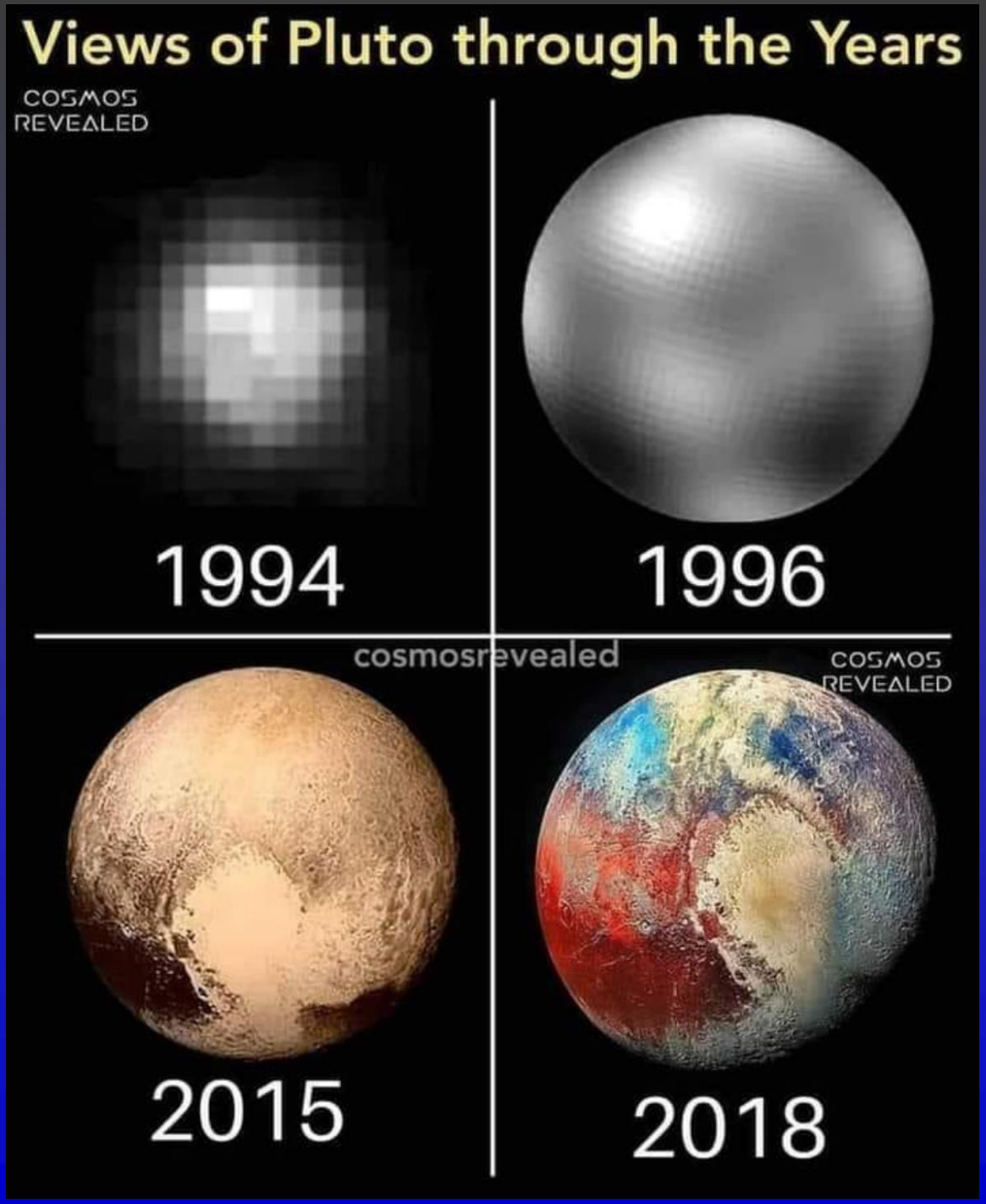
Bessel A. van der Kolk MD & Licia Sky
Trauma Research Foundation www.traumaresearchfoundation.com
www.besselvanderkolk.com

The origins of the diagnosis "PTSD"

PTSD

- Extraordinary event outside ordinary range of human experience
- Memory diagnosis
- DSM III: Too imprecise to ever be used for insurance or forensic purposes


Views of Pluto through the Years
COSMOS
REVEALED
1994
1996
cosmosrevealed
COSMOS
REVEALED
2015
2018

The expression of traumatic stress is highly influenced by cultural context


LUE

Dissociation
The body keeps the score

- Cutting yourself off from you pain, as well as your shame about that pain.
- Lived out in heartbreaking and gut wrenching physical experiences.
- Managing unbearable sensations: 60% of combat vets suffer form drug and alcohol addiction .
- Manifests itself as physical diseases,
- domestic violence, bullying and harassment of others, indiscriminate sexual activity, and self-harming, violent, or adrenaline-seeking behavior

Scope of Childhood Trauma

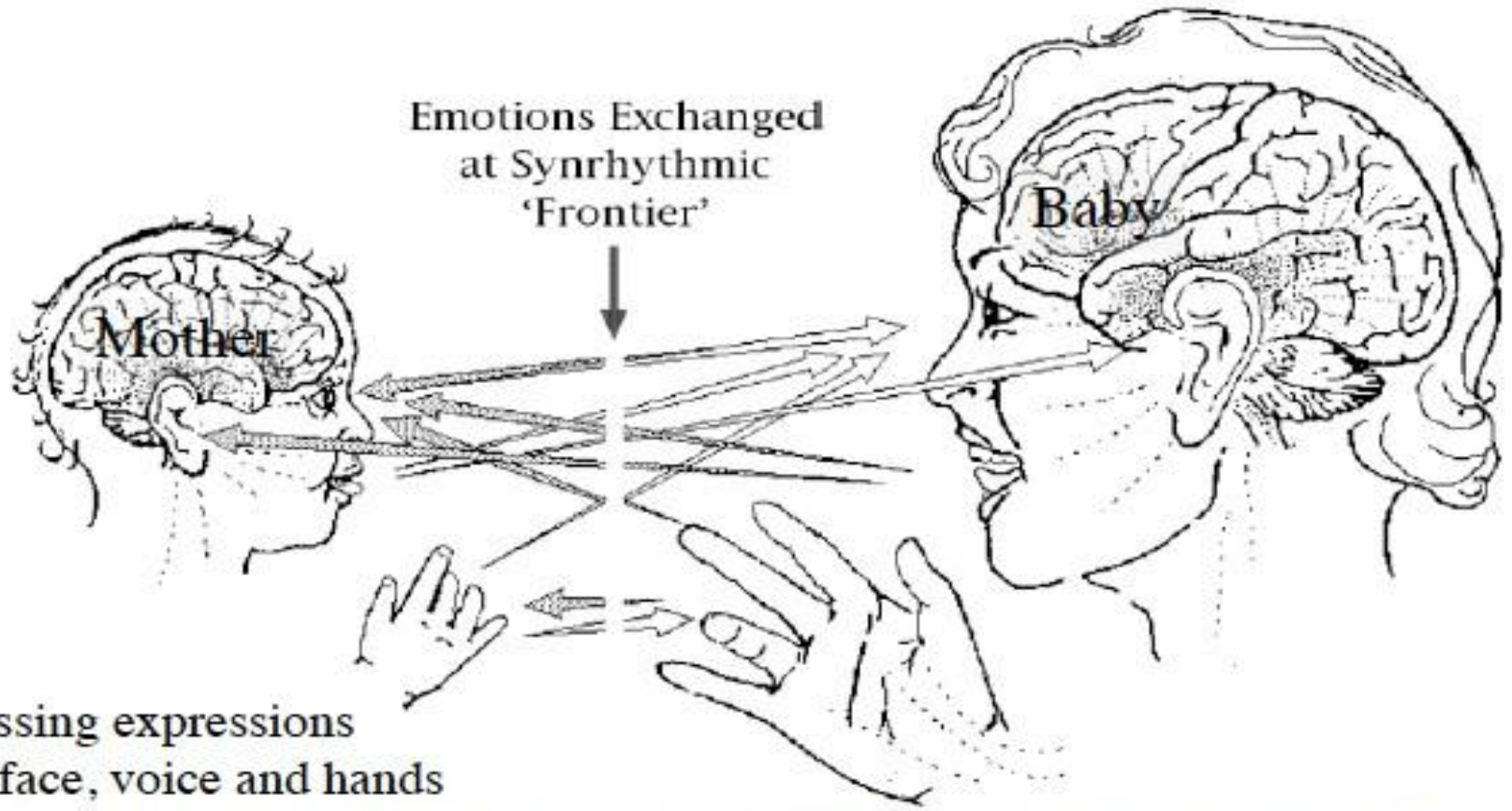
- The U.S. Centers for Disease Control (CDC) estimates that **1 in 8 children** between ages 2 and 17 is a victim of maltreatment.
- Developmental Victimization Study finds that **71%** of U.S. children had at least one form of victimization
- Gun related deaths leading cuase in children and adolescents in US
- March 2016 Pediatrics: **50%** of children in Asia, Africa and North America witness violence each year.

That is: over 1,000,000,000 children each year.

Attachment:

The critical variable

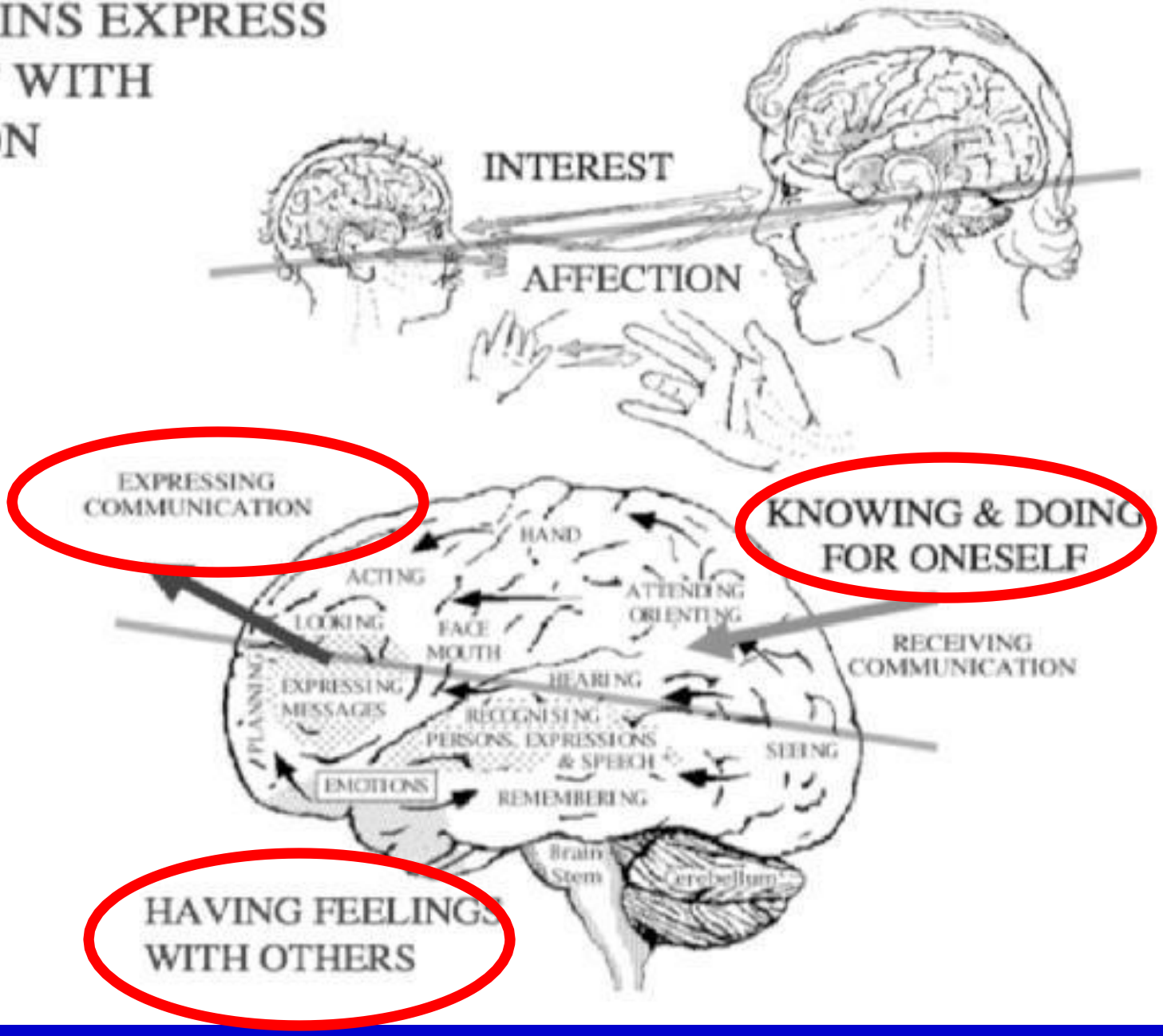
SYNRHYTHMIC REGULATION: Mother and infant can communicate **psychologically**, regulating sympathy by expressions of emotion.

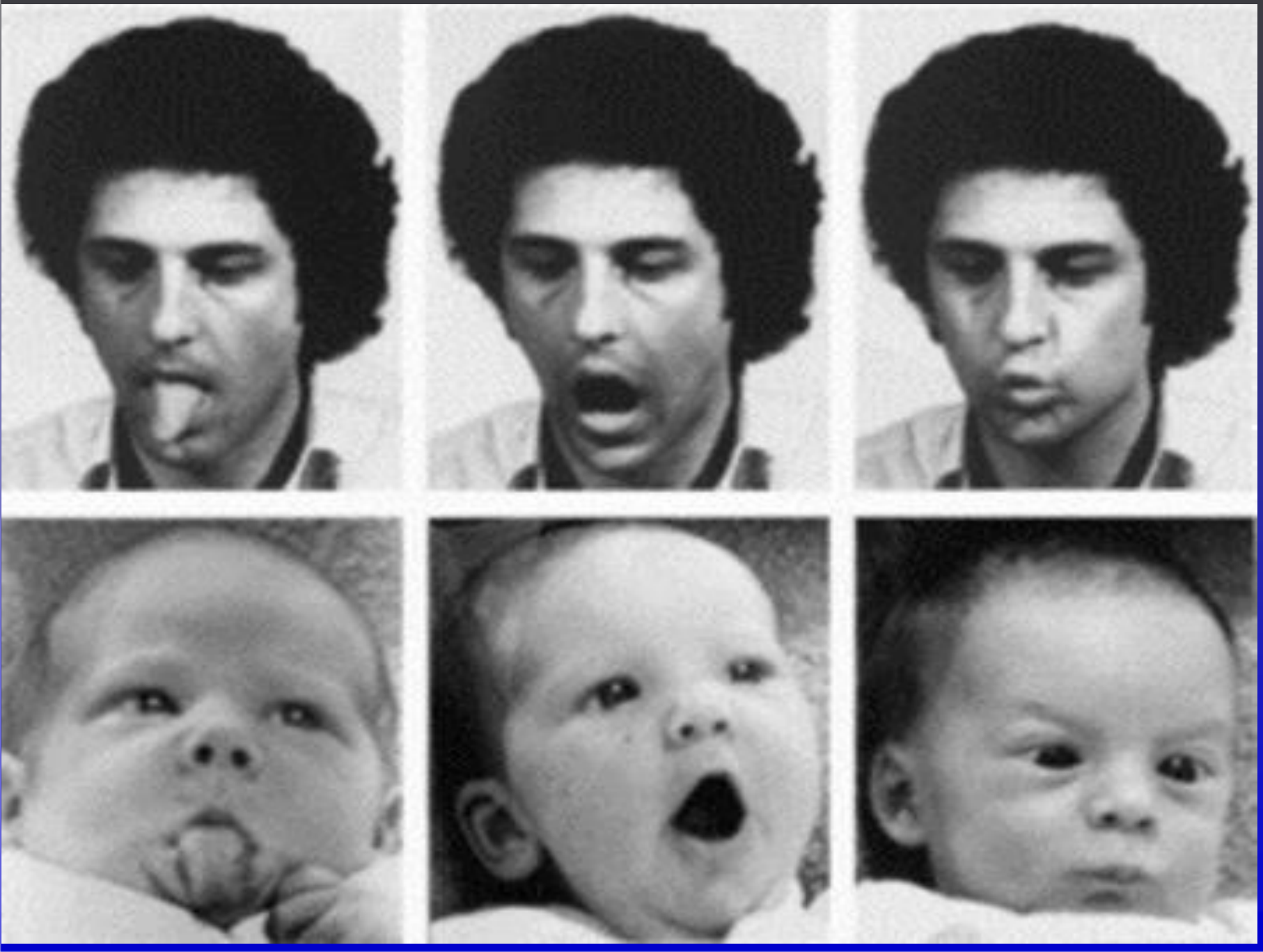


Passing expressions
of face, voice and hands
back and forth, rhythmically, imagining each other, participating in feelings

Telling and acting out stories with emotion, listening to thoughts and imitating actions is how humans learn -- in shared vitality and awareness.

HOW BRAINS EXPRESS INTEREST WITH AFFECTION





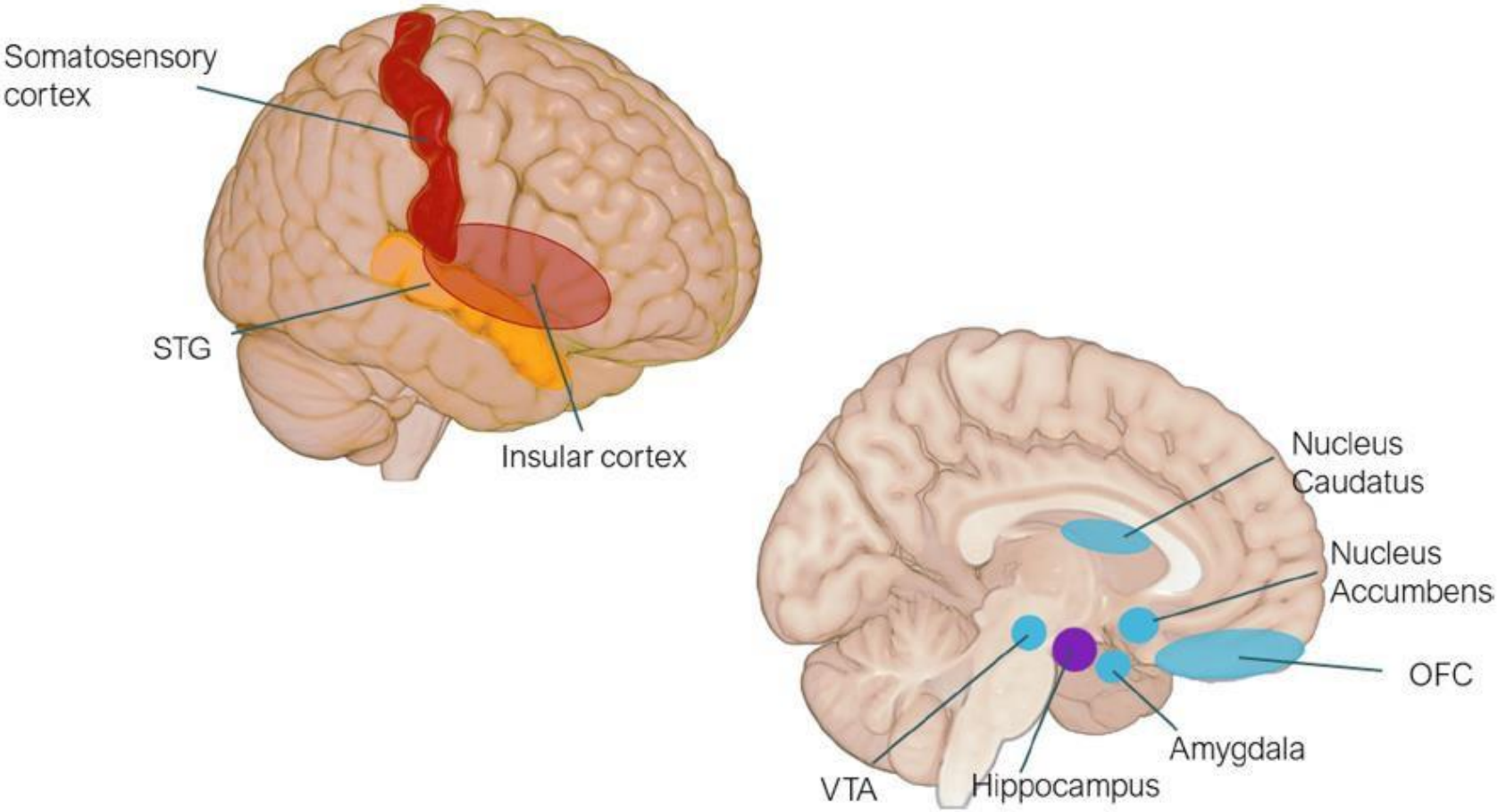


Fig. 1. Brain regions associated with touch processing after trauma. Red represents evidence for significant hyperactivity in response to CT-suboptimal interpersonal touch in trauma-exposed individuals, purple represents evidence for significant hypoactivity in response to CT-optimal interpersonal touch (Maier et al., 2020b). Orange indicates increased responses to interpersonal and impersonal CT-optimal and CT-suboptimal touch in the superior temporal gyrus (STG) after trauma exposure (Strauss et al., 2019b). Previous studies did not observe significant trauma-related responses to social touch in reward areas or the amygdala (marked in blue). We hypothesise that trauma-associated changes in these areas are context-dependent (e.g. changes may become evident if reward areas are more strongly activated irrespective of trauma). Abbreviations: orbitofrontal cortex (OFC), superior temporal gyrus (STG), and ventral tegmental area (VTA).

ACE study
Turning gold into lead

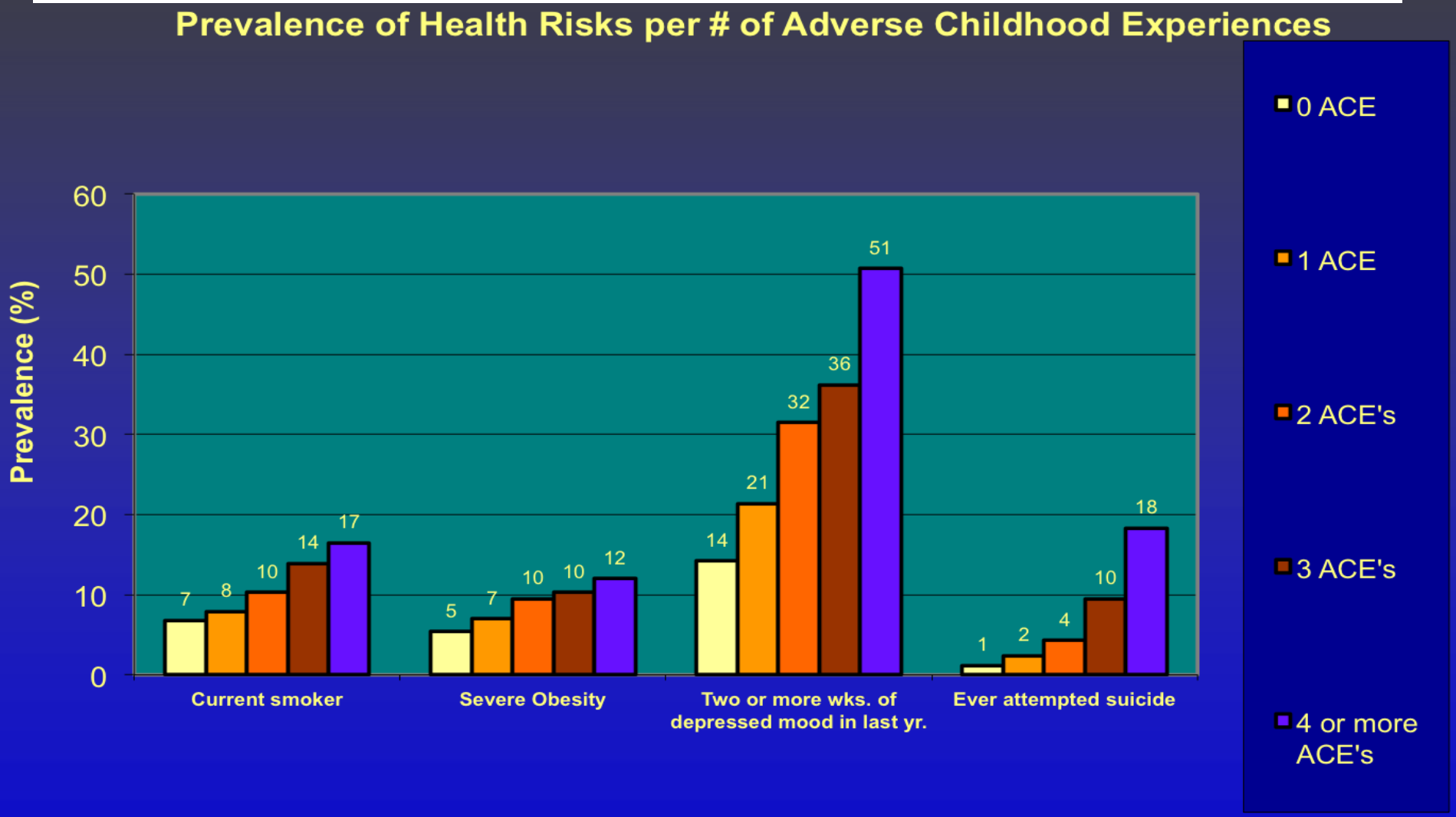
How does one turn this

Into this

in twenty years?

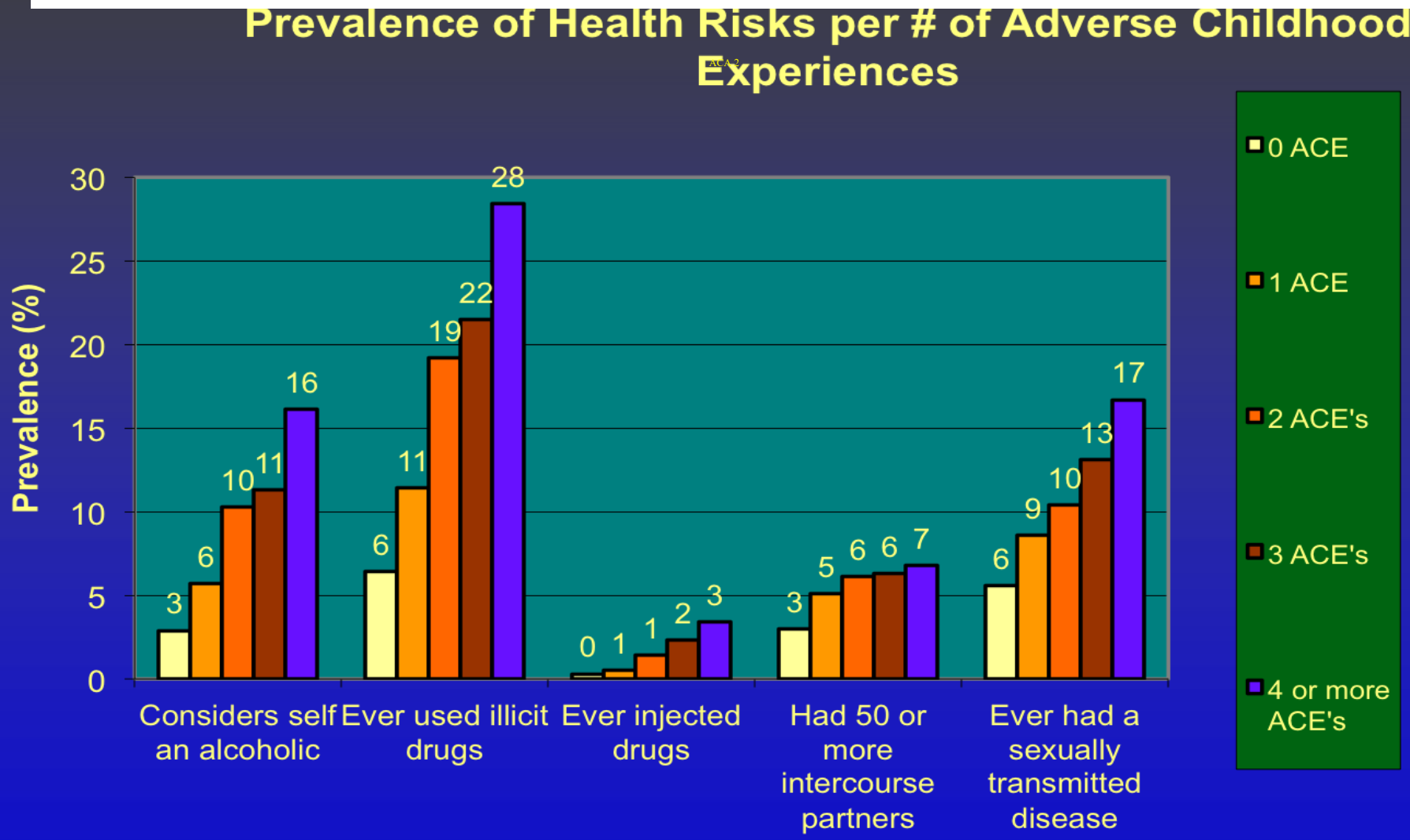
ACE Study	N=17,337
Emotional abuse 10.6 (Did a parent or other adult in the household . . .) 1) Often or very often swear at you, insult you, or put you down? 2) Sometimes, often, or very often act in a way that made you fear that you might be physically hurt?	10.6
Physical 28.3 (Did a parent or other adult in the household . . .) 1) Often or very often push, grab, slap, or throw something at you? 2) Often or very often hit you so hard that you had marks or were injured?	28.3
Sexual 20.7 (Did an adult or person at least 5 years older ever . . .) 1) Touch or fondle you in a sexual way? 2) Have you touch their body in a sexual way? 3) Attempt oral, anal, or vaginal intercourse with you? 4) Actually have oral, anal, or vaginal intercourse with you?	20.7
Household dysfunction Substance abuse 26.9 1) Live with anyone who was a problem drinker or alcoholic? 2) Live with anyone who used street drugs?	26.9
Mental illness 19.4 1) Was a household member depressed or mentally ill? 2) Did a household member attempt suicide?	19.4
Mother treated violently 12.7 (Was your mother (or stepmother)): 1) Sometimes, often, or very often pushed, grabbed, slapped, or had something thrown at her? 2) Sometimes, often, or very often kicked, bitten, hit with a	12.7

Effects of Child Maltreatment on Health



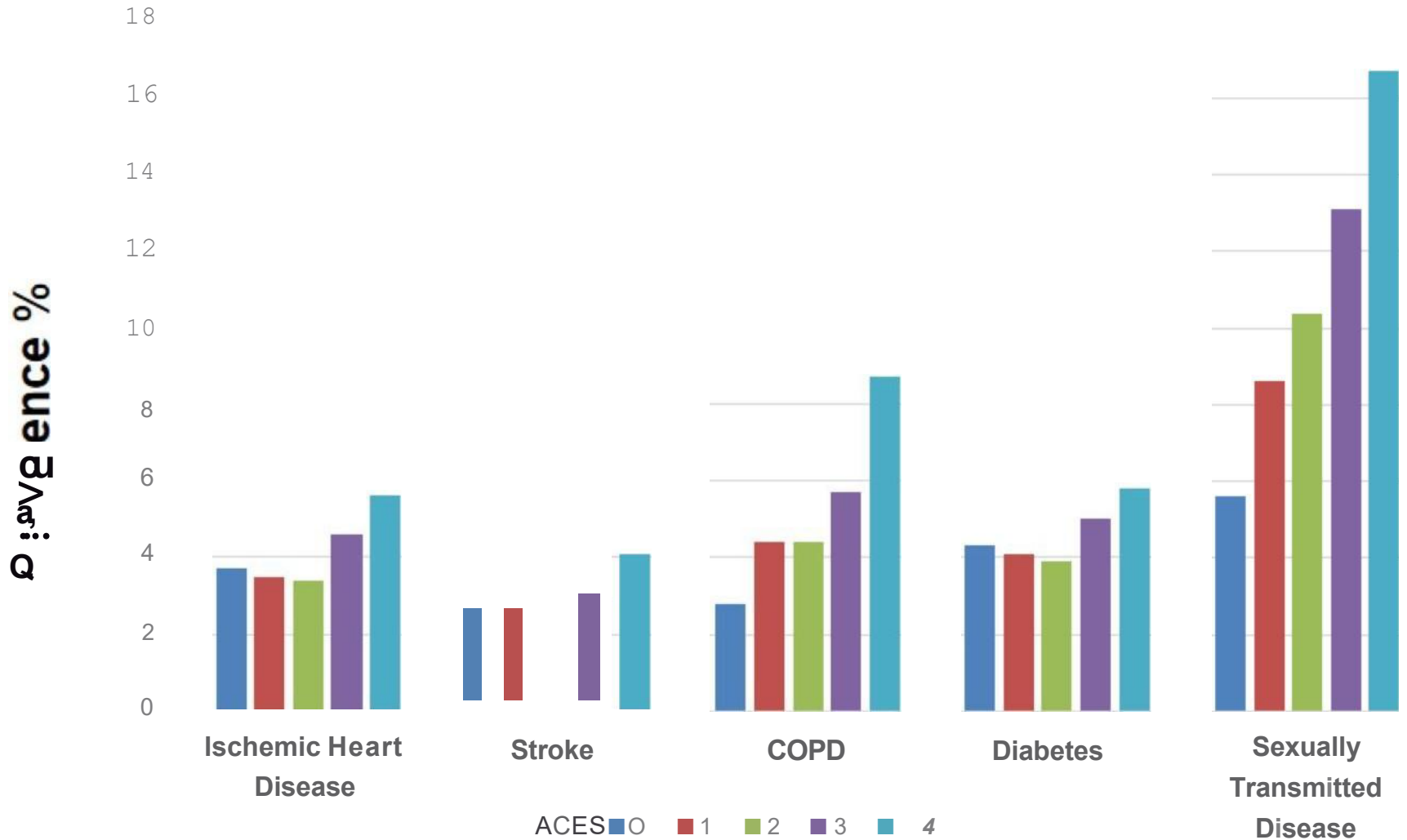
Felitti, et al (1998). Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults. *Am J Prev Med* 14(4).

Effects of Child Maltreatment on Health



Felitti, et al (1998). Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults. *Am J Prev Med* 14(4).

Cumulative ACES & Chronic Disease[1]



Impact of Cumulative **ACES** & Social Dysfunction[1]

- Lower educational, occupational attainment.
- Increased social service costs.
- Increased medical costs.
- Shortened life span.
- Increased risk for HIV, teen pregnancy, maternal depression[2].
- Intergenerational transmission of ACES to offspring.

[1]IOM (Institute of Medicine) and NRC (National Research Council). 2013.

Pervasive problems

More than 50% with ACE scores of 4 or higher had learning or behavioral problems in school, (cf. 3 % of those with a score of zero.

Children do not “outgrow” the effects of their early experiences.

High ACE scores correlated with higher workplace absenteeism, financial problems, pain medications, antidepressants, anti psychotics, and lower lifetime income.

Felitti: “Traumatic experiences are often lost in time and concealed by shame, secrecy, and social taboo”

Estimates of the Population Attributable Risk* (PAR) of ACEs for Selected Outcomes in Women

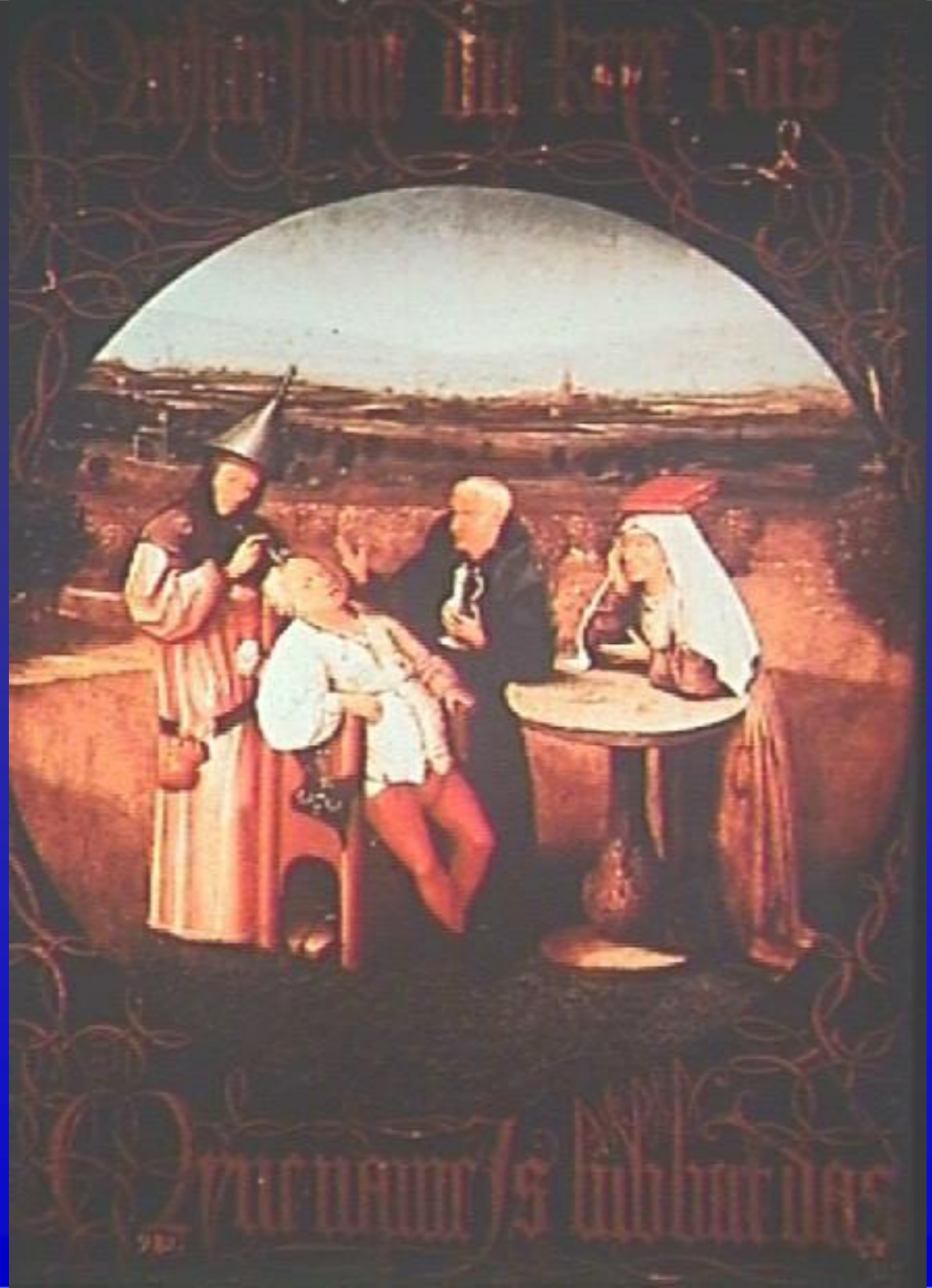
Mental Health:	PAR
Current depression	54%
Suicide attempt	58%
Drug Abuse:	
Alcoholism	65%
Drug abuse	50%
IV drug abuse	78%
Crime Victim:	
Sexual assault	62%
Domestic violence	52%

*Based upon the prevalence of one or more ACEs (62%) and the adjusted odds ratio ≥ 1 ACE

CDC
SAFER · HEALTHIER · PEOPLE

What is trauma?


TO COMMEMORATE
THE DISCOVERY
THAT THE INHALING OF ETHER
CAUSES INSENSIBILITY TO PAIN·
FIRST PROVED TO THE WORLD
AT THE
MASS· GENERAL HOSPITAL
IN BOSTON
OCTOBER A·D· MDCCCXLVI·



Victory over Pain - pre-anesthetic surgery

George Wilson, Doctor of medicine, 1847

"Several years ago I was required to prepare, on a very short warning, for the loss of a limb by amputation.

I at once agreed to submit for the operation, but asked for a week to prepare --- simply because it was so probable that the operation would be followed by a fatal issue.

"Of the agony it occasioned, I will say nothing.

Suffering so great as I underwent cannot be expressed in words, and thus cannot be recalled.

The particular pangs are now forgotten; but the black whirlwind of emotion, the horror of great darkness, and the sense of desertion by God and man, bordering close upon despair, which swept through my mind and overwhelmed my heart, I can never forget, however gladly I would do so…..

Further, during the operation, in spite of the pain it occasioned, my senses were preternaturally acute..

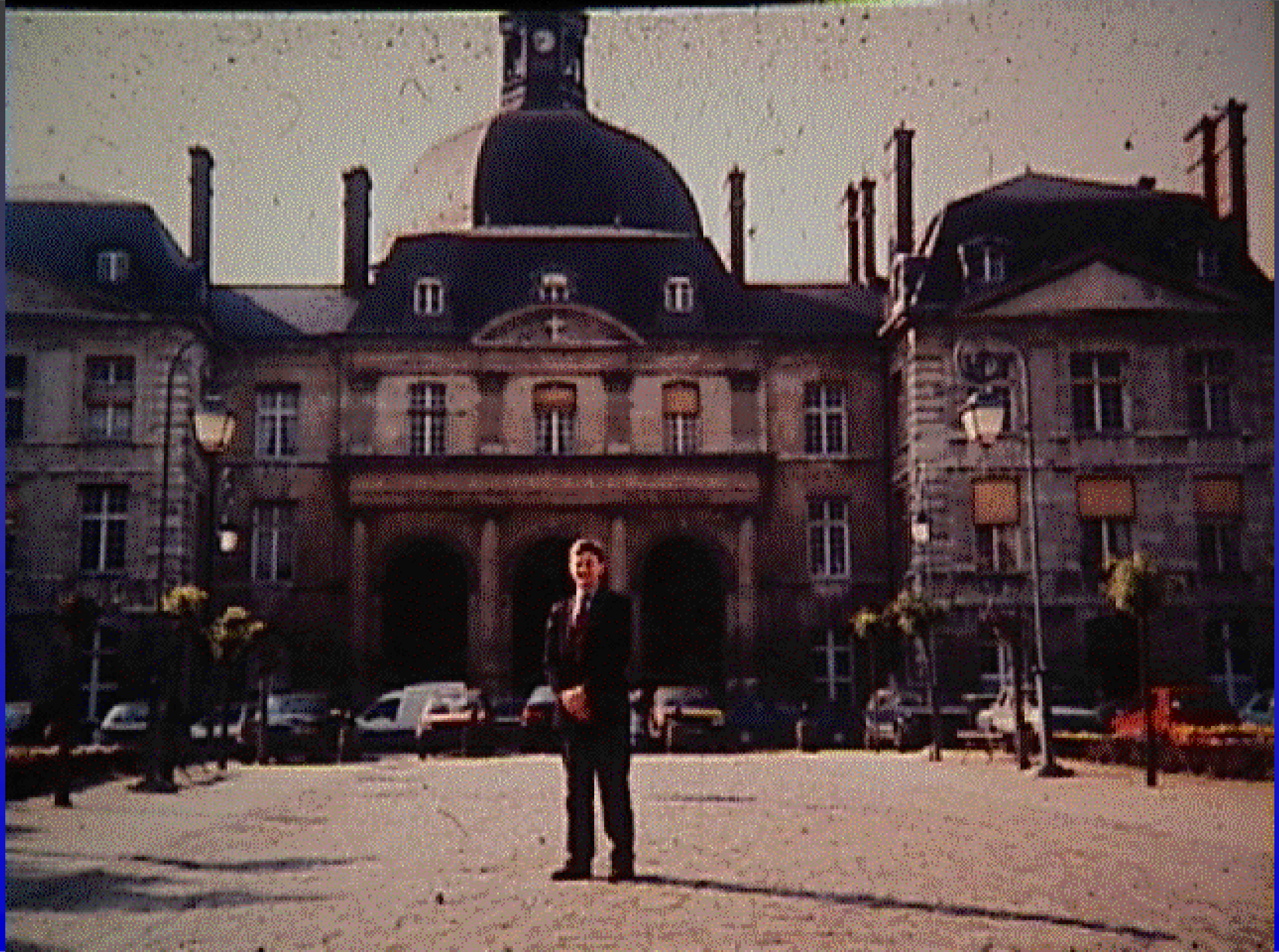
I still recall with unwelcome vividness the spreading out of the instruments; the twisting of the tourniquet; the first incision; …… and the bloody dismembered limb lying on the floor.

George Wilson, Doctor of medicine, 1847.

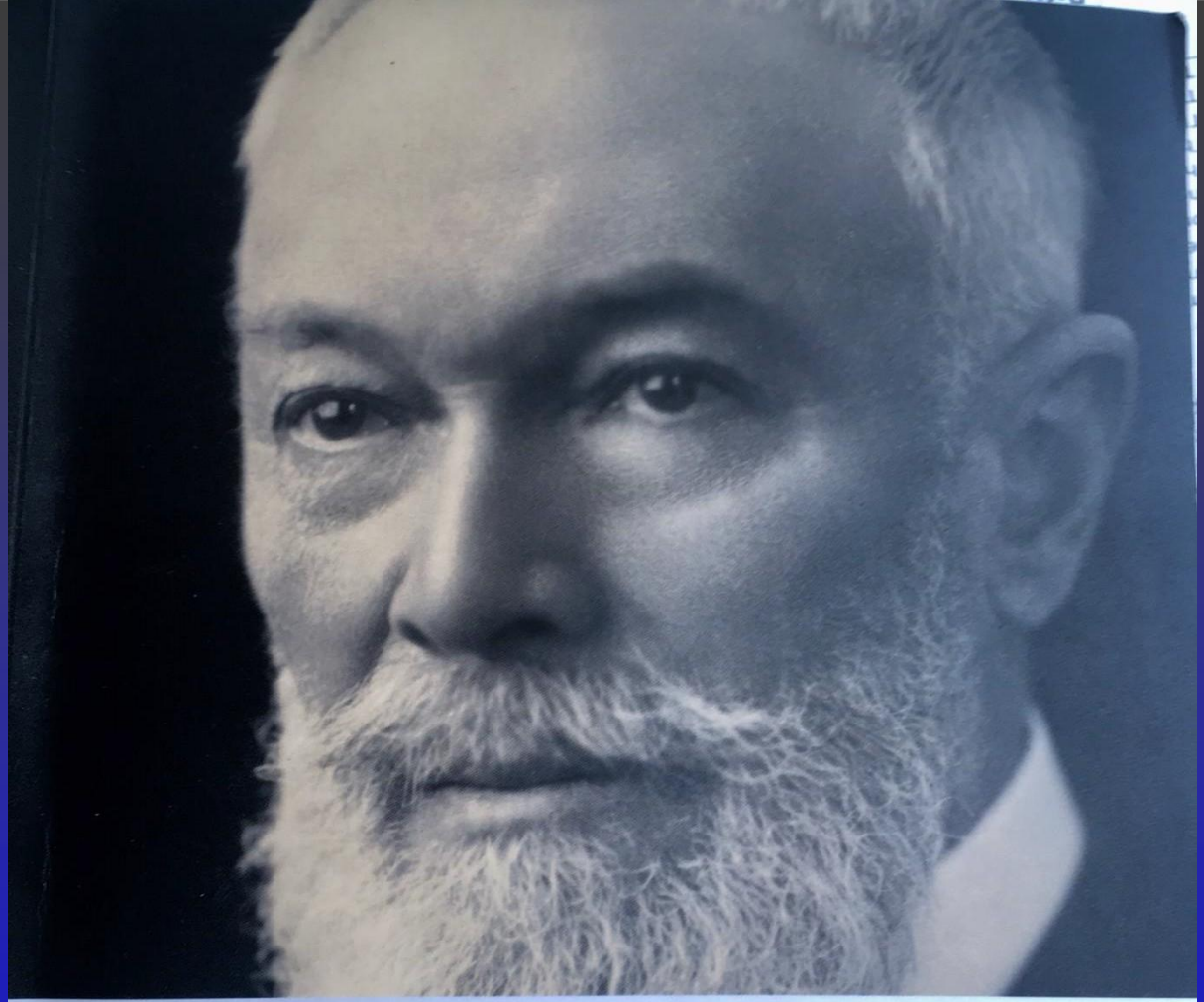
“These are not pleasant remembrances. For a long time they haunted me, and even now they are easily resuscitated;

and though they cannot bring back the suffering attending the events which gave them a place in my memory, they can occasion a suffering of their own, and be the cause of disquiet which favours neither mental nor bodily health”

Traumatic memories



Bessel



REDISCOVERING PIERRE JANET

Trauma, Dissociation, and a New Context for Psychoanalysis

Edited by Giuseppe Craparo, Francesca Ortu,

Pierre Janet on Traumatic Memories

L'Automatisme Psychologiques (1889)

"(1894)

I was led to recognize in many patients the role of events that had been accompanied by *intense emotions*. Failure to master these overwhelming emotions led them to react to stress with excessive and irrelevant responses(1889).

"automatisms"

"The remembrance of these events absorbed a great deal of energy and played a role in a persistent weakening of the self"

The integration of experience

- **When people are too upset to translate their experience into words, their memories cannot be transformed into a simple story about something that happened long ago:**
- **The memories of those experiences then are split off from conscious awareness and voluntary control.**
- **Fragments of those unintegrated events then later show up as automatic motor actions, images and sensations.**
- **Until about 1990 hypnosis was the treatment of choice**

Janet: Fixation on the Trauma

"Unable to integrate the traumatic memories, they seem loose their capacity to integrate other experiences, as well" (1919).

"It is as if their personality development has stopped at a certain point and cannot continue to expand by the assimilation of new experiences" (1911):

"All traumatized people seem to have the evolution of their lives halted: they are attached to an insurmountable obstacle" (1919)

The Etiology of Hysteria, 1893

Breuer & Freud

The .. memory of the trauma .. acts like a foreign body which long after its entry must be regarded as an agent that is still at work”

The fading of a memory or the losing of its affect depends on various factors. The most important of these is whether there has been an energetic reaction to the event that provokes an affect.

"If a **(physical)** ***reaction*** *is suppressed [the affect] stays attached to the memory"*

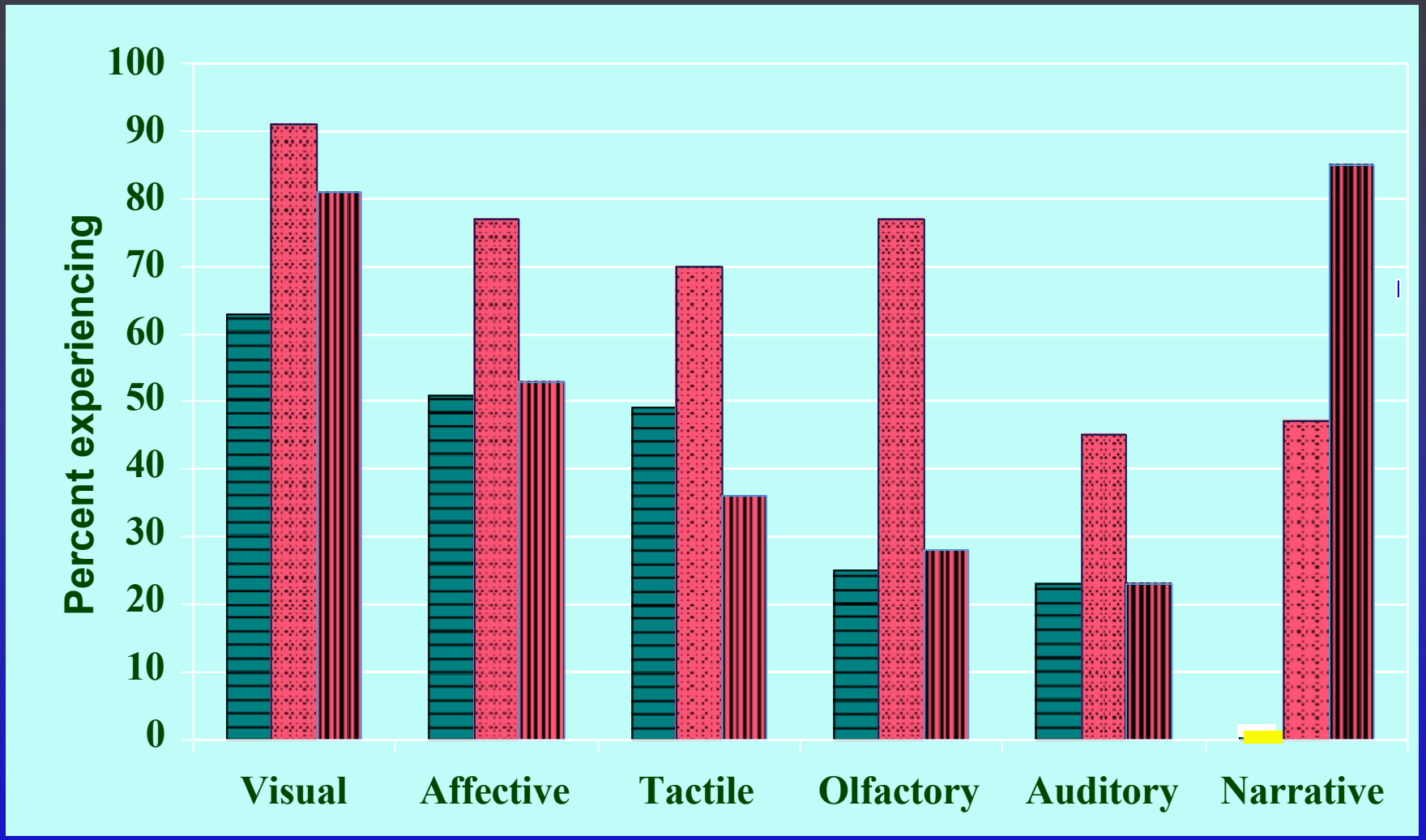
The defining statement of 20th (& 21st) century psychology

"But language serves as a substitute for action: with its help, an affect can be 'abreacted' almost as effectively".

"It brings to an end the operative force of the idea which was not abreacted in the first instance, by allowing it strangulated affect to find a way out through speech;

"and it creates an associative correction by introducing it into normal consciousness.

First TRAUMA CLINIC MEMORY STUDY, J. Trauma Stress, 1995



Sensory modalities in which trauma was experienced initially, at peak, and currently

Nobody wants to remember trauma

Patients themselves

Professional societies

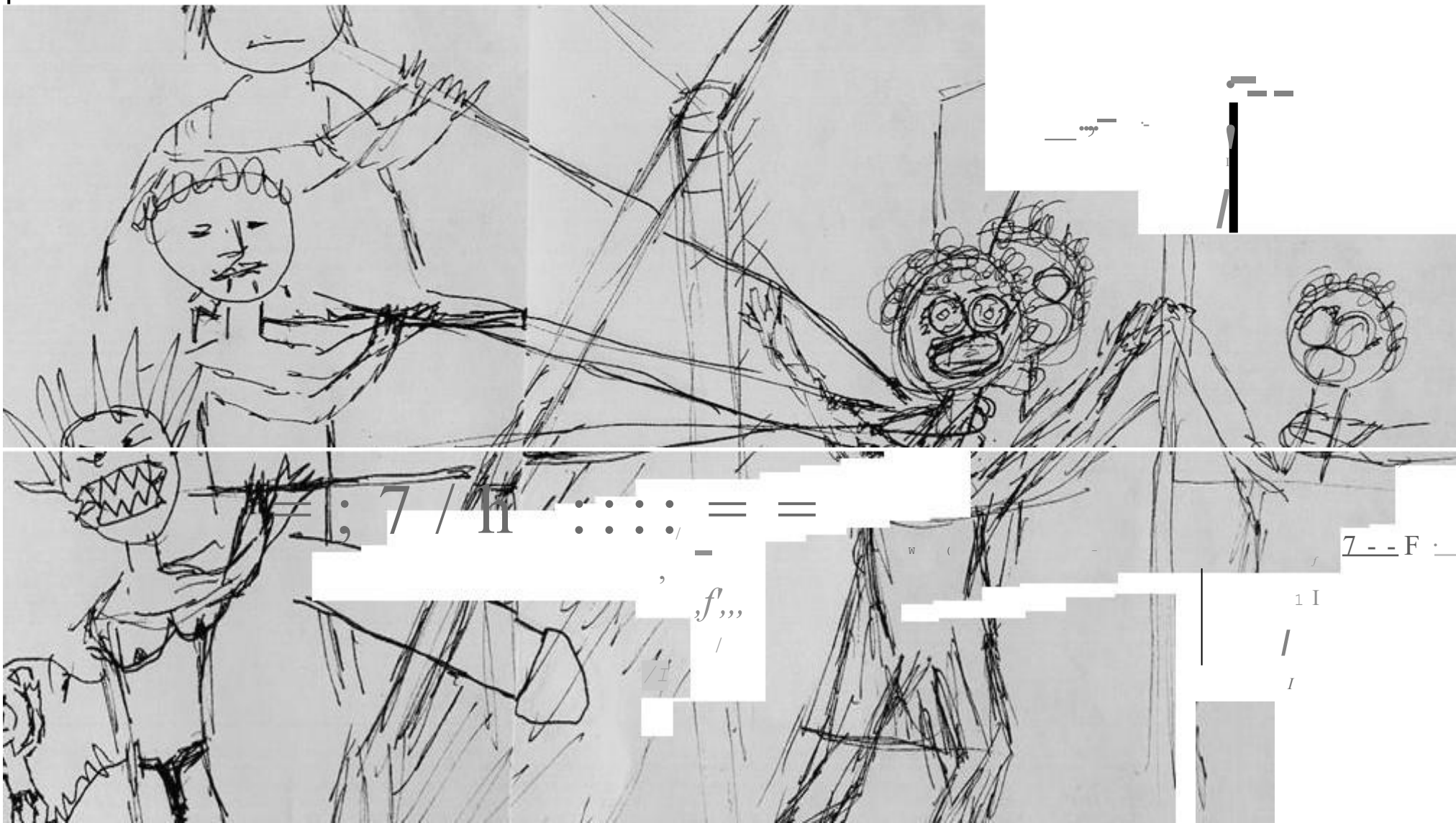
Freedman, Kaplan & Sadock's Comprehensive Textbook of Psychiatry, II. 1975

Friedman & Kaplan

Incest in the United States: one out of 1.1 million women

'There is little agreement about the role of father-daughter incest as a source of serious subsequent psychopathology.

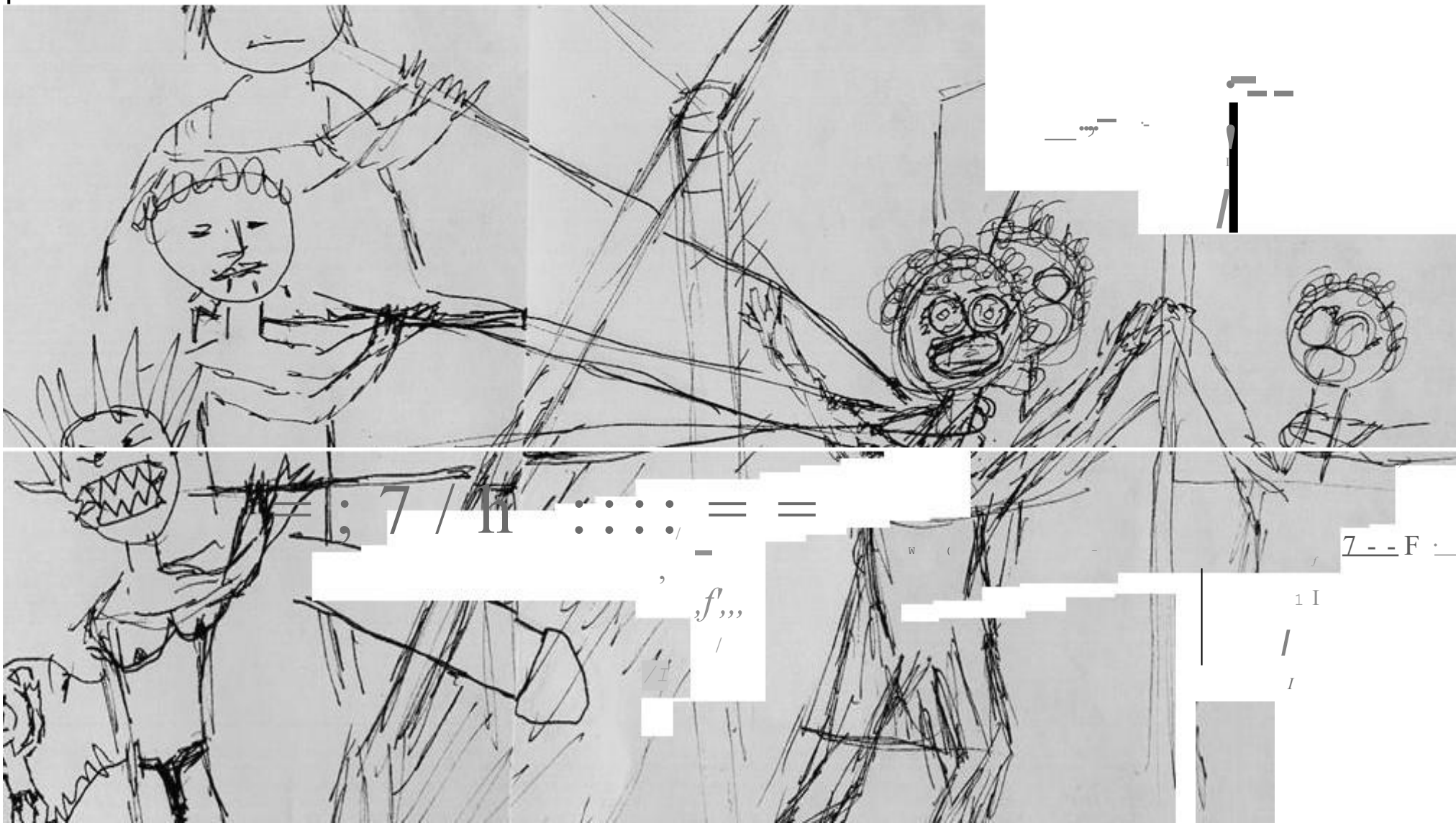
The father-daughter liaison satisfies instinctual drives in a setting where mutual alliance with an omnipotent adult condones the transgression. .. The act offers an opportunity to test in reality an infantile fantasy whose consequences are found to be gratifying and pleasurable..... such incestuous activity diminishes the subject's chance of psychosis and allows for a better adjustment to the external world.



Immune function in women with incest histories

van der Kolk, Wilson, Burbridge & Kradin

		mean	SD	#observ	sign
CD3	patients	69.7	12.8	12	.813
	controls	68.6	9.1	12	
CD4	patients	47.6	12.4	12	.905
	controls	48.1	7.3	12	
CD8	patients	23.2	9.0	12	.604
	controls	25.2	9.6	12	
CD25	patients	3.9	1.9	12	.450
	controls	4.5	1.8	12	
CD45RA	patients	50.8	12.1	12	.157
	controls	57.9	11.9	12	
CD45RO	patients	36.8	11.3	12	.092
	controls	30.2	6.3	12	
RA:RO ratio	patients	1.5	0.51	12	.046
	controls	2.0	0.65	12	



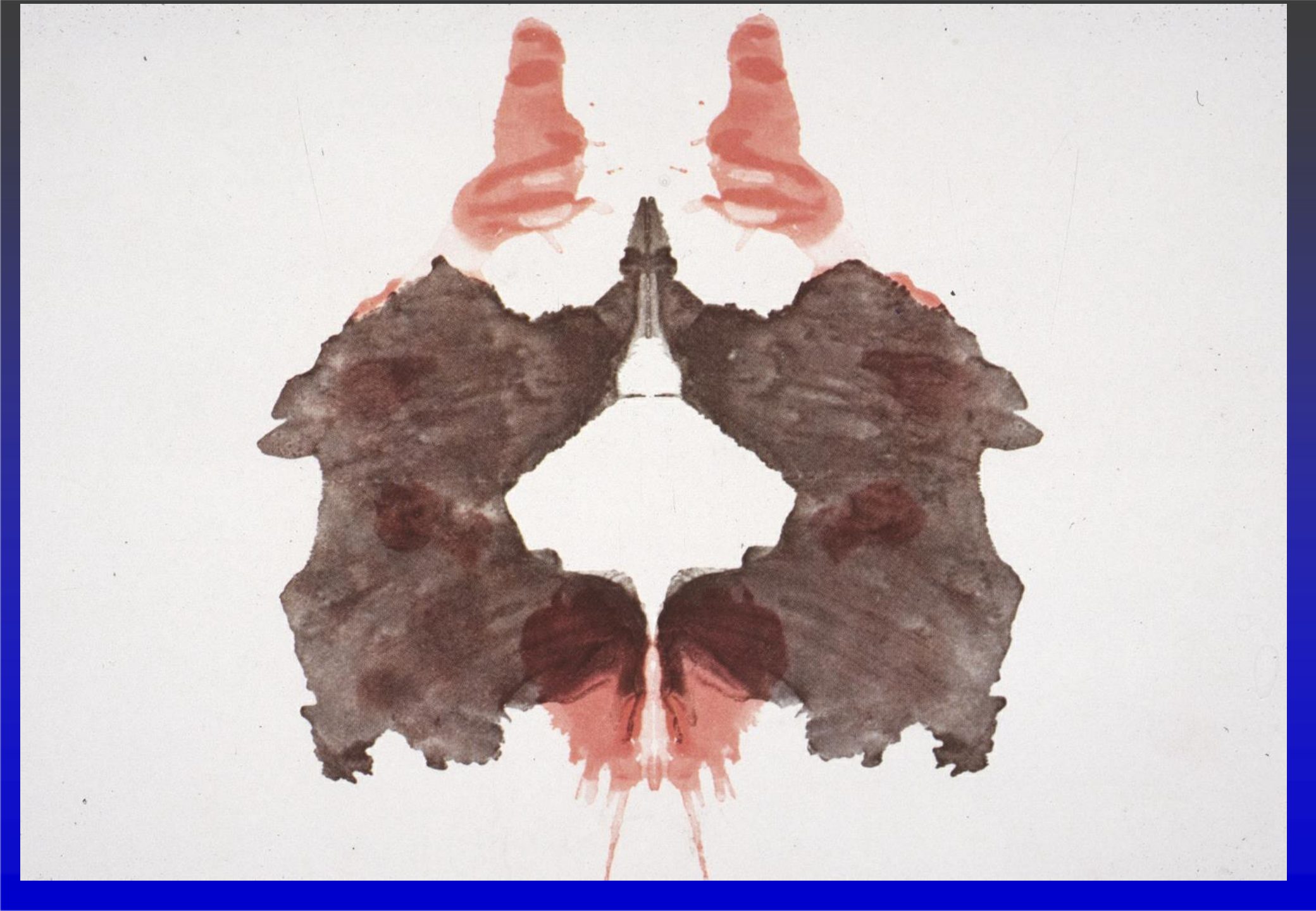
After you have been traumatized you live in a different universe

How do you measure the inner world that we inhabit?

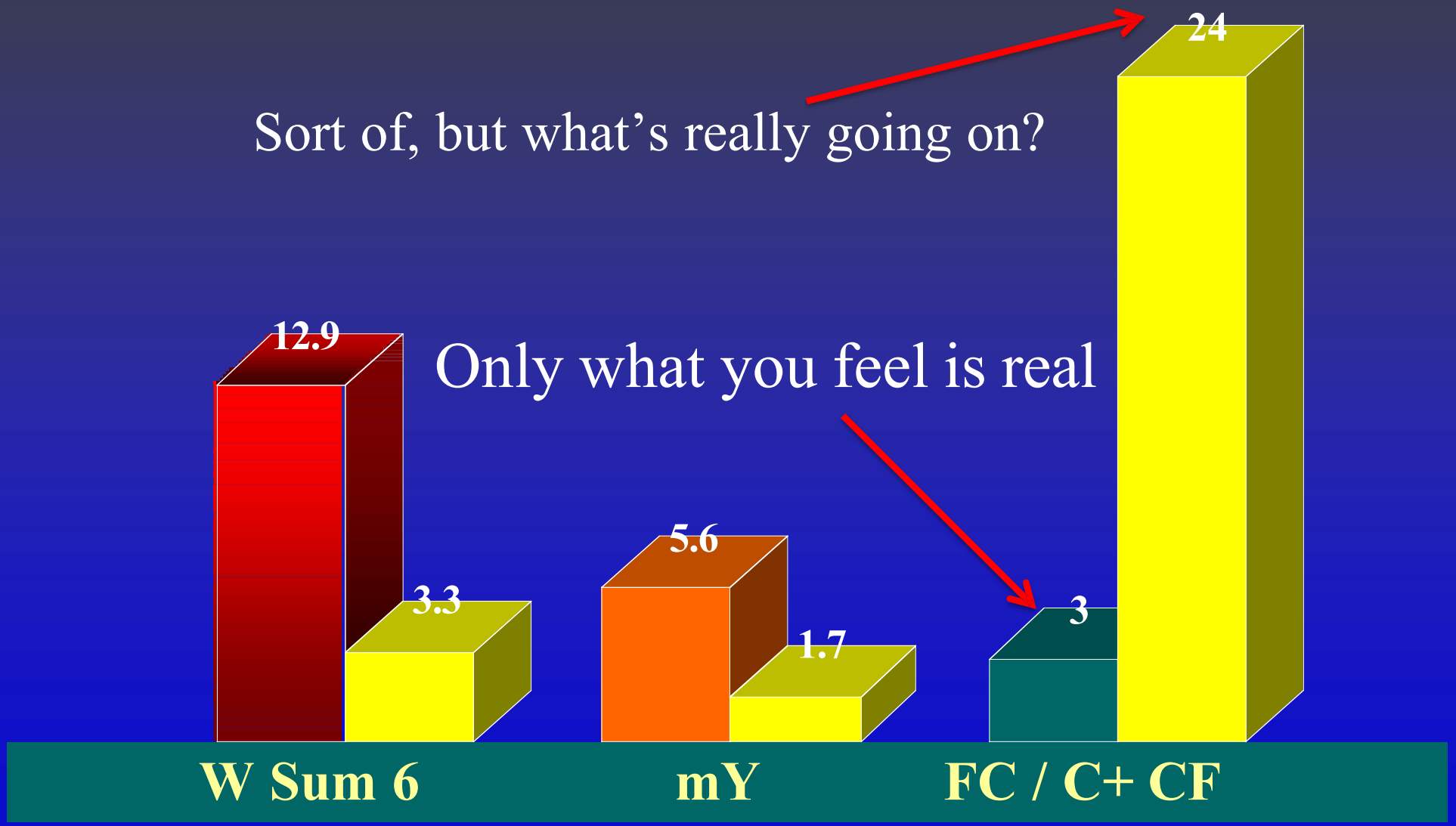
Self-report?

Brain scans?

Projective testing

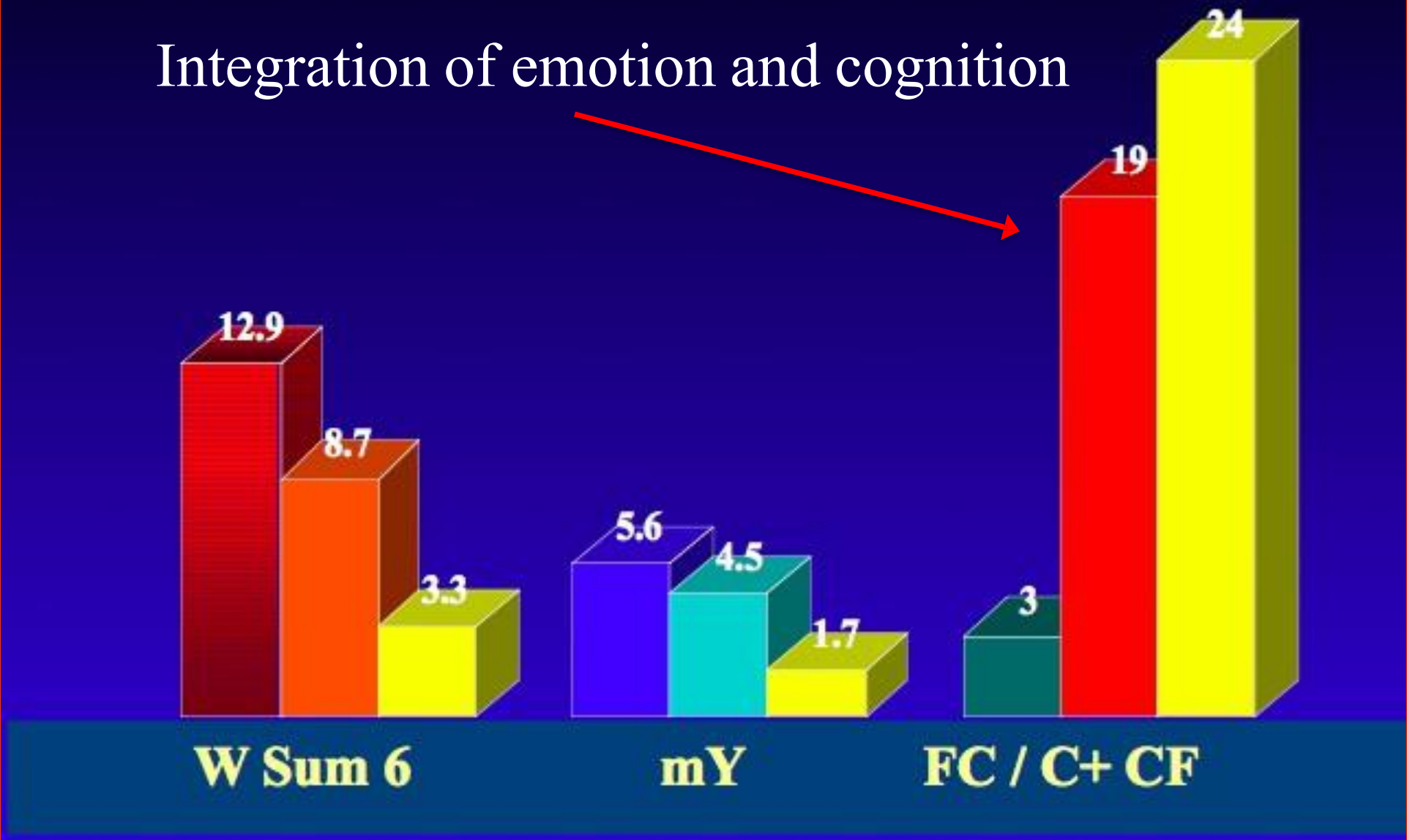


RORSCHACH DETERMINANTS: EXNER NORMS VS PTSD



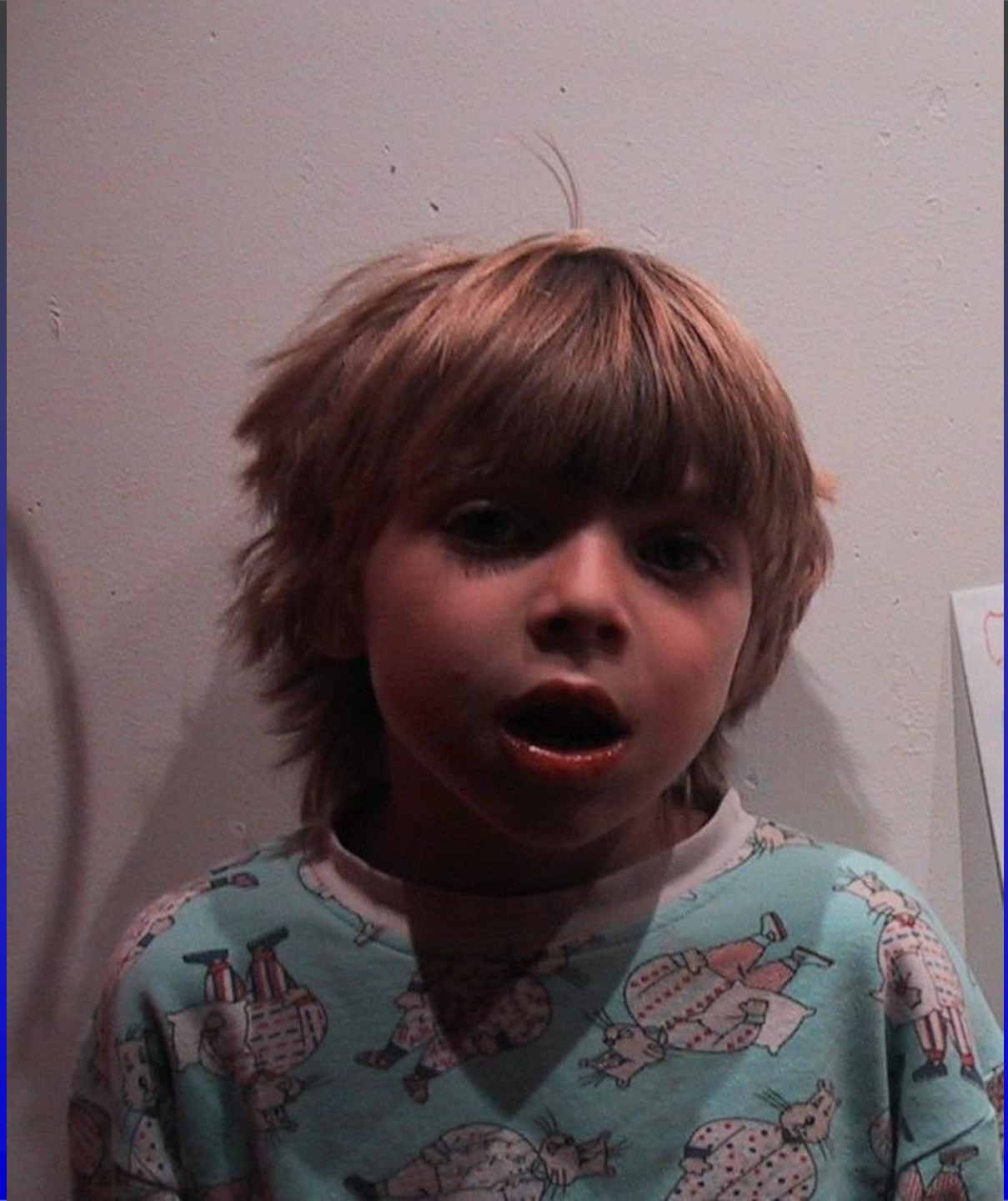
Recovery from traumatic stress

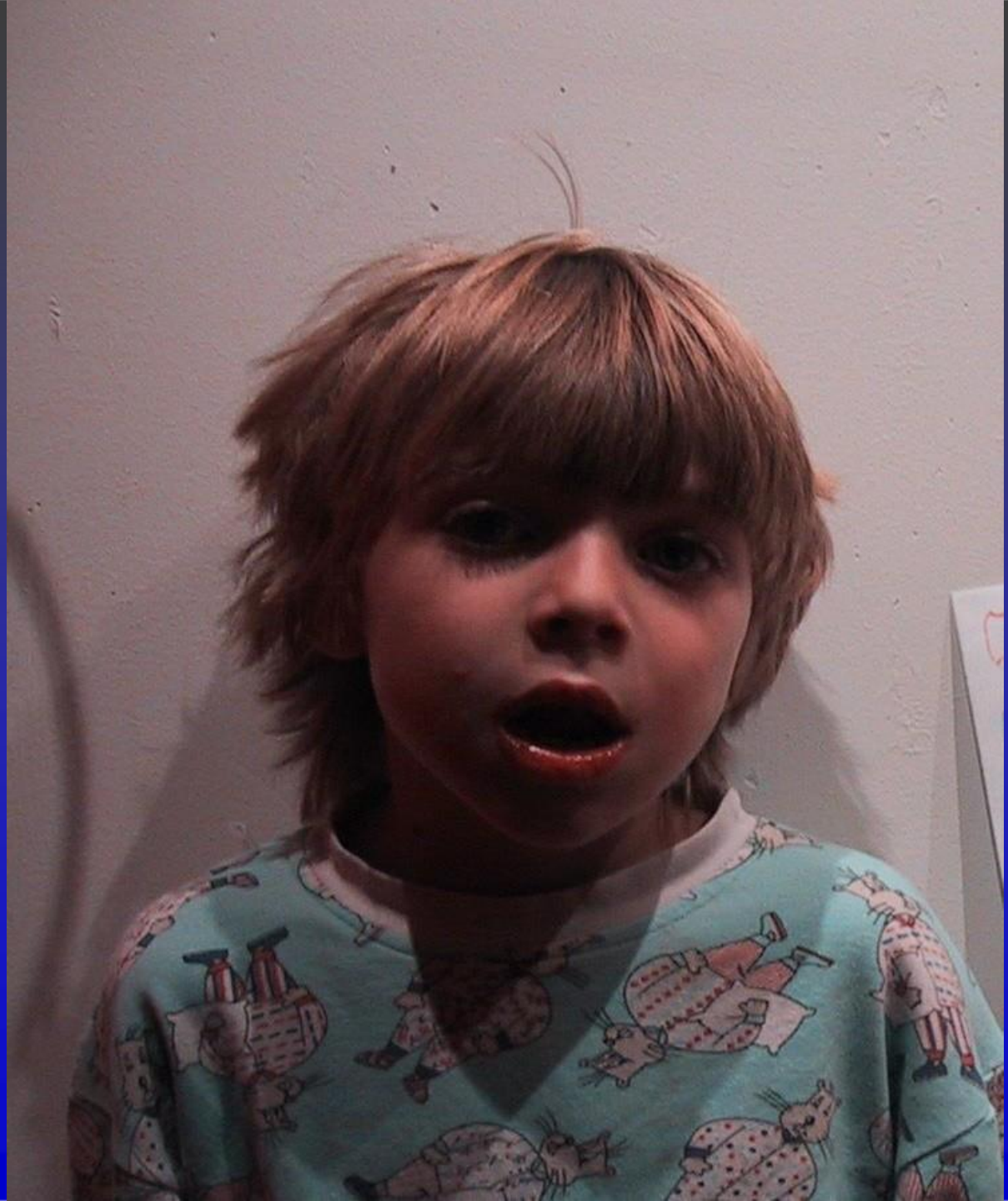
Integration of emotion and cognition



How do children deal with trauma?

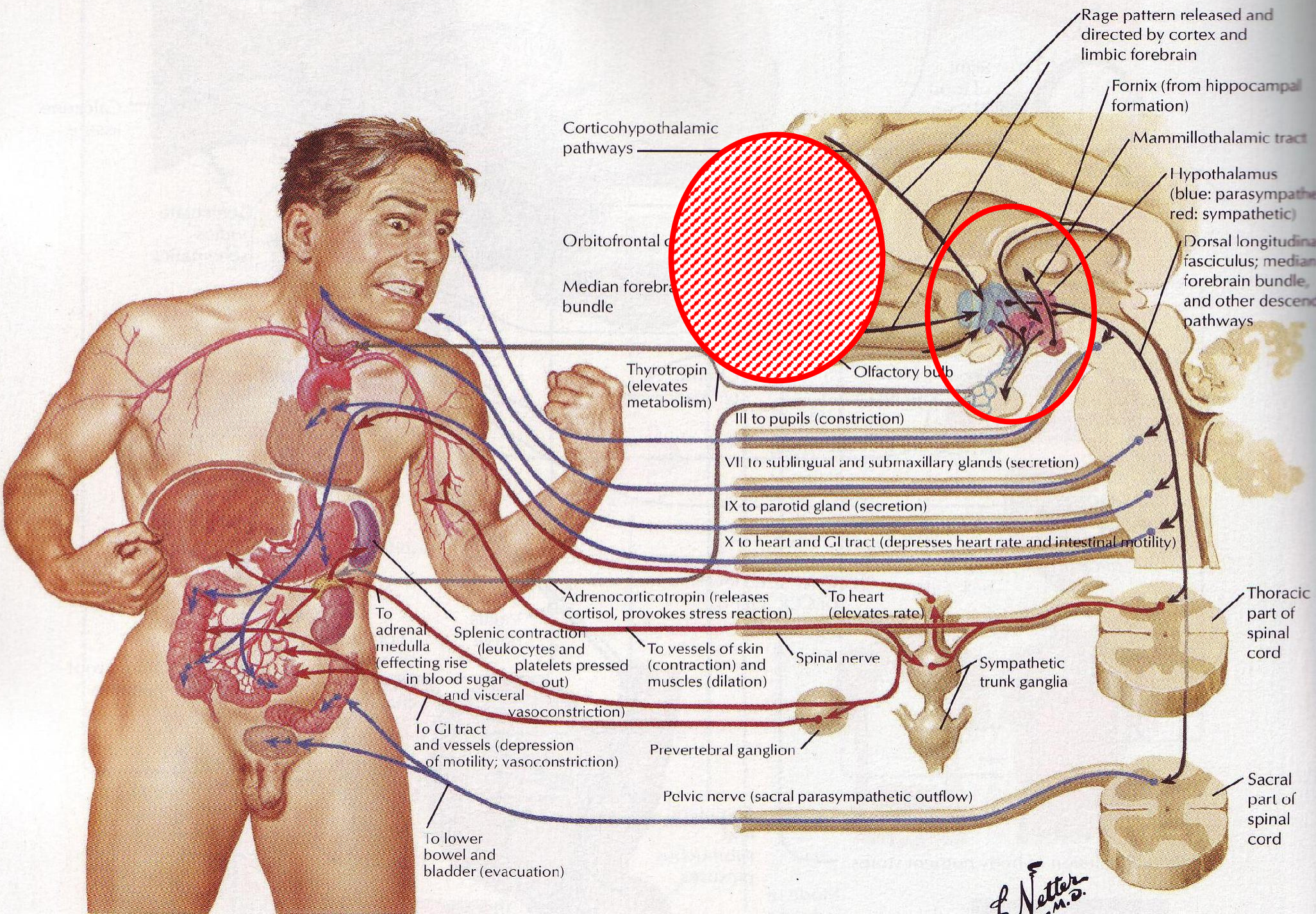
- It all depends on the quality of their attachment system.

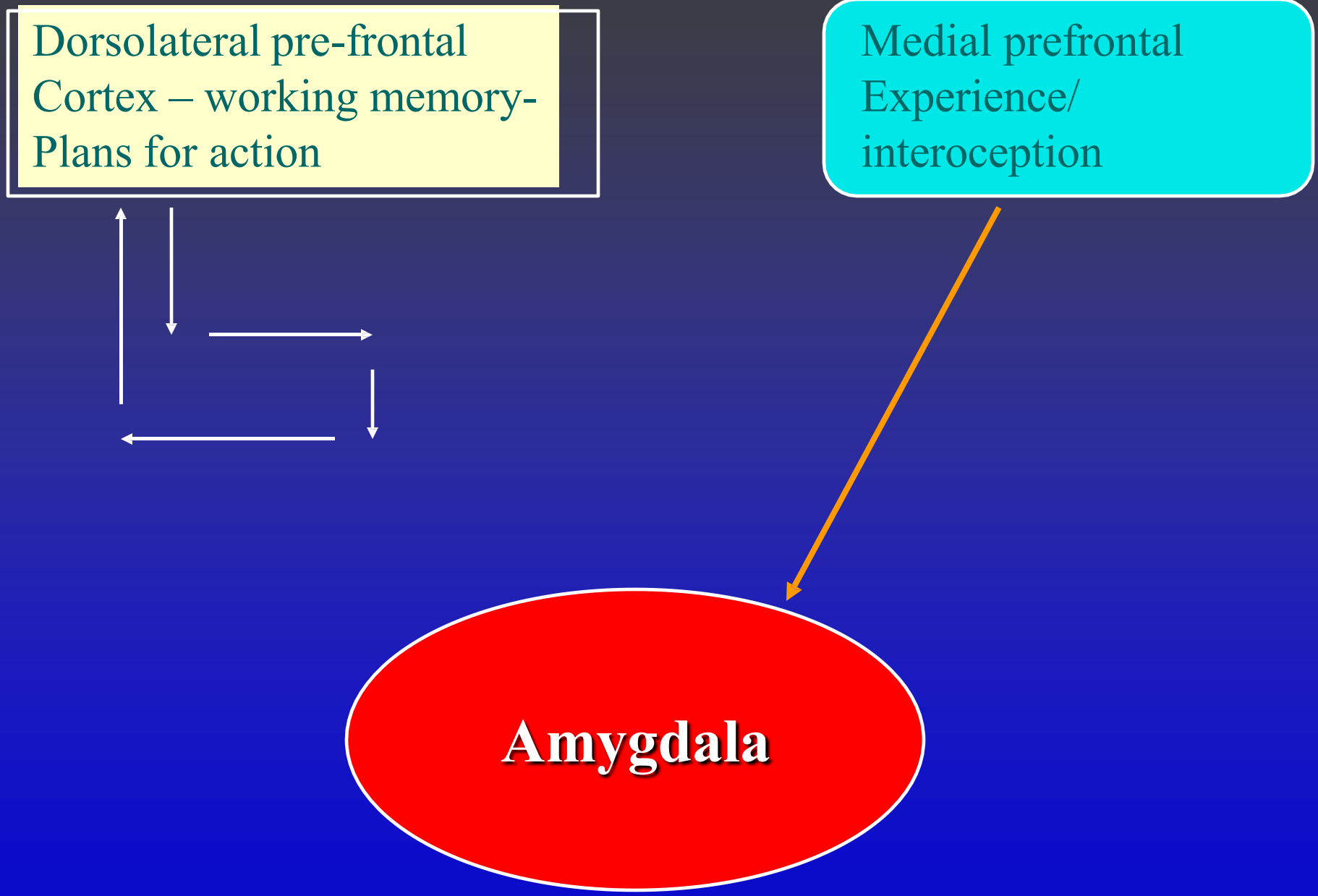


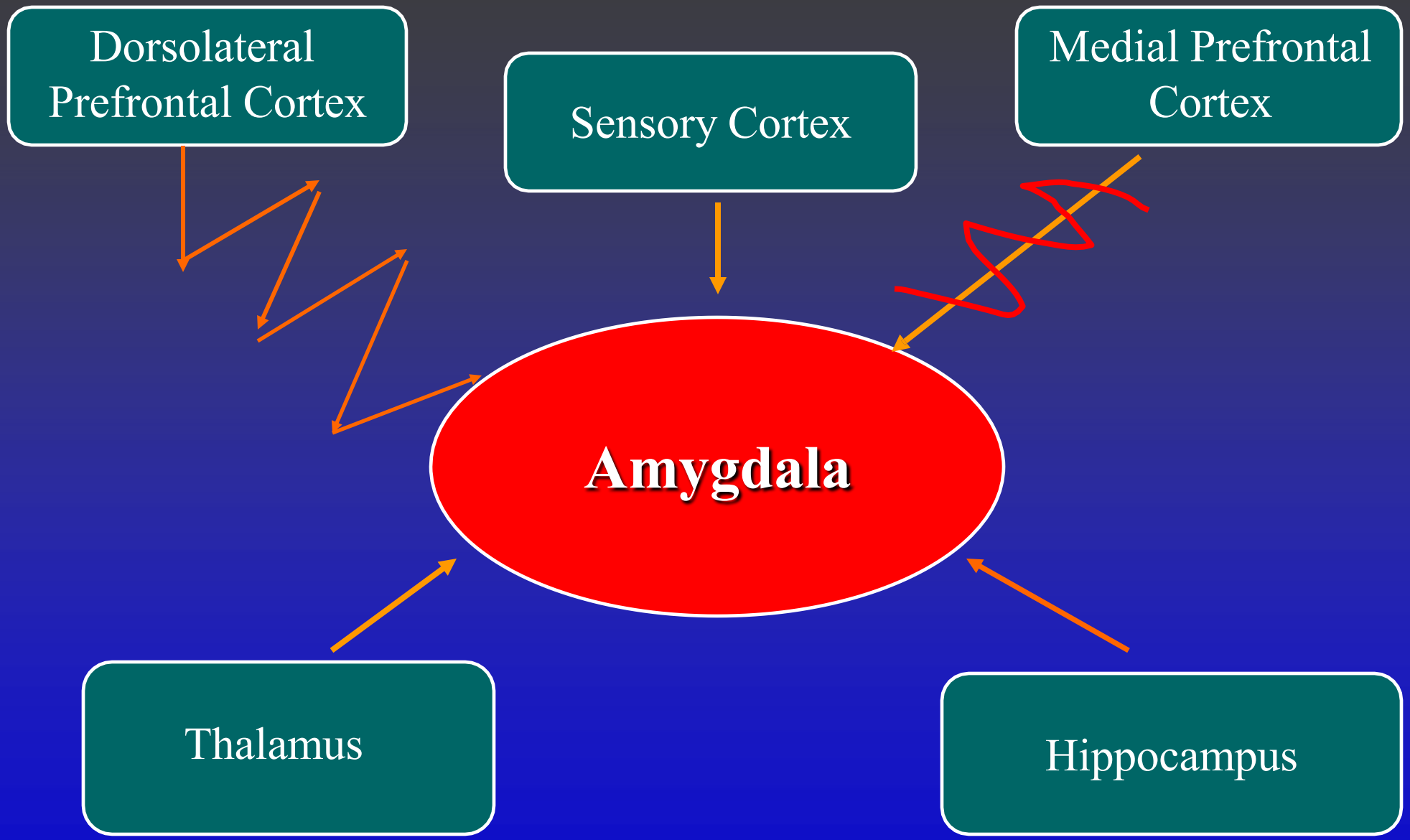



WARNING!

!!


Rage pattern released and directed by cortex and limbic forebrain
Fornix (from hippocampal formation)
Mammillothalamic tract
Hypothalamus (blue: parasympathe red: sympathetic)
Dorsal longitudina fasciculus; median forebrain bundle, and other descend pathways
Corticohypothalamic pathways
Orbitofrontal c
Median forebra bundle
Thyrotropin (elevates metabolism)
Olfactory bulb
III to pupils (constriction)
VII to sublingual and submaxillary glands (secretion)
IX to parotid gland (secretion)
X to heart and GI tract (depresses heart rate and intestinal motility)
Adrenocorticotropin (releases cortisol, provokes stress reaction)
To heart (elevates rate)
To adrenal medulla (effecting rise in blood sugar and visceral vasoconstriction)
Splenic contraction (leukocytes and platelets pressed out)
To vessels of skin (contraction) and muscles (dilation)
Spinal nerve
Sympathetic trunk ganglia
Thoracic part of spinal cord
To GI tract and vessels (depression of motility; vasoconstriction)
Prevertebral ganglion
Pelvic nerve (sacral parasympathetic outflow)
Sacral part of spinal cord
To lower bowel and bladder (evacuation)


Dorsolateral pre-frontal
Cortex – working memory-
Plans for action
Medial prefrontal
Experience/
interoception
Amygdala


Dorsolateral Prefrontal Cortex
Sensory Cortex
Medial Prefrontal Cortex
Amygdala
Thalamus
Hippocampus

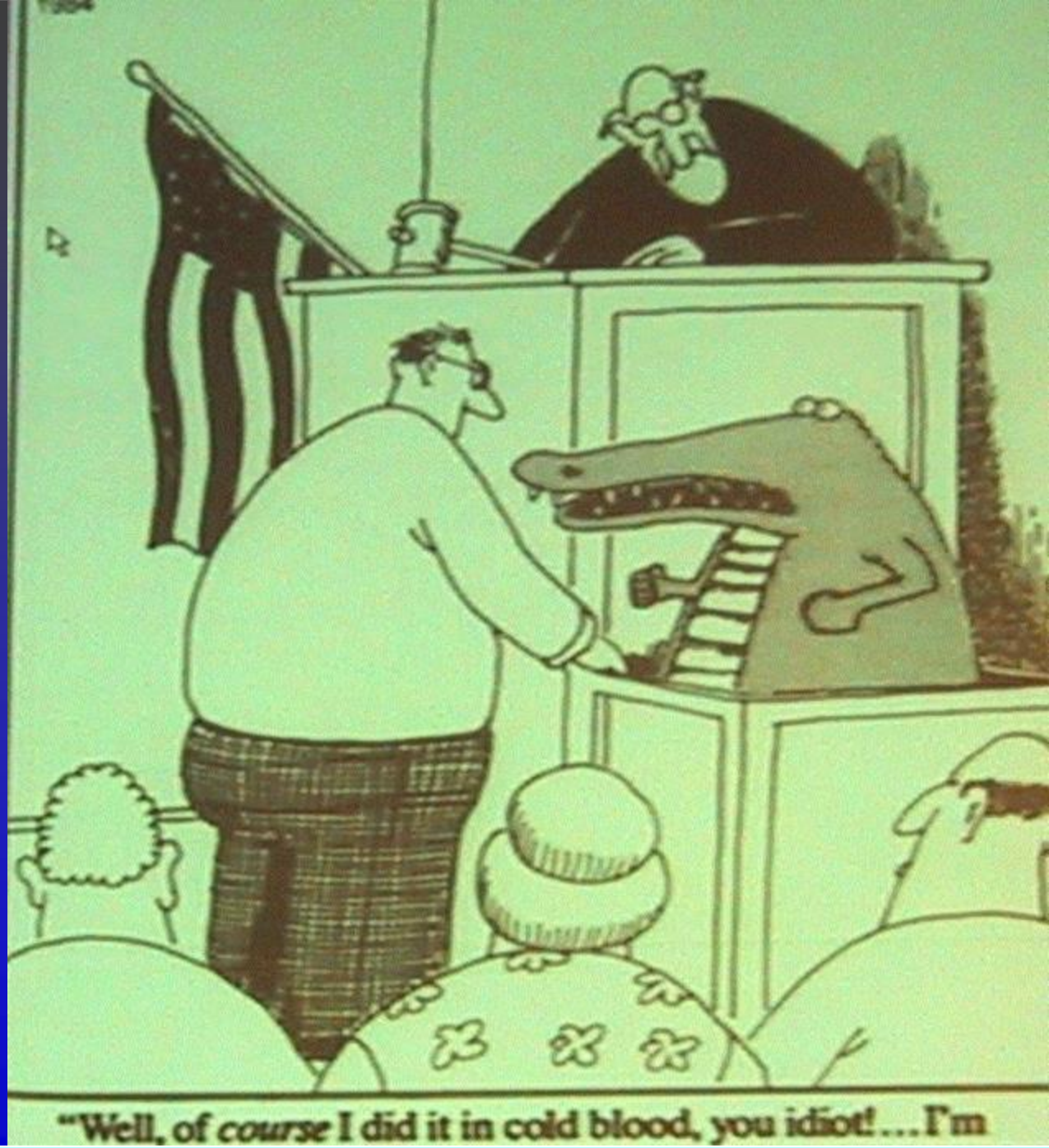
- Our survival brains keep feeding our addictions, family violence, infidelity and workaholism.
- Disordered eating & sleeping.
- Use of substances in attempt to gain control
- Physical insensitivity and hypersensitivity.
- Damaging bodies through too much or not enough exercise,
- Thrill-seeking or self-harming behavior
- Putting their pain onto others through violent, abusive & unethical, behavior.
- Freud: ”and that is their way of remembering”.

Thinking brain dominant strategies

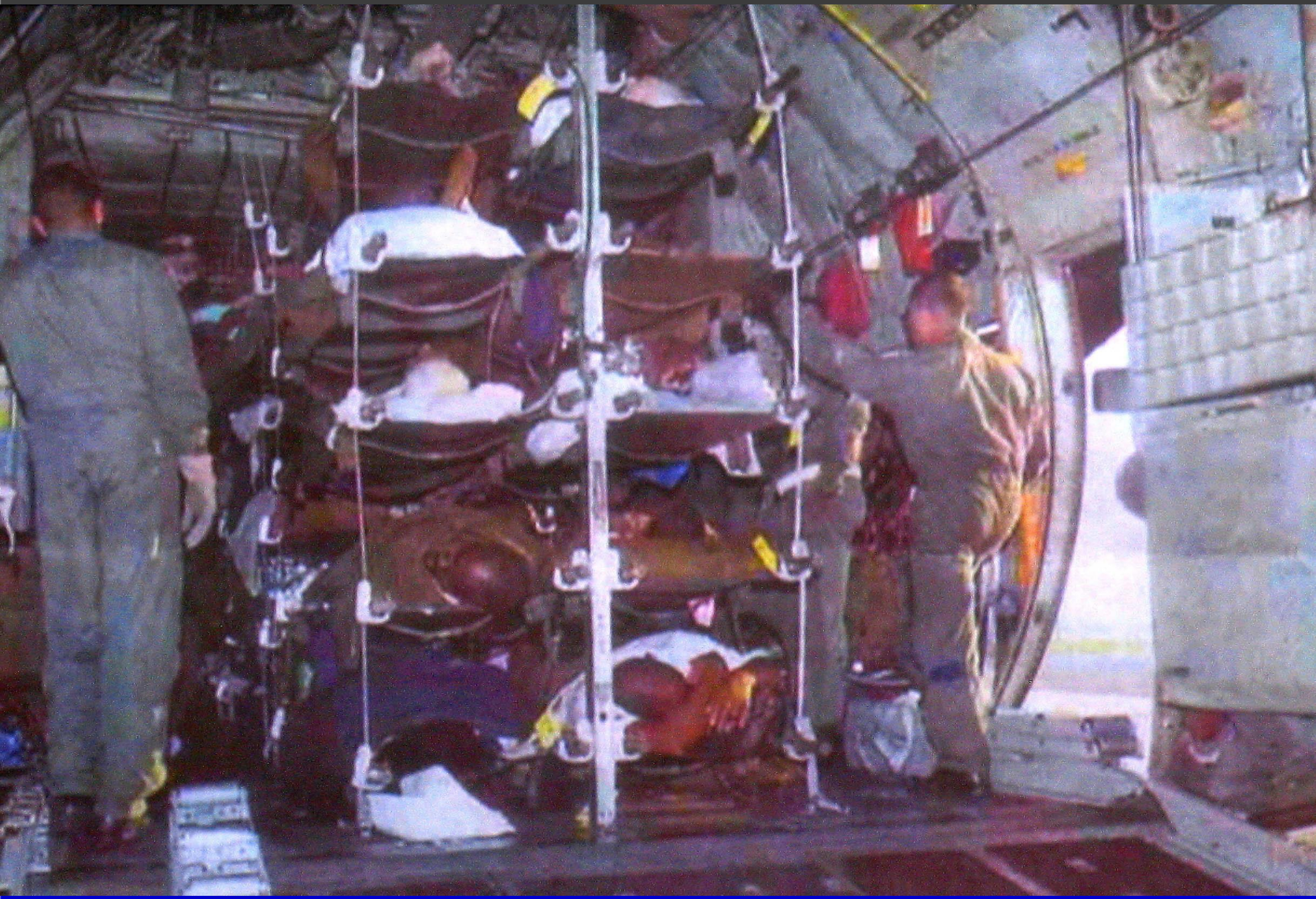
Cognitive-behavioral therapy (CBT), cognitive processing therapy, goal-setting, “broadening and building” positive emotions, are all based on thinking brain-dominant techniques.

. None has shown empirical efficacy for reducing dysregulation or negative emotions.

Aggression: A phylogenetic explanation.



a reptile



Imagination is central to recovery

Without an inner imagination of an alternative future there is no place to go.

Imagination is central to recovery:

1) Art therapy
2) Sandtray
3) Theraplay
4) Theater
5) Improv
6) PBSP
7) etc

NCTSN The National Child Traumatic Stress Network

How do you take a trauma history?

TRAUMATIC ANTECENDENTS QUESTIONNAIRE I

I. Demographics

- current household composition, occupation, etc.
- who do you rely on for practical help
- who do you rely on for emotional help

II. Current Health

III. Family of origin demographics

- who in your family was affectionate with you
- who recognized you as a special person
- was there anyone you felt safe with growing up?

IV. Childhood caretakers and separations

Herman and van der Kolk

TRAUMATIC ANTECENDENTS QUESTIONNAIRE II

V. Peer relationships and childhood strength

VI. Family Alcoholism

VII. Family discipline and conflict resolution

- **who made the rules and enforced discipline at home**
- **description of family rules**
- **usual ways of disciplining children: scolding, withholding privileges, spanking, verbal abuse, hitting, hitting with objects**
- **usual way parents solved disagreements: never angry, talking, yelling, threatening to hit, breaking and throwing, hitting**

VIII. Early sexual experiences

Intake data from the TAQ Trauma Center; May-June, 2000

	0 to 6	7-12	13-18	Age 19+	Lifetime
Neglect	58.2	71.4	81.1	xx.x	91.4
Separations	47.1	61.4	81.4	xx.x	98.6
Emotional abuse	51.4	77.1	85.7	82.9	85.7
Physical abuse	41.4	54.3	55.7	50.0	80.0
Sexual abuse	25.7	41.4	41.4	44.3	74.3
Witnessing	54.3	71.4	78.6	70.0	87.1
Fam. substance ab.	40.0	50.0	67.1	65.7	75.7
Other traumas	50.0	55.7	65.7	82.9	91.4

"Matthews ... we're getting another one of those strange 'aw blah es span yol' sounds."

Herman, van der Kolk & Perry,

Childhood trauma in borderline personality disorder.

Am J Psychiat. 1989

Findings :
Childhood trauma and borderline personality disorder.

Herman, van der Kolk & Perry, 1989

- 87 % of subjects with BPD had histories of severe childhood abuse and/or neglect starting prior to age 7.
- Other Personality Disorders did not have significant relations to childhood abuse and neglect.

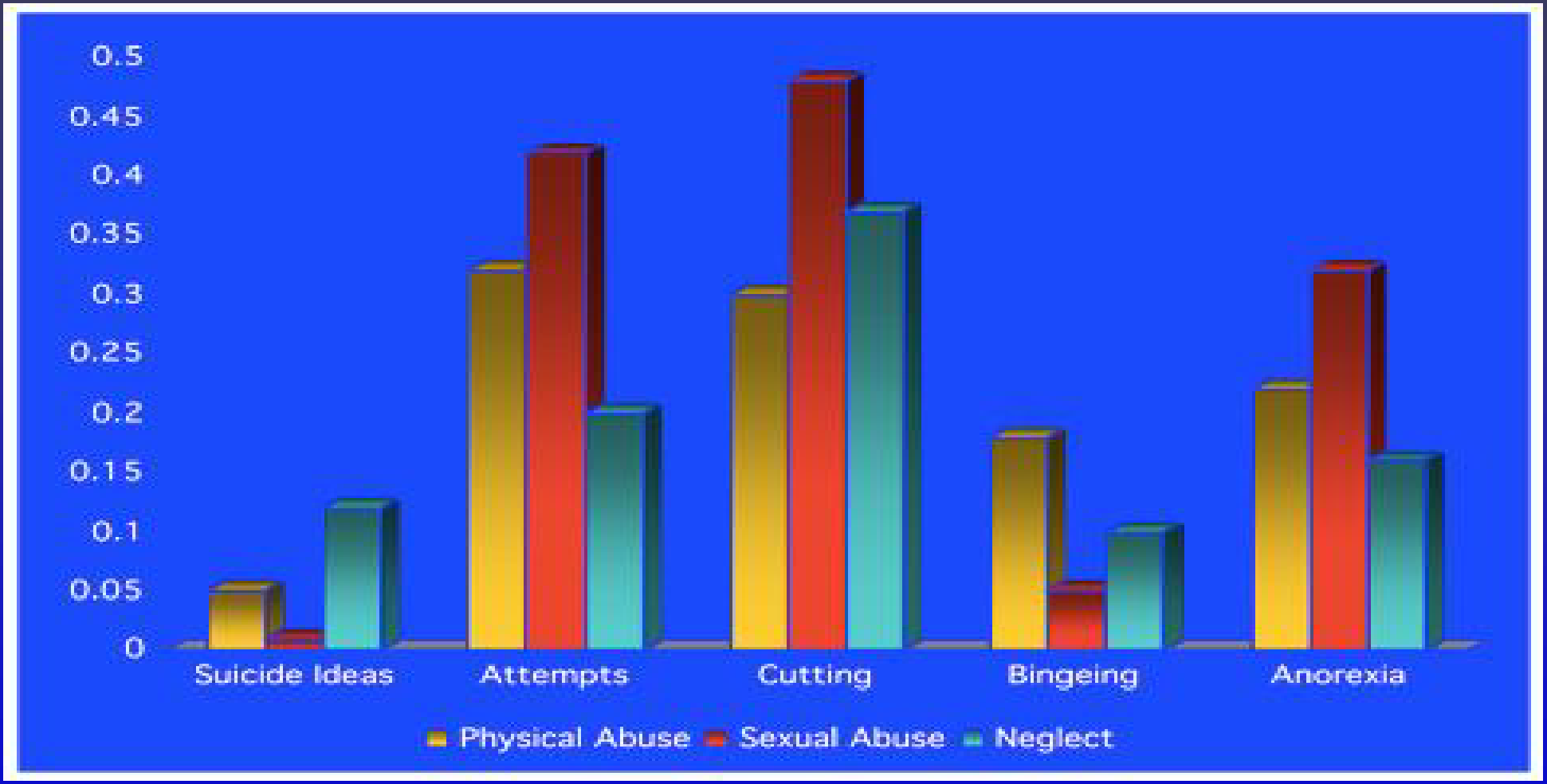
Childhood trauma and self-destructive behavior

Bessel Van der Kolk, Judith Herman
& Christopher Perry

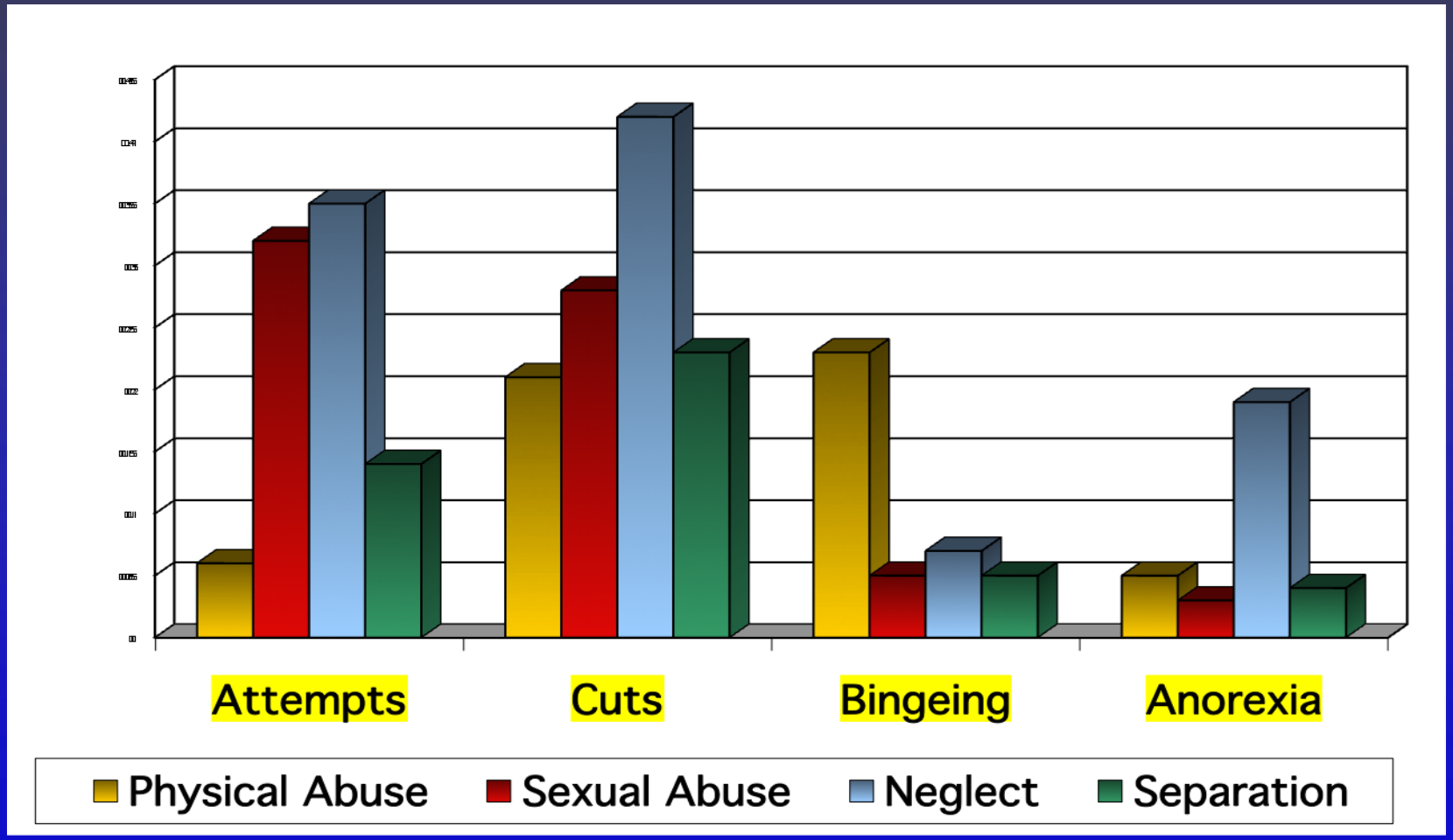
Am J Psychiat 1991

Childhood antecedents of self-destructive behavior

(van der Kolk, Perry & Herman, Am J Psychiat, 1991)



Predictors of persistence of self-destructive behavior over four year follow-up



Getting in touch

EMDR

My first exposure to a treatment that does not primarily rely on

- narratives,
- [relationship?],
- or drugs


12:36PM
JAN. 19 1995

EMDR vs. fluoxetine vs. placebo
R01MH58363

Bessel van der Kolk MD

Joseph Spinazzola PhD

James Hopper PhD

Margaret Blaustein, PhD

Elisabeth Hopper PhD

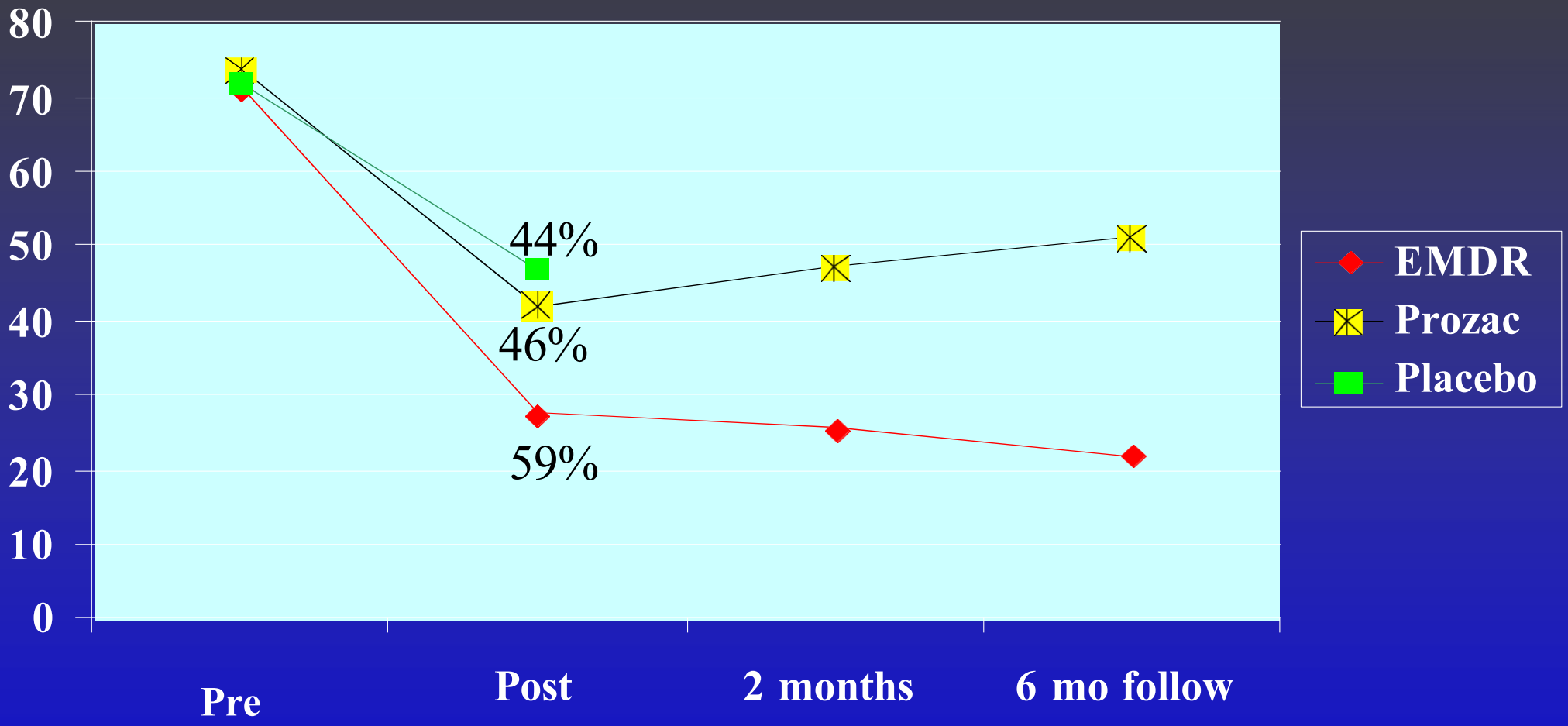
Deborah Korn PhD

Jose Hidalgo MD

William Simpson PhD

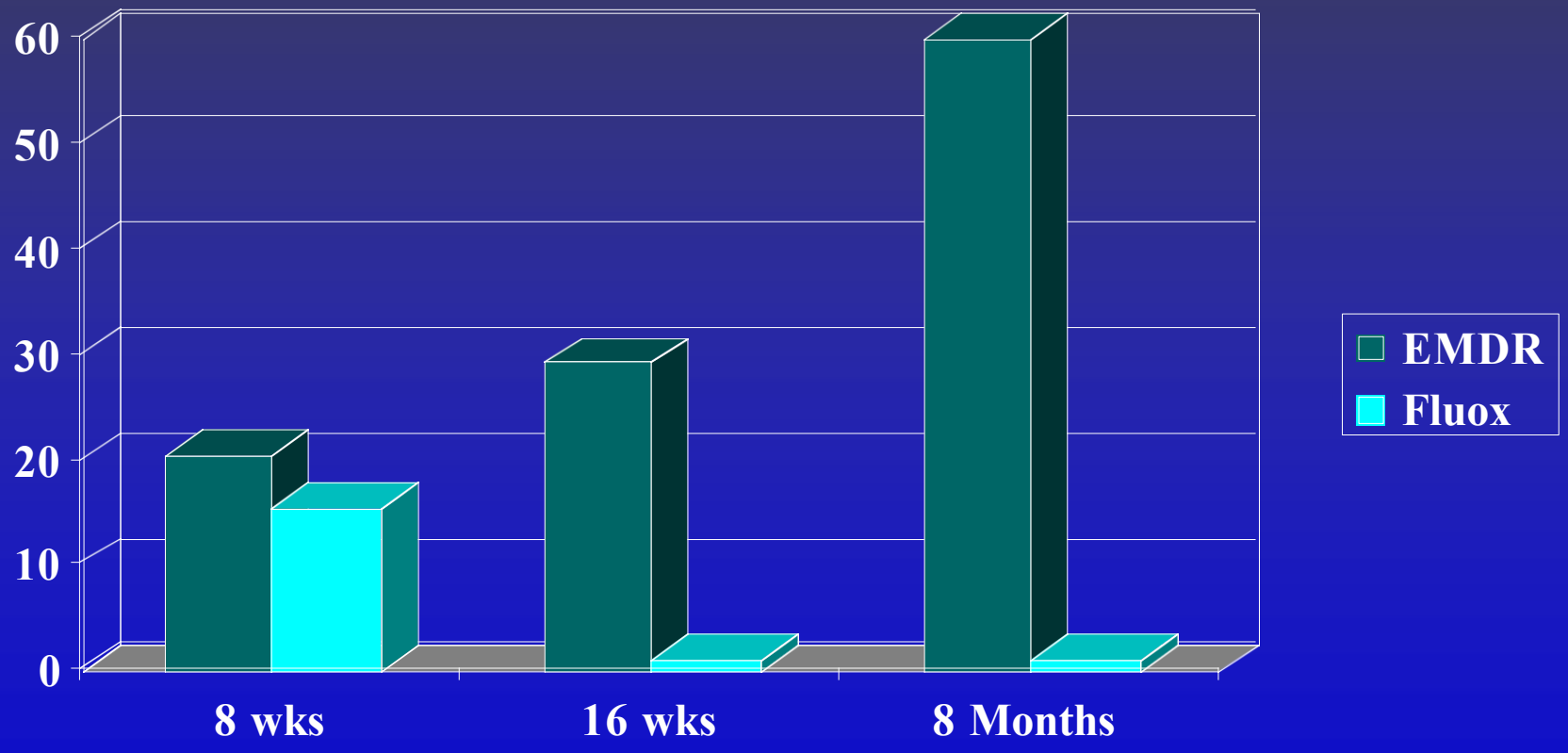
Jellica Markovic, Jeff Weir, Deborah Rozelle, Caren Swift,
Miriam Kissin, Dan Siskind

EMDR vs. fluoxetine vs. Placebo

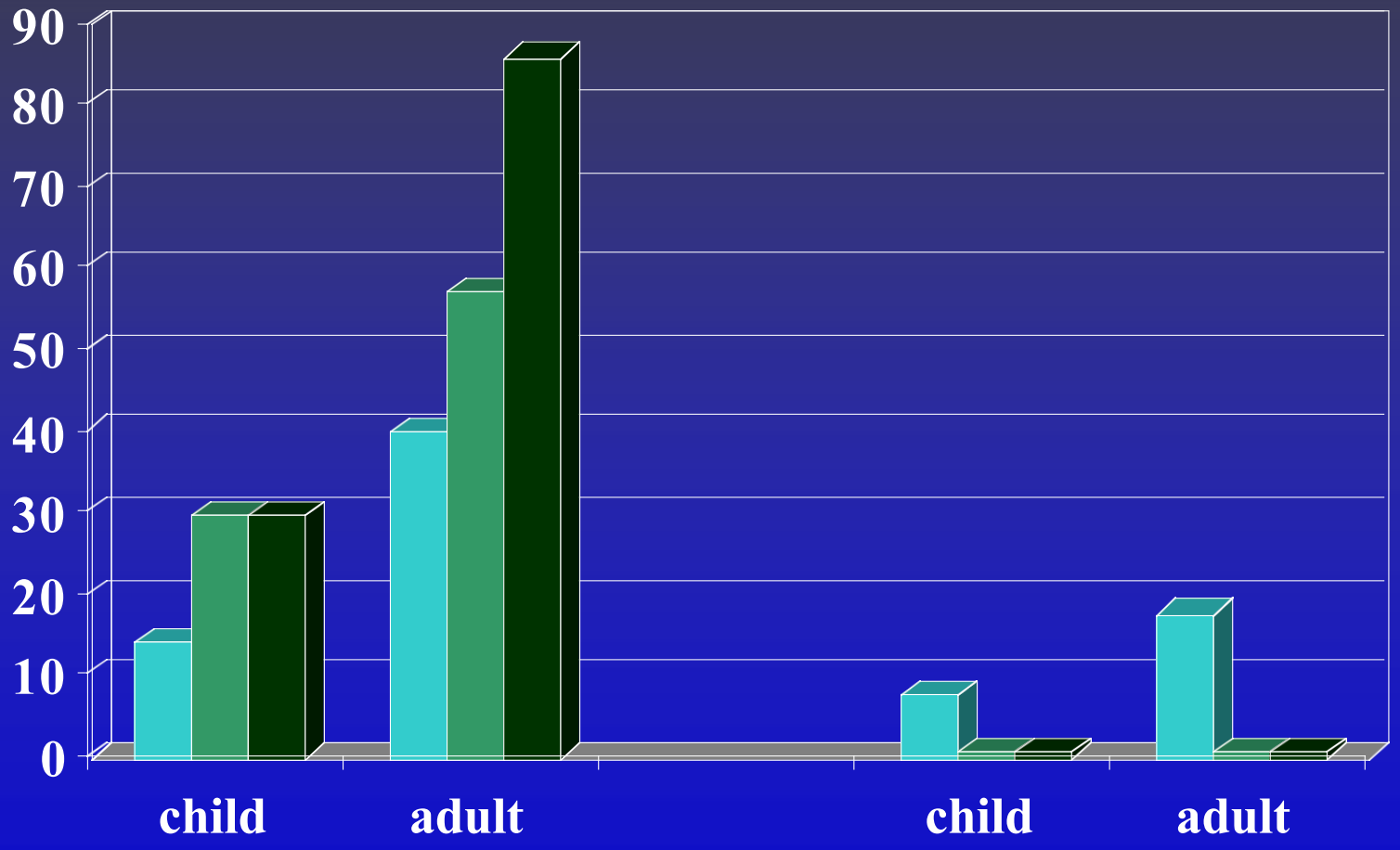


CAPS Scores pre-treatment, Post treatment (12 wks), 2 month Follow- up and 6 month follow up

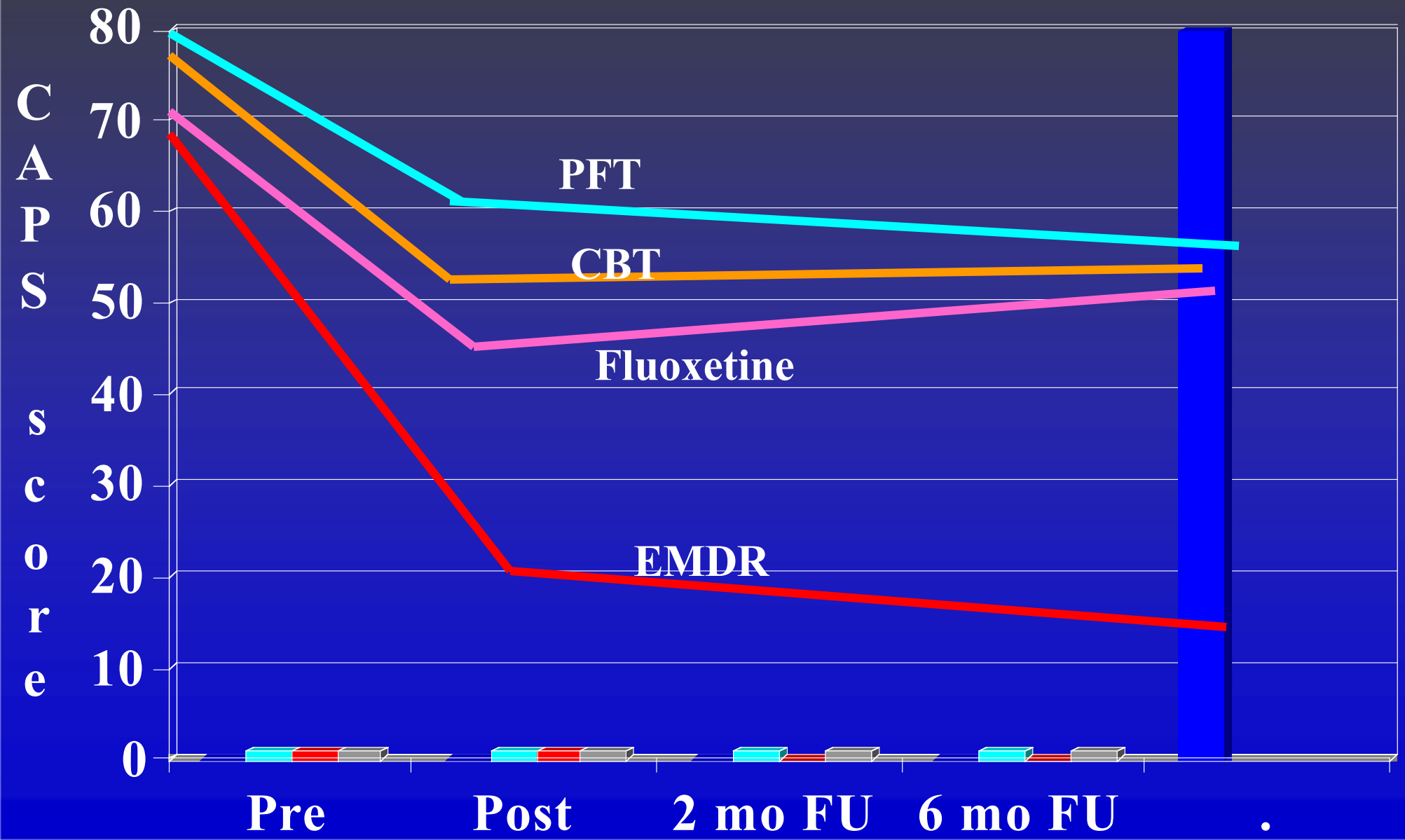
Good end-state function: CAPS score below 20

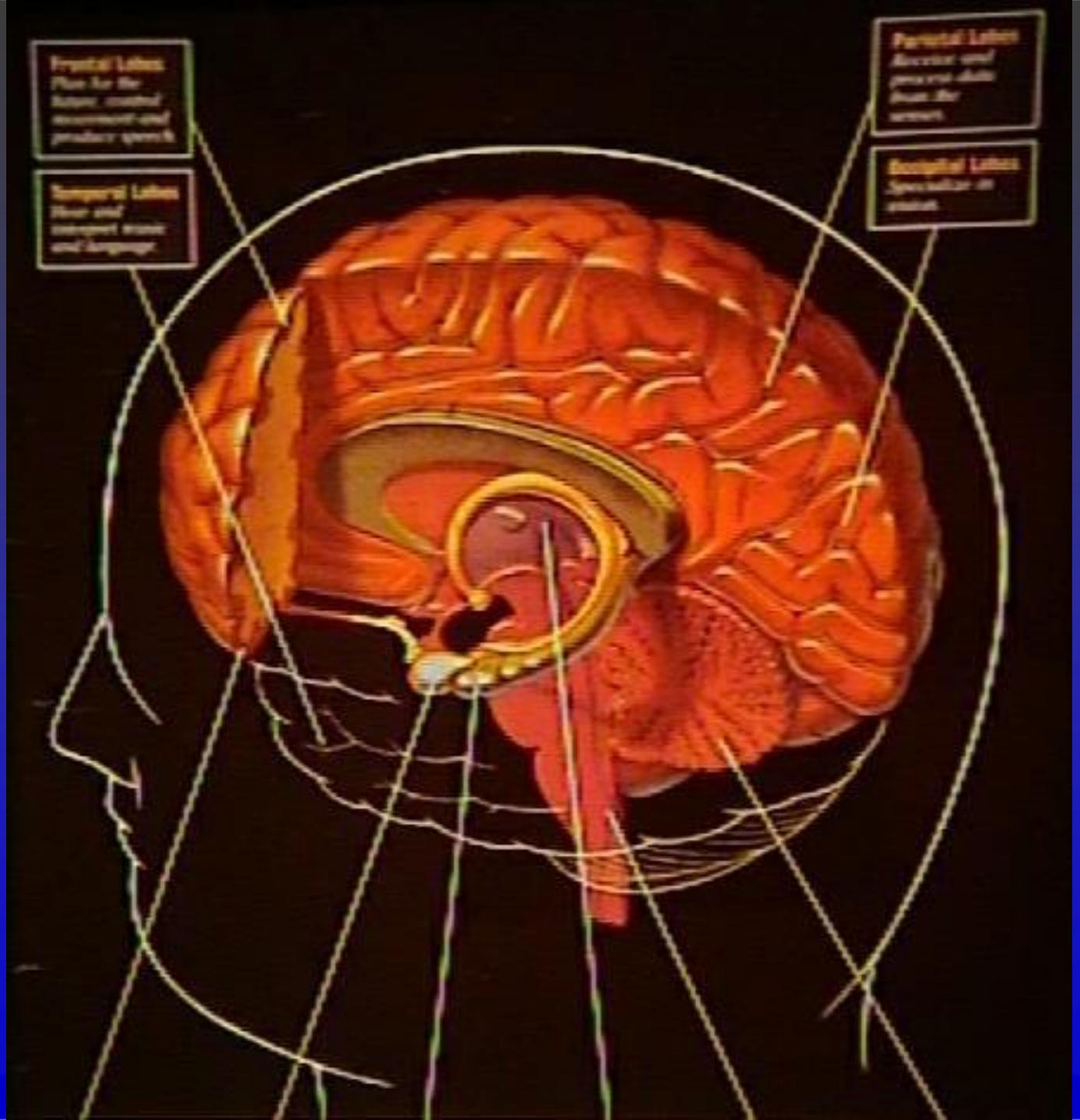


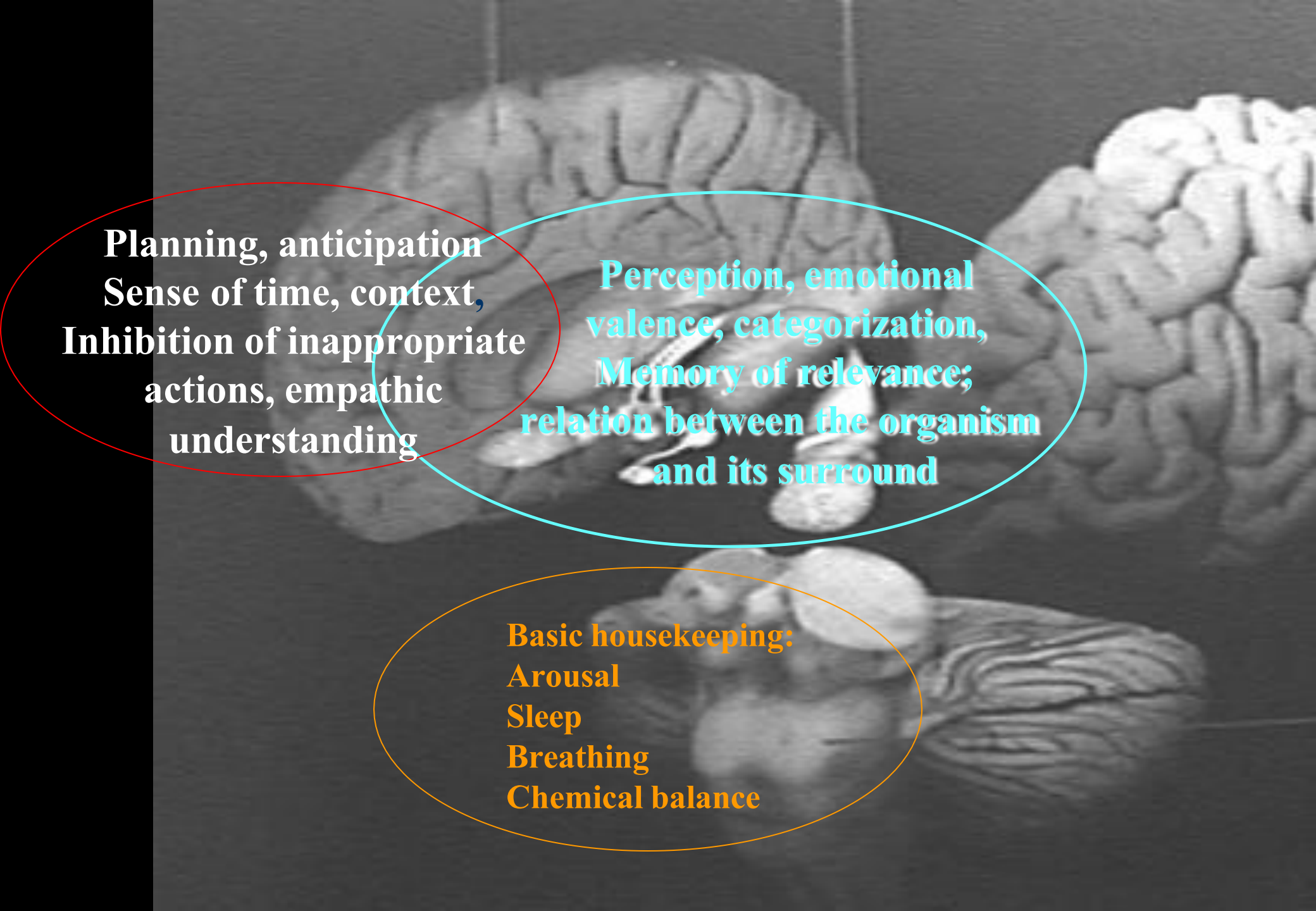
Positive end-state function (CAPS < 20)



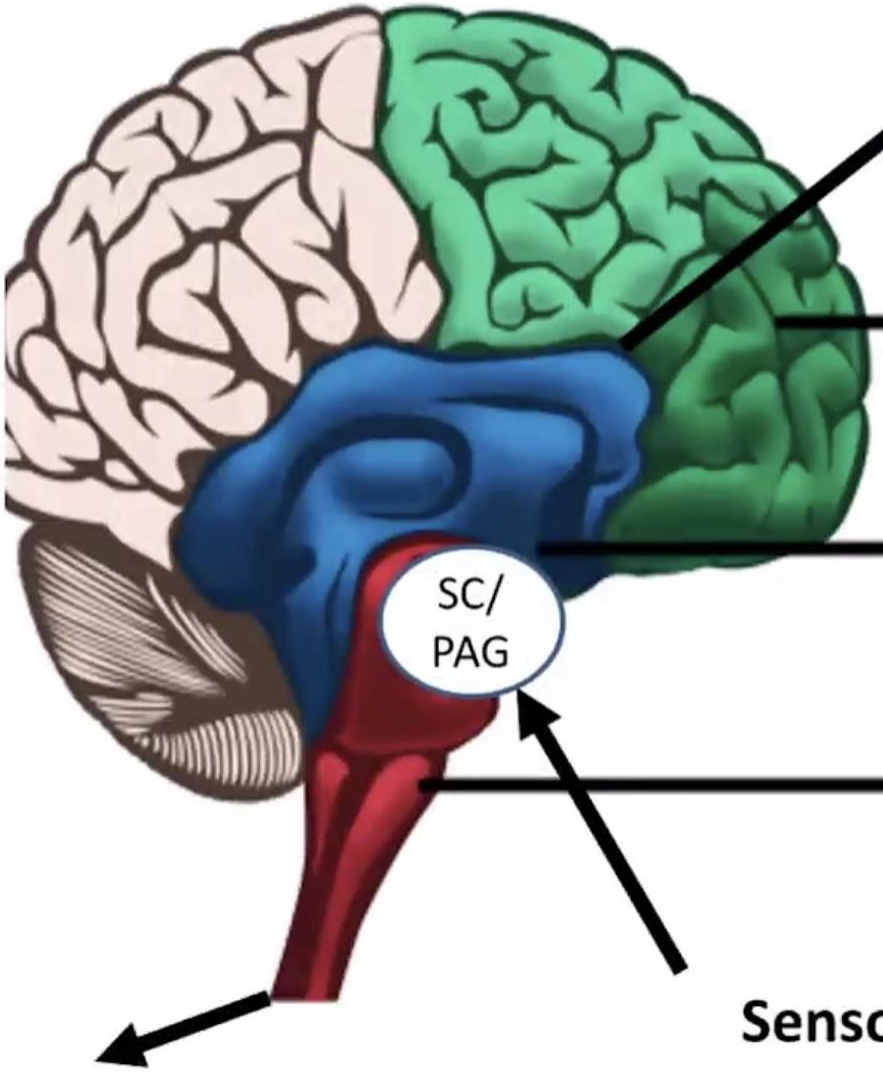
Comparison EMDR vs Prozac (van der Kolk et al, 2007) and CBT vs PFT (Schnurr et al, 2007)




Frontal Lobes
Parietal Lobes
Temporal Lobes
Occipital Lobes


Planning, anticipation
Sense of time, context,
Inhibition of inappropriate
actions, empathic
understanding
Perception, emotional
valence, categorization,
Memory of relevance;
relation between the organism
and its surround
Basic housekeeping:
Arousal
Sleep
Breathing
Chemical balance

Sensory Processing



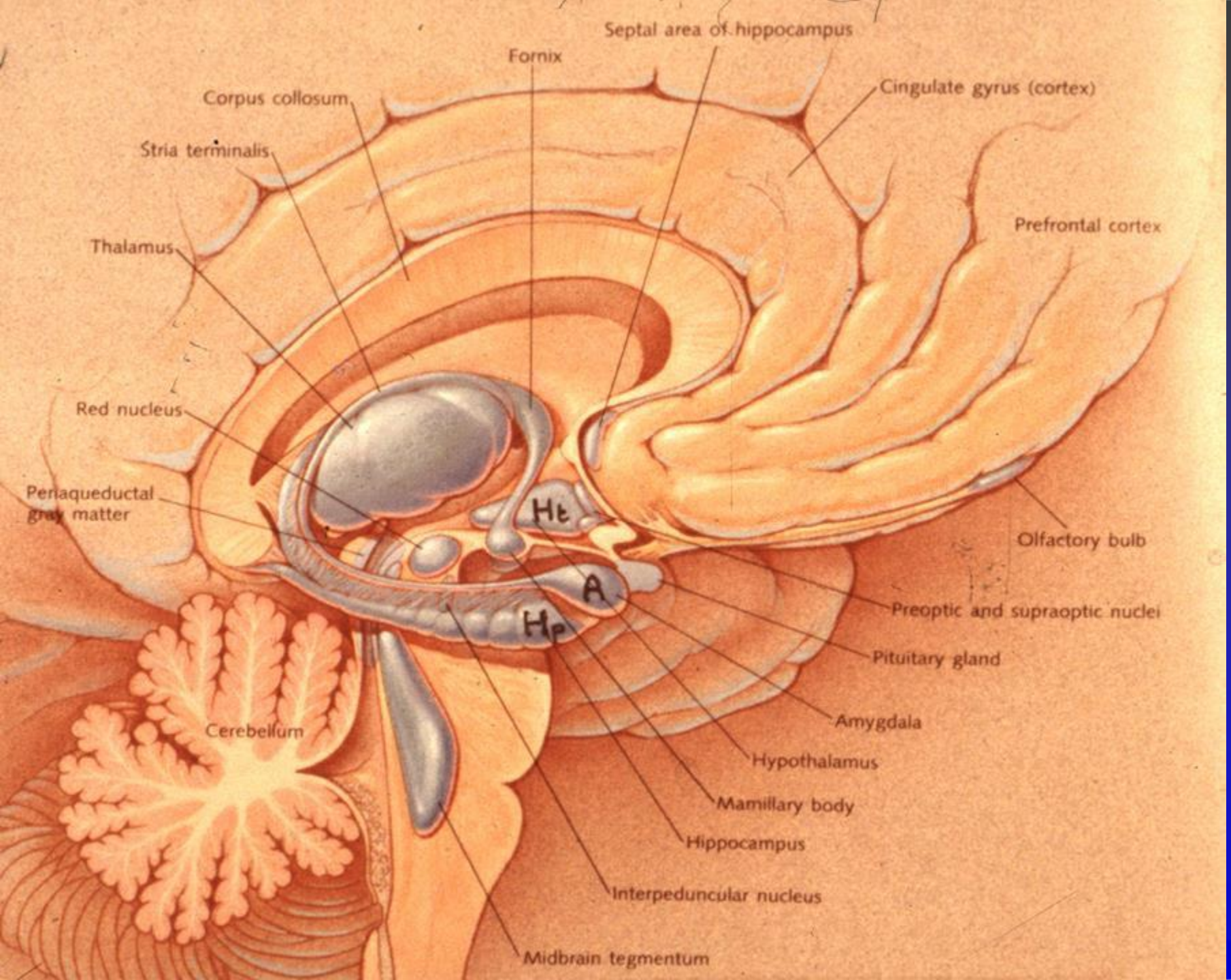
Conscious Awareness of
Sensory Experience Emerges
(Anterior Insula)

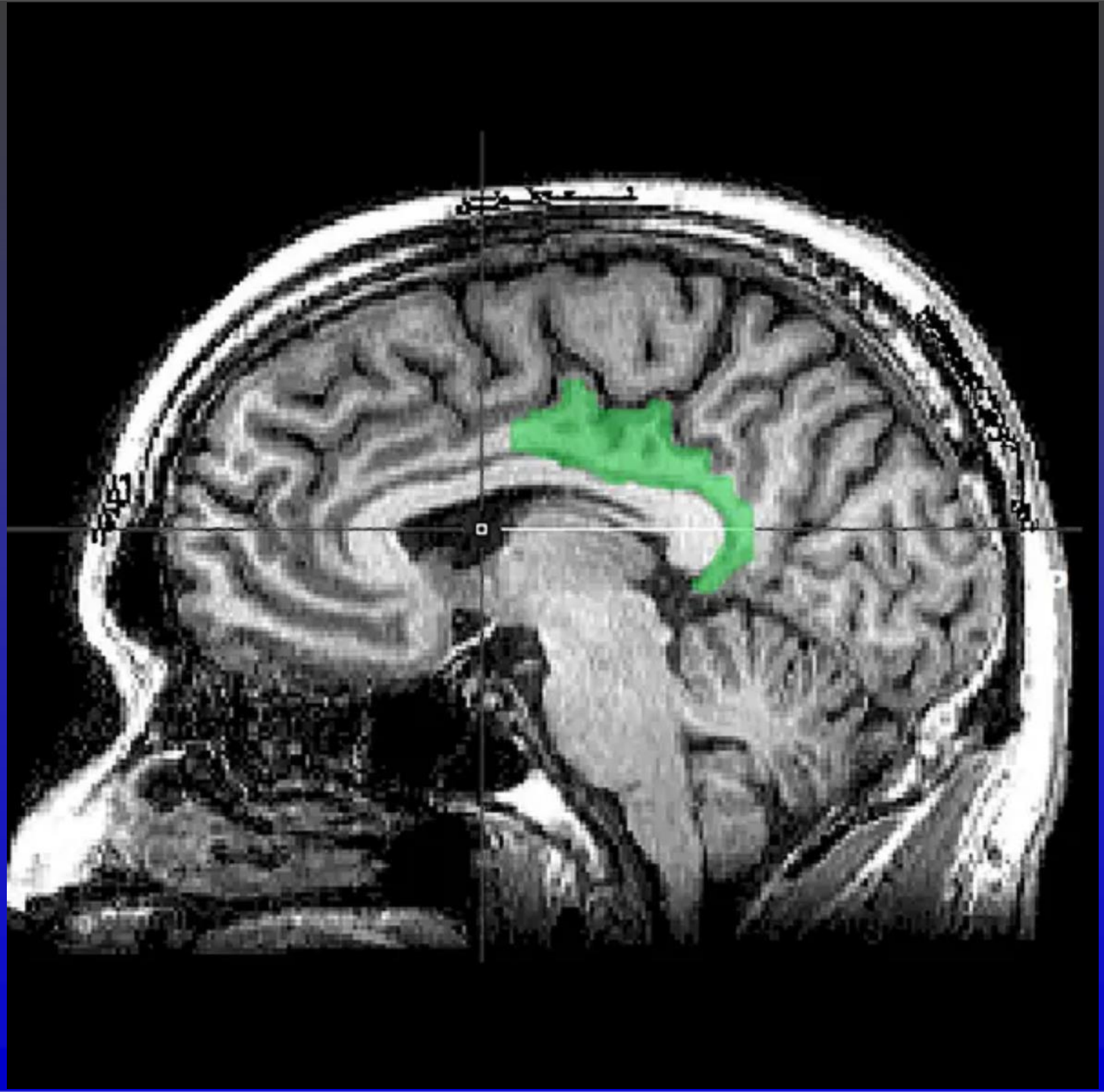
Executive State
Prefrontal Lobes
What can I learn from this?

Emotional State
Limbic System
Am I loved?

Survival State
Brain Stem
Am I safe?

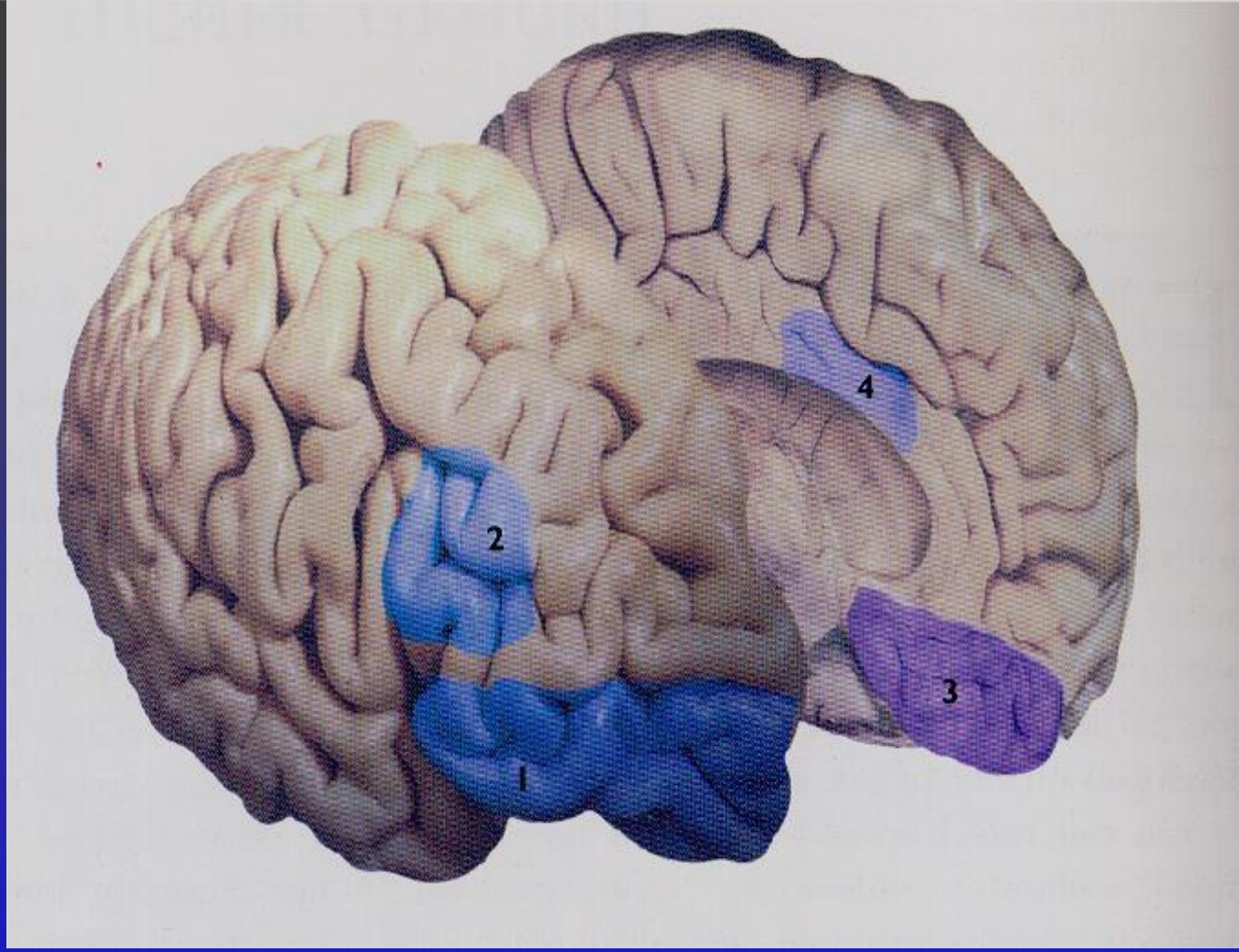
Sensory information from body


Septal area of hippocampus
Fornix
Corpus collosum
Cingulate gyrus (cortex)
Stria terminalis
Prefrontal cortex
Thalamus
Red nucleus
Periaqueductal gray matter
Ht
A
Hp
Olfactory bulb
Preoptic and supraoptic nuclei
Pituitary gland
Amygdala
Cerebellum
Hypothalamus
Mamillary body
Hippocampus
Interpeduncular nucleus
Midbrain tegmentum



1) Orbitofrontal cortex. Inhibits inappropriate action; helps postpone reward seeking.

2) Dorsolateral pre-frontal cortex. Here things are "held in mind" and manipulated to form plans and concepts.
Helps set priorities.



3) Ventromedial Prefrontal cortex. Here Emotions are registered and meaning bestowed on perceptions.

4) Anterior cingulate. Helps focus Attention. Integrates cognition and affect. Tunes into thoughts; Awareness of "self"

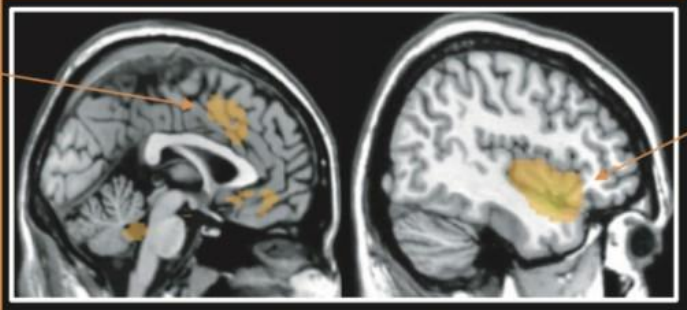
Networks in the brain

Determine relevance, attention, information processing and self-experience

Salience Network

dACC

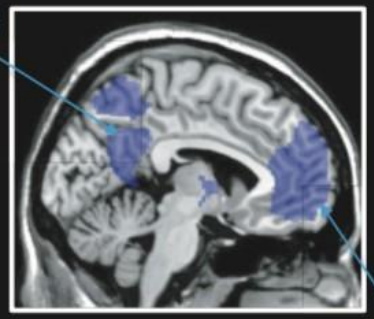
Insula



- **Clinical Markers**
  - Hyper –/Hypoarousal
- **Clinical Treatment**
  - Mindfulness
- **Neural Treatment**
  - NFB, TMS
- **Pharmacotherapy**

Default Mode Network

PCC

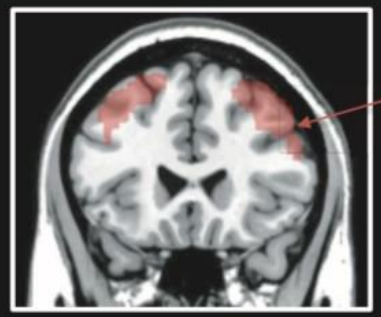


mPFC

- **Clinical Markers**
  - Sense of Self
- **Clinical Treatment**
  - Psychotherapy to ↑ self–reflective functioning
- **Neural Treatment**
  - NFB, TMS
- **Pharmacotherapy**

Anticorrelated

Central Executive Network



dlPFC

- **Clinical Markers**
  - Executive Dysfunction
- **Clinical Treatment**
  - Cognitive Remediation
- **Neural Treatment**
  - NFB, TMS
- **Pharmacotherapy**

Three intrinsic connectivity networks (ICN) crucial to understanding higher cognitive function.

- **Central Executive Network** (CEN) crucial to verbal learning
- **Salience (SN)**, consists of dorsal anterior cingulate cortex and the fronto-insular cortex: directing behavior to the most pertinent actions
- **Default Mode Network (DMN)** anterior and posterior medial cortices and lateral parietal lobes. Self-referential processing, autobiographical memory & social cognition
- Responses of these ICNs generally increase and decrease proportionally and antagonistically during cognitive and emotional-processing.
- **The anterior insula** of the SN mediates engagement of CEN and disengagement of the DMN:t he dynamic interplay between externally- and internally-focused attention and cognitive-affective processing

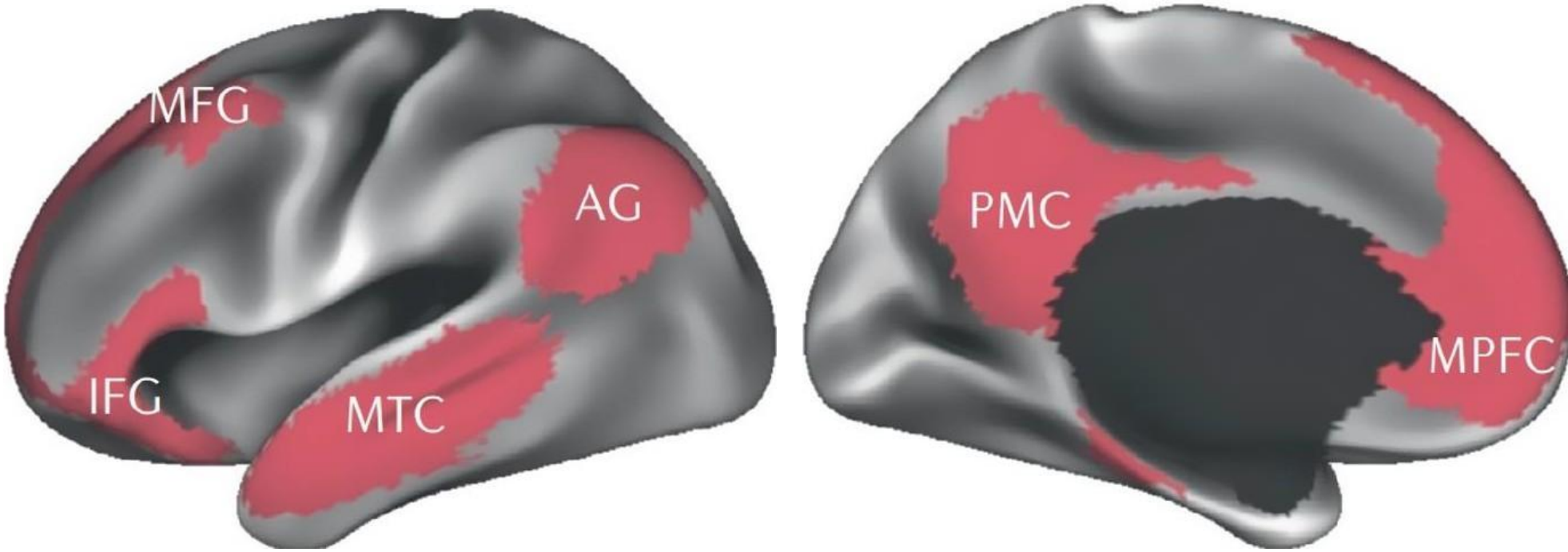
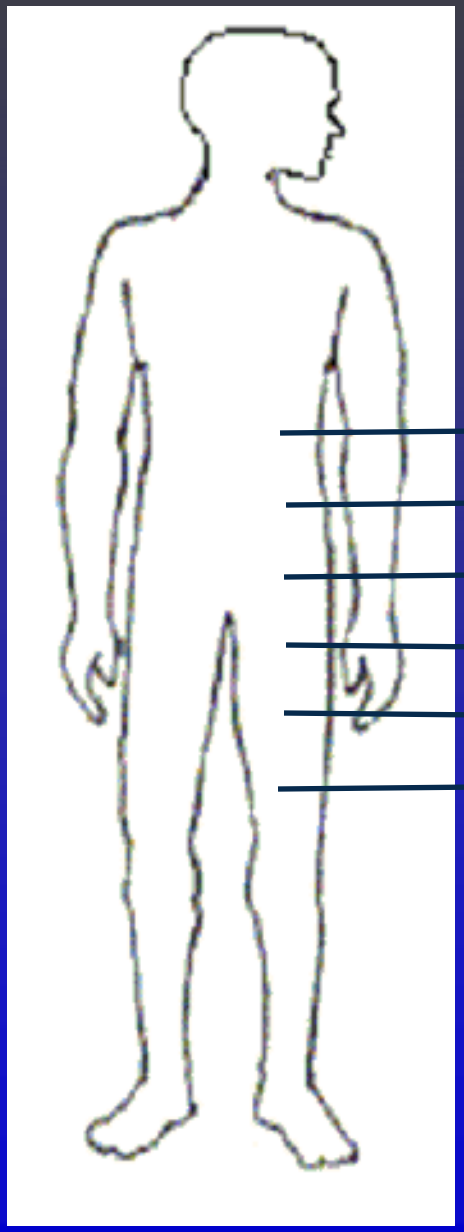


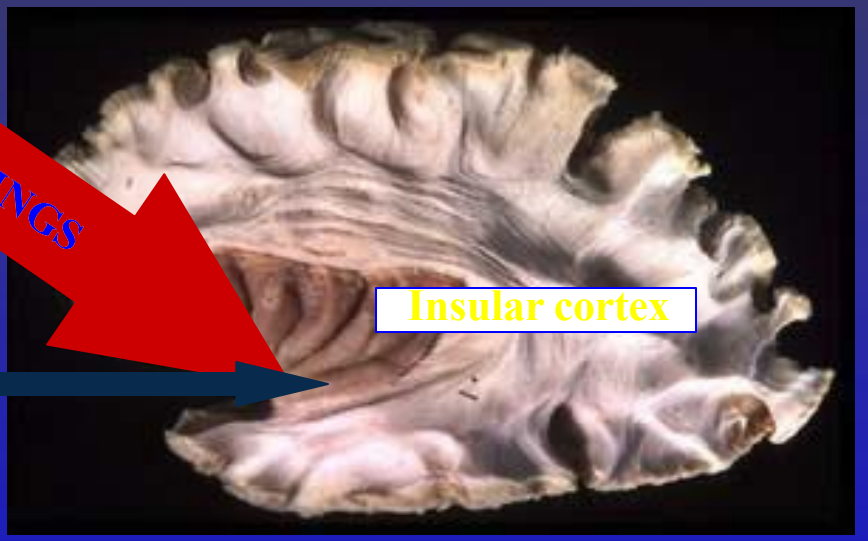
Figure 1. Reprinted by permission from [Springer Nature]: Nature [Nature Reviews Neuroscience]. The default mode network in cognitic a topographical perspective, Smallwood et al. (2021). Brain regions of the DMN based on the coherence of their temporal activity, measured at rest. These regions are the posteromedial cortex (PMC), the medial prefrontal cortex (MPFC), angular gyrus (AG), middle temporal cortex (MTC), middle frontal gyrus (MFG), and inferior frontal gyrus (IFG).

Insula



Sensations
Pain
Body temperature
Viscera
Striated Muscles
Vestibular System

CONTENT OF FEELINGS



Conveys bodily states to the brain

Insula shut-down

Emotional experience critical for salience detection

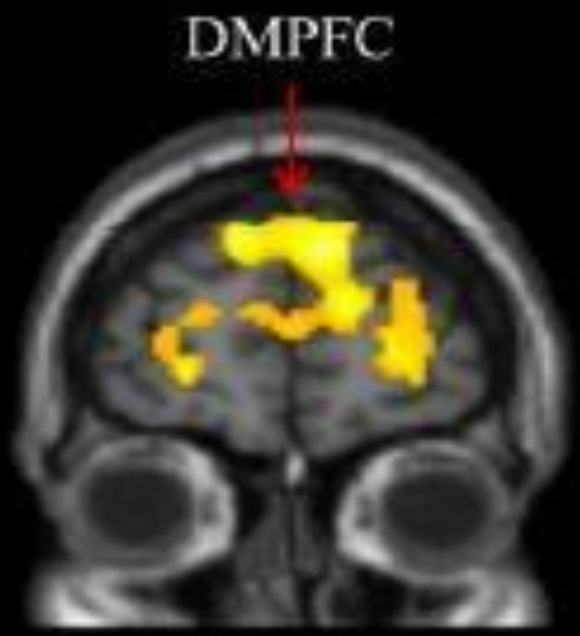
Emotions crucial to directing behavior and physiological states

Trauma interferes with capacity to pursue salient endeavors in the present.

How can we help traumatized pple to awaken from shutdown and restore interoceptive awareness and salience detection?

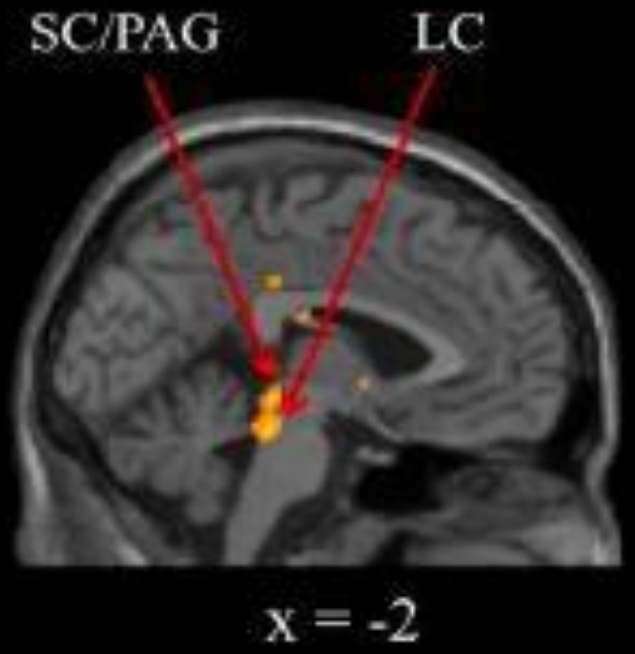
REACTIONS TO MEETING A DARK HANDSOME STRANGER

Controls:



On seeing an attractive stranger

PTSD:



What changes in the brain as a result of trauma ?

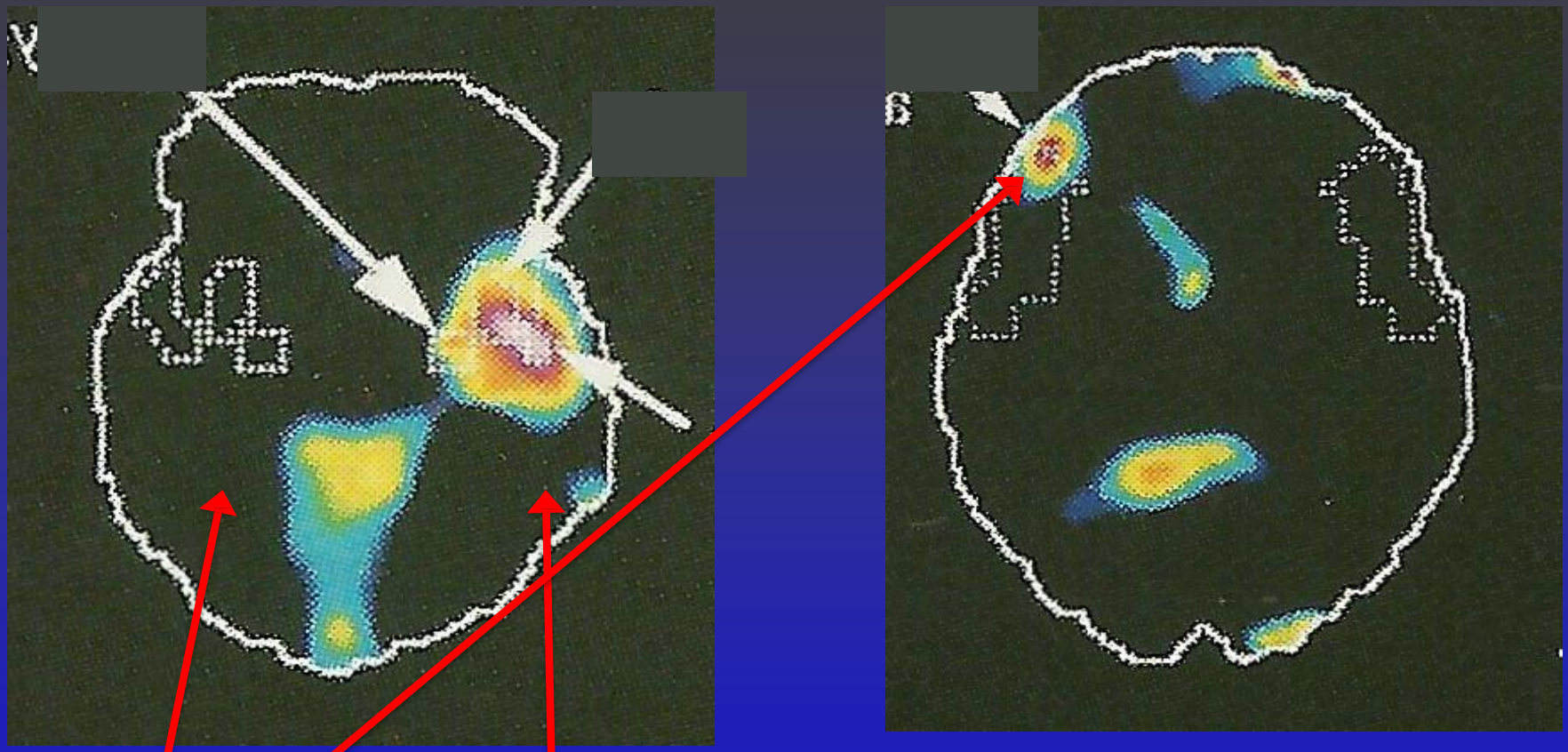
1. Speechless terror

TRAUMA SCRIPT II.

You are in the hospital emergency room lying on a stretcher, but feeling as if you were standing on its head. You hear doctors' words echoing, asking if you are pregnant. You try hard to understand, but just can't remember. Your little boy is talking to someone in another room, but you don't hear Katie.

When the doctor comes in, you know something is wrong. He tells you you have been in an accident. Your heart skips a beat, and you feel sweaty and nauseous. Then you hear him say: ' we could not do anything for your little girl. She is dead.' Your body feels heavy and you start to cry.

Neuroimaging in PTSD Rauch, van der Kolk et al, 1994



De-activation of Left hemisphere

Imprint of trauma on Right

Left anterior prefrontal cortex (Broca's area) goes off-line (speechless terror, dumbfounded)

PROPERTIES OF THE LEFT HEMISPHERE

- Organizes memory and problem-solving.
- Creates symbols: transcribes personal experience into culturally shared meaning.
- Creativity the distinguishing feature of L-hemisphere cognition.
- Lack of left hemisphere functioning in PTSD responsible for alexithymia: not knowing what you feel.


SAD
HAPPY
DISTRAUGHT
HILARIOUS
OUTRAGED
SOMBER
JOVIAL
GRIEF STRICKEN

The Nature of Traumatic Memories I.

"At a certain point my father would cut off my breathing; then these feelings would become intolerable….

"My mind would come to that certain point and then disintegrate

"All these intrusive recollections have an experiental quality to them- I get lost, confused and I hear things.

"When I have these flashbacks they are not explainable – I cannot make things sequential

The Nature of Traumatic Memories III.

“The tragedy is the loneliness; the inability to convey the inner experience, and knowing that I cannot get out of it without going through it again.

Going through it by myself over and over again has certainly not done it”

The Experience of Dissociation

Although I know and understand many things now I am limited by the fact that a large number of things I do not know at the same time.

It does me no good to have knowledge without having a sense of time. I do not know the things that I know simultaneously.

I need help from outside for somebody to hold what I know – from the outside. That allows me to have continuity of understanding which is crucial for me to go anywhere

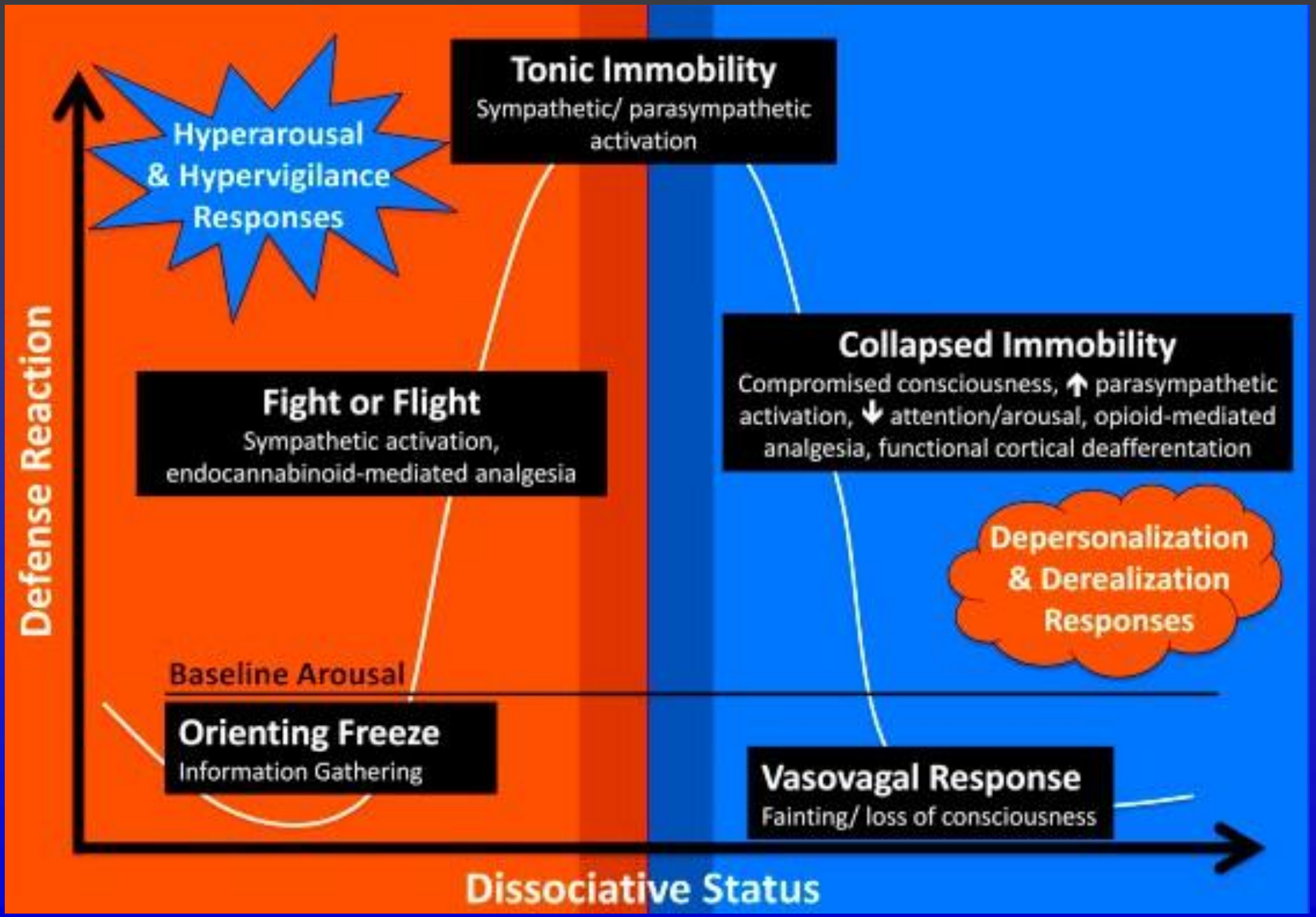
The Experience of Dissociation II

A lot of my work and struggles is in chunks:

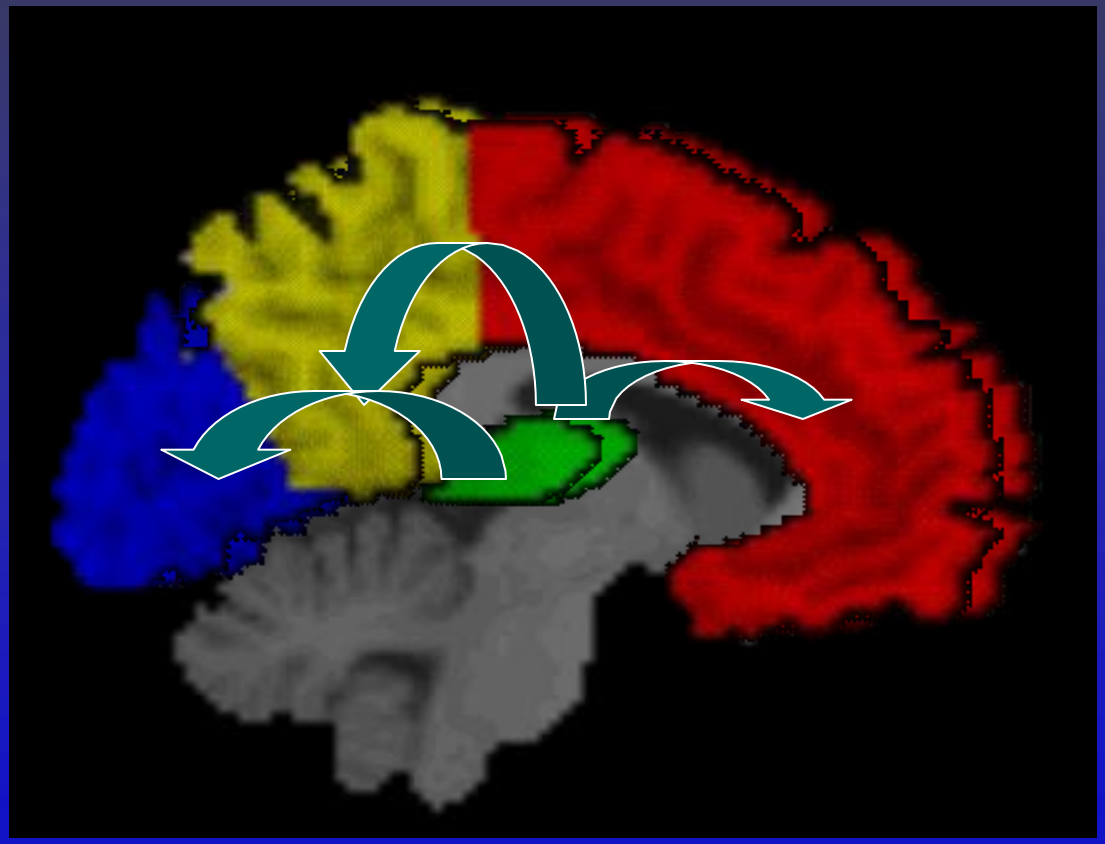
I am so afraid of action.

Action that comes from me is bound to be evil, evil, evil.

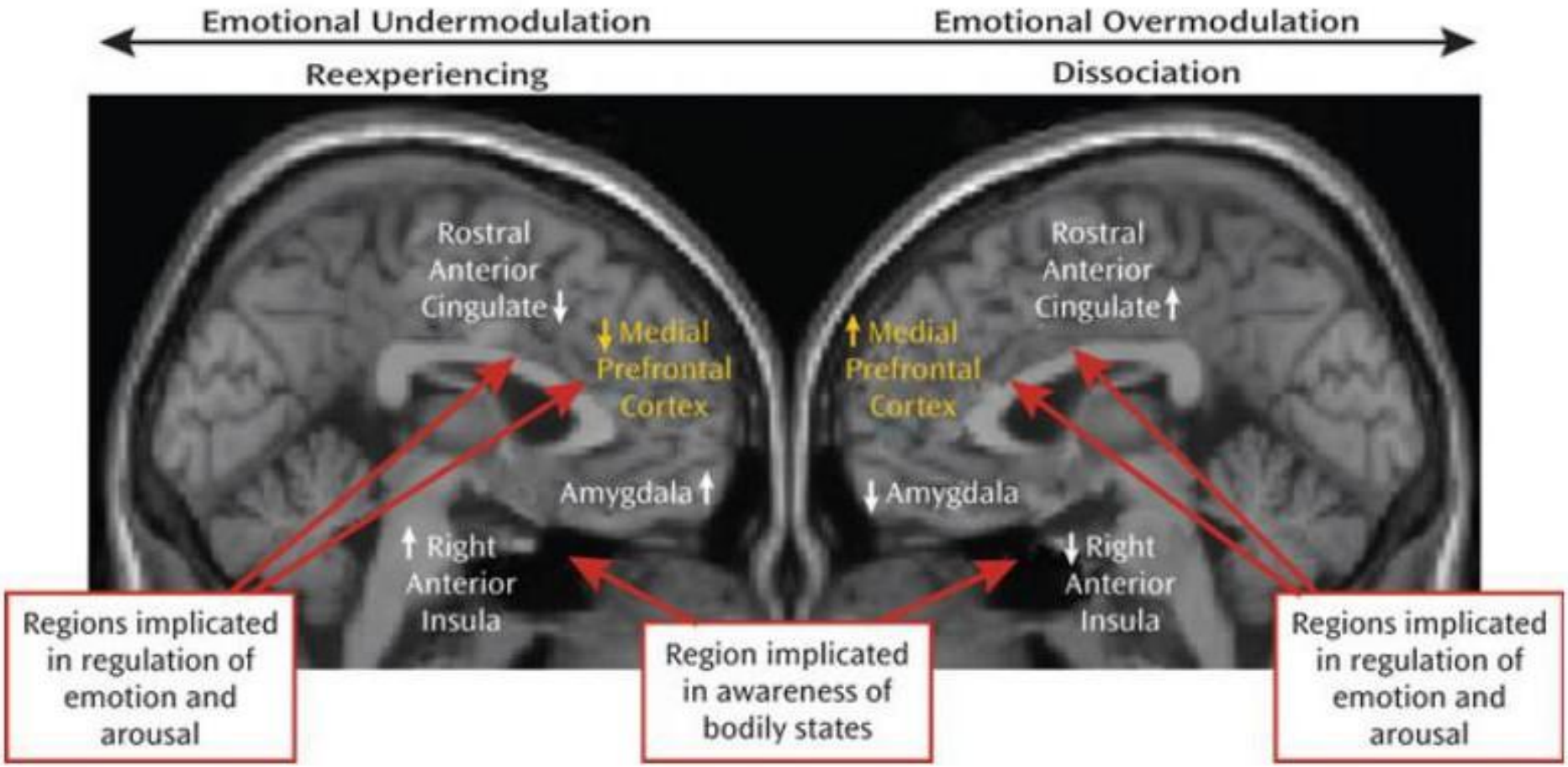
My spend my life between pieces of effective Action.


Tonic Immobility
Sympathetic/ parasympathetic activation
Hyperarousal & Hypervigilance Responses
Collapsed Immobility
Compromised consciousness, ↑ parasympathetic activation, ↓ attention/arousal, opioid-mediated analgesia, functional cortical deafferentation
Fight or Flight
Sympathetic activation, endocannabinoid-mediated analgesia
Depersonalization & Derealization Responses
Baseline Arousal
Orienting Freeze
Information Gathering
Vasovagal Response
Fainting/ loss of consciousness
Defense Reaction
Dissociative Status

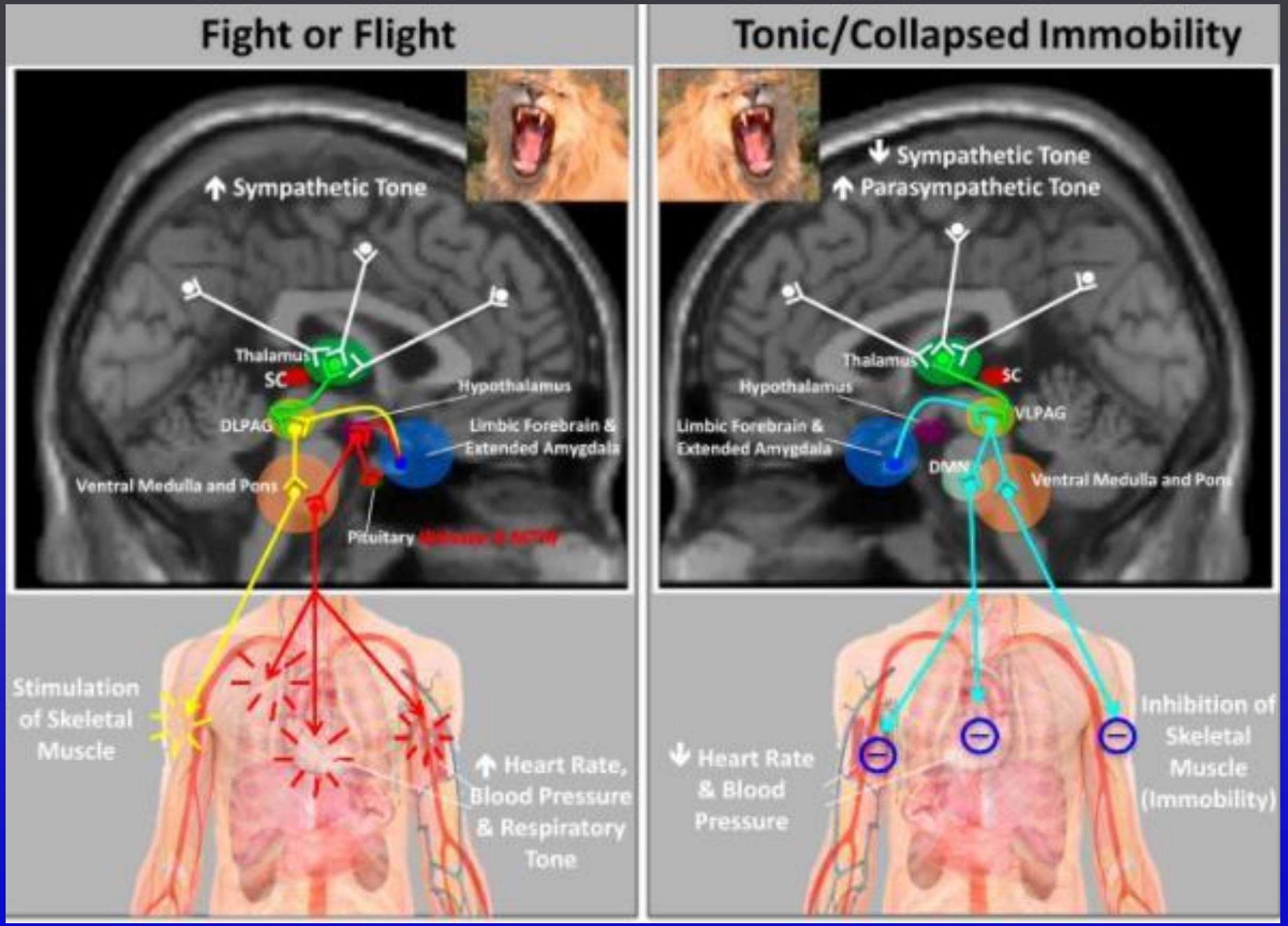
Temporal Binding



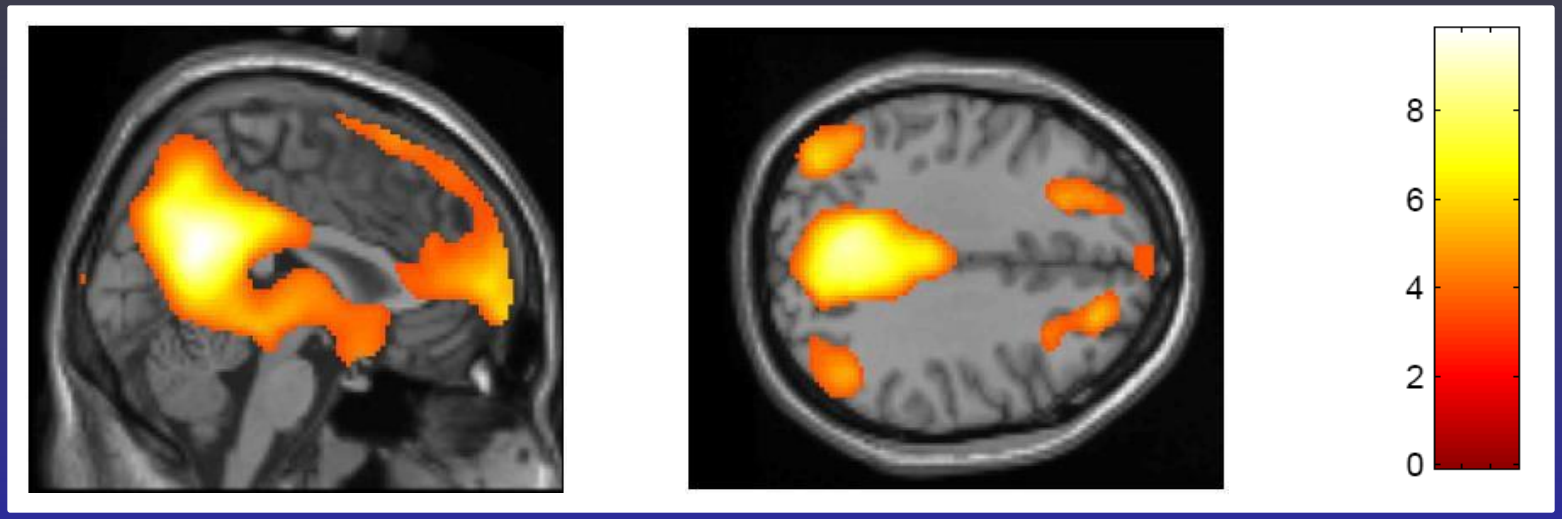
Thalamocortical rhythms integrate information across regions at 80mHz



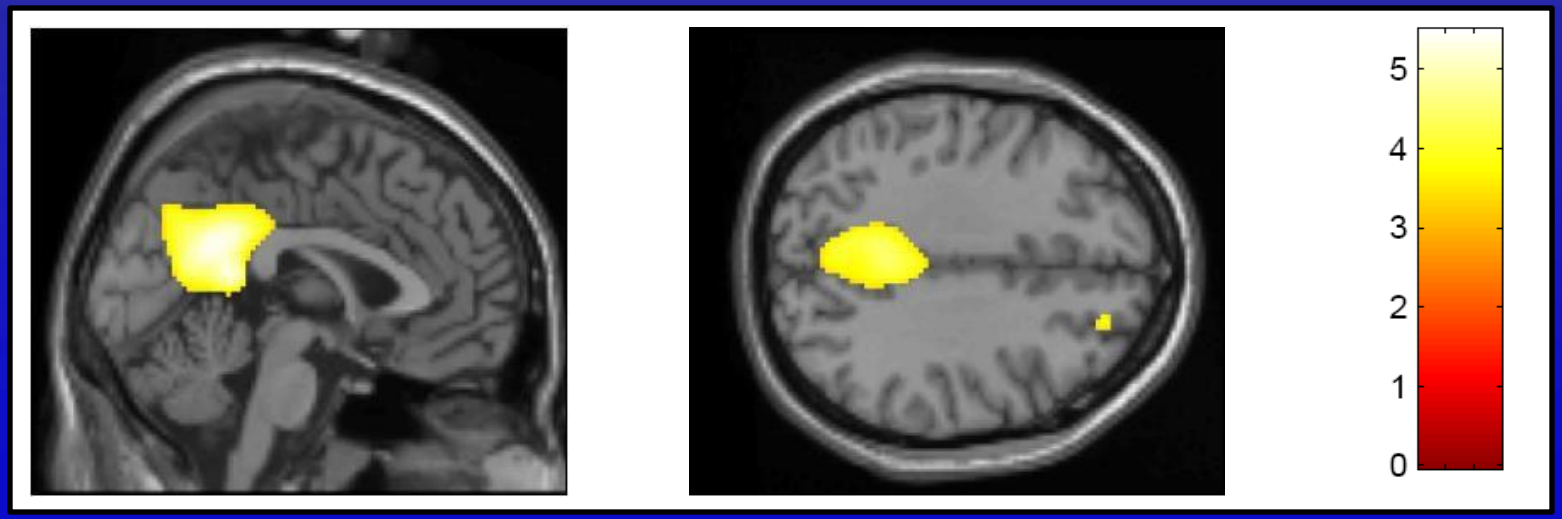
otional under- and overmodulation in PTSD (Reprinted with permission from the American Jou
©2010). American Psychiatric Association)


Fight or Flight
Sympathetic Tone
Thalamus
SC
Hypothalamus
DLPAG
Limbic Forebrain & Extended Amygdala
Ventral Medulla and Pons
Pituitary
Stimulation of Skeletal Muscle
Heart Rate, Blood Pressure & Respiratory Tone
Tonic/Collapsed Immobility
Sympathetic Tone
Parasympathetic Tone
Thalamus
SC
Hypothalamus
VLPAG
Limbic Forebrain & Extended Amygdala
DMN
Ventral Medulla and Pons
Heart Rate & Blood Pressure
Inhibition of Skeletal Muscle (Immobility)

Controls (n=16): Positive Correlation



PTSD (n=18): Positive Correlation



Default Mode Network

DMN is a key brain network underlying

a) continuous experience of the sense of self across time and into the future,

b) envisioning the future,

c) conceiving the perspectives of others

d) dissociative experiences involve brain regions associated with the DMN, including the medial prefrontal cortex, medial parietal lobe, and the temporo-parietal junction

(Frewen & Lanius, 2015)

How Balance and Action orientation become Disabled During Trauma

- Action would have been futile
- Having been physically overpowered
- Resistance could have led to more trauma
- The individual dissociated
- Conditioning from prior trauma led to automatic submission and obedience or to freezing

Ogden, 1999

Perception and Self-experience

- Conscious emotional experience is based on the perception of physical sensations/bodily states arising from musculoskeletal, autonomic nervous, and endocrine system mediated by the anterior insula[1].
- Mapping what physical sensations are associated with specific emotions - help individuals identify what is going on.
- Specific maps of bodily sensations are associated with different emotions
- Increasing awareness of bodily sensations is important strategy to deal wit emotional detachment and thus restore salience detection. insula and SN functioning
- Meditators exhibit greater gray matter thickness of the insula as compared to non-meditator Increase in right insula cortical thickness that correlated with decreased levels of alexithymia in mindfulness-based stress reduction

Nummenmaa, Glerean, Hari, & Hietanen, 2014). (Santarnecchi et al., 2014).

Emotional undermodulation & hyperarousal

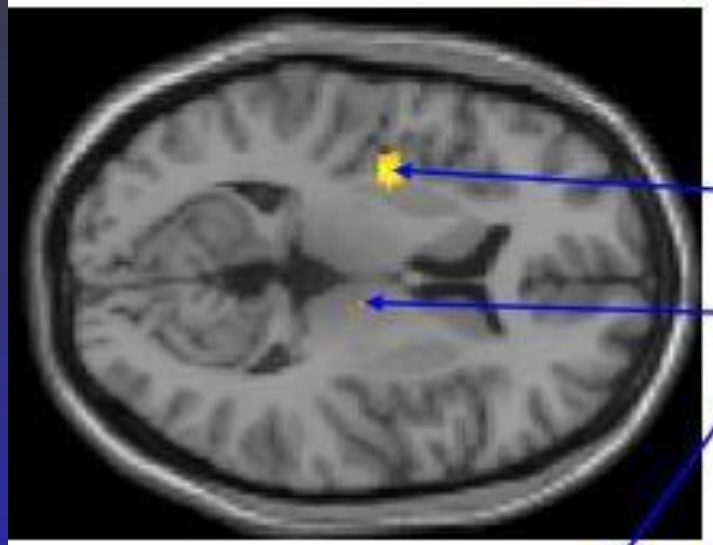
Hypervigilance, increased interoceptive awareness, salience detection, and heightened insula activation.

Increased insula activation alters SN: hypervigilance & hyperarousal.

Identity

- “I have permanently changed for the worse,”
- “I will never be able to feel normal emotions again,”
- “I don’t know myself anymore”
- Somatically-based alterations in self-referential processing, such as depersonalization
- “I feel as if I am outside my body,”
- “I feel dead inside,”
- “I feel like my body does not belong to me”

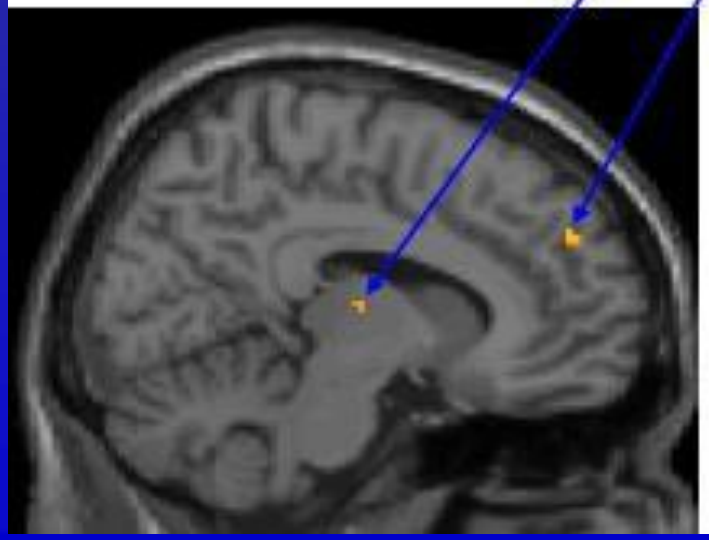
Yoga Participants(n=6) Greater Than Control(n=2),
Post-Yoga Greater Than Pre-Yoga

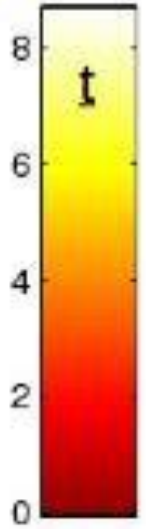


Left Insula

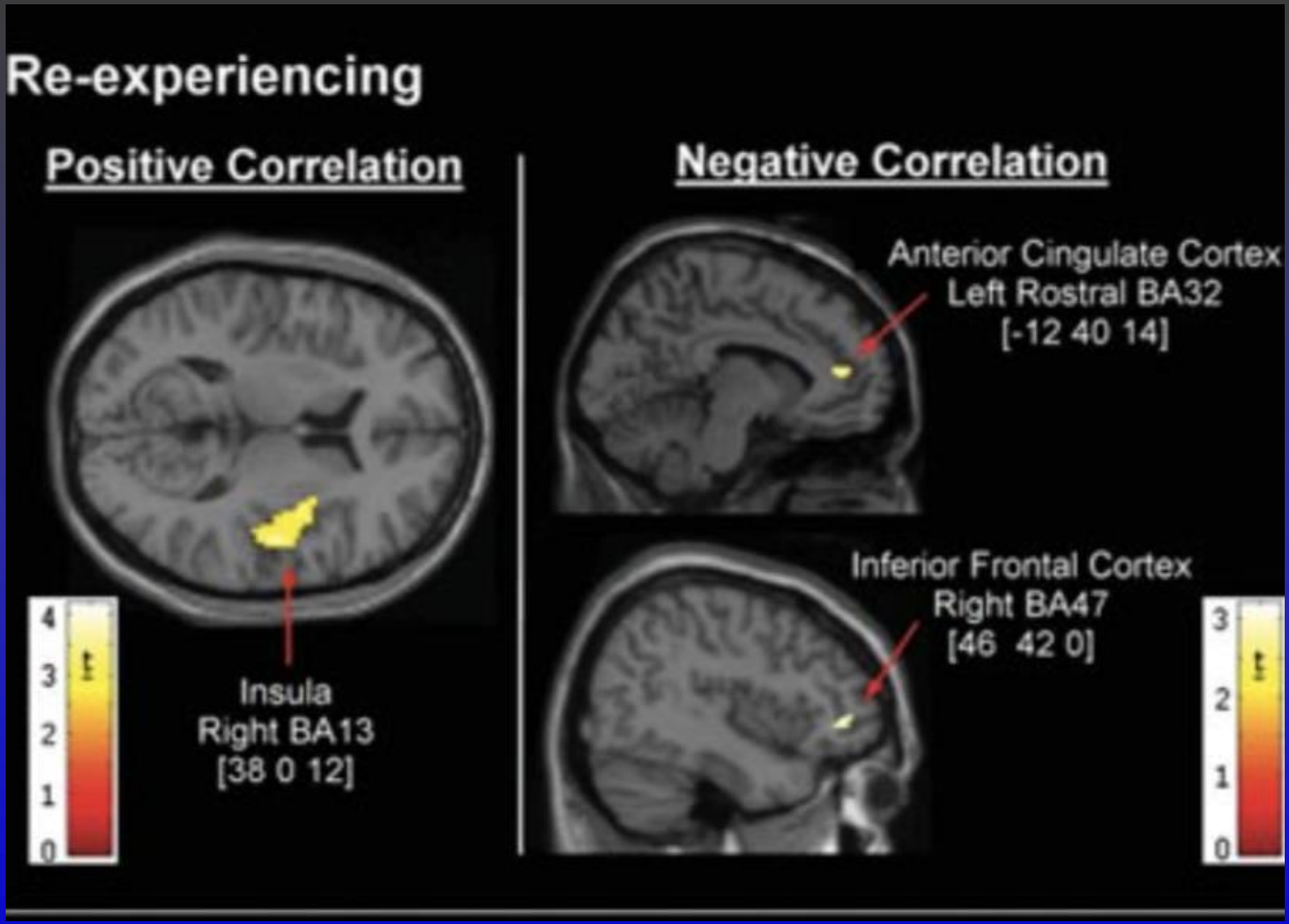
Right Thalamus

Right Dorsomedial Prefrontal Cortex



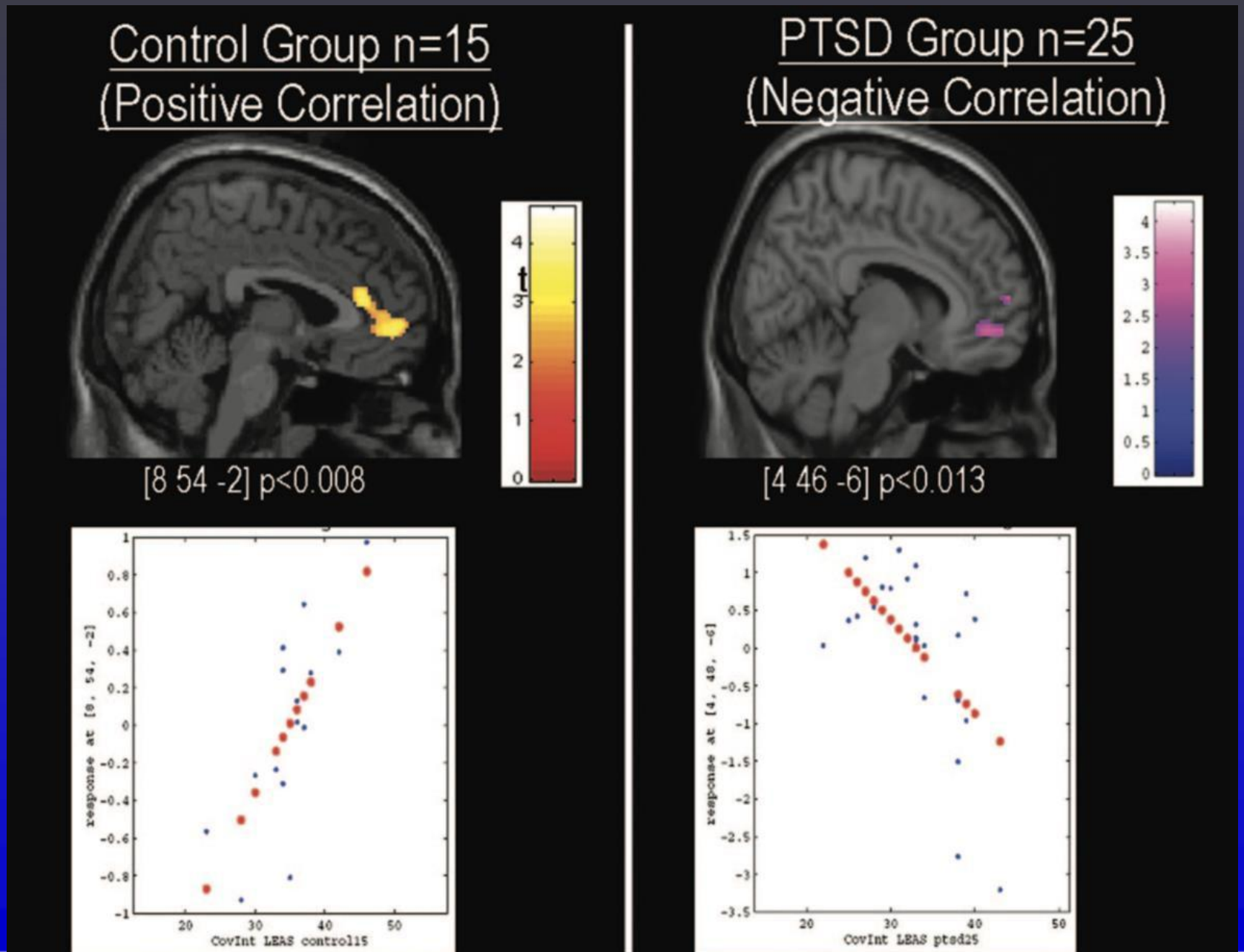


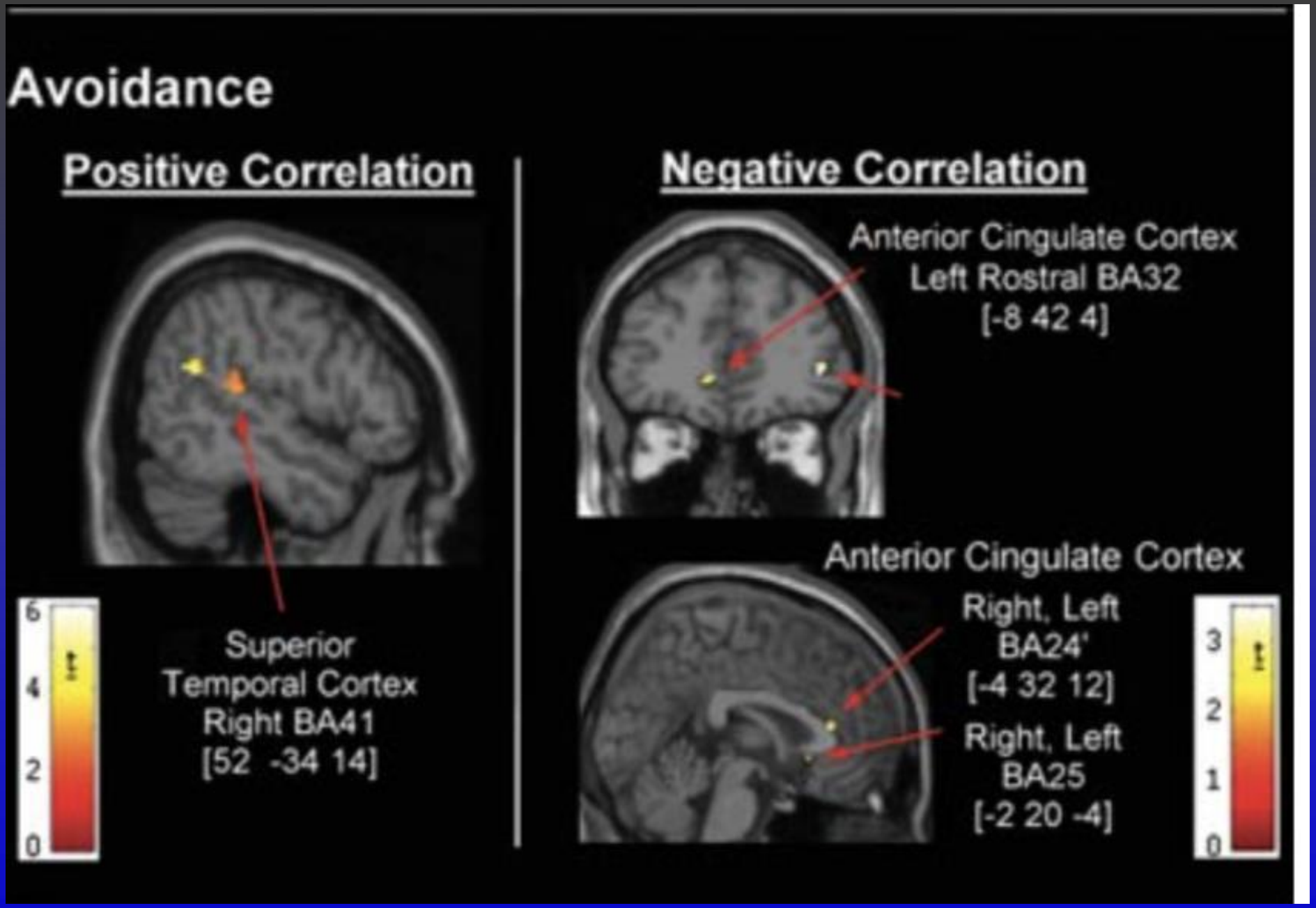
Van der Kolk & Lanius 2012



Hopper, Frewen, van der Kolk & Lanius

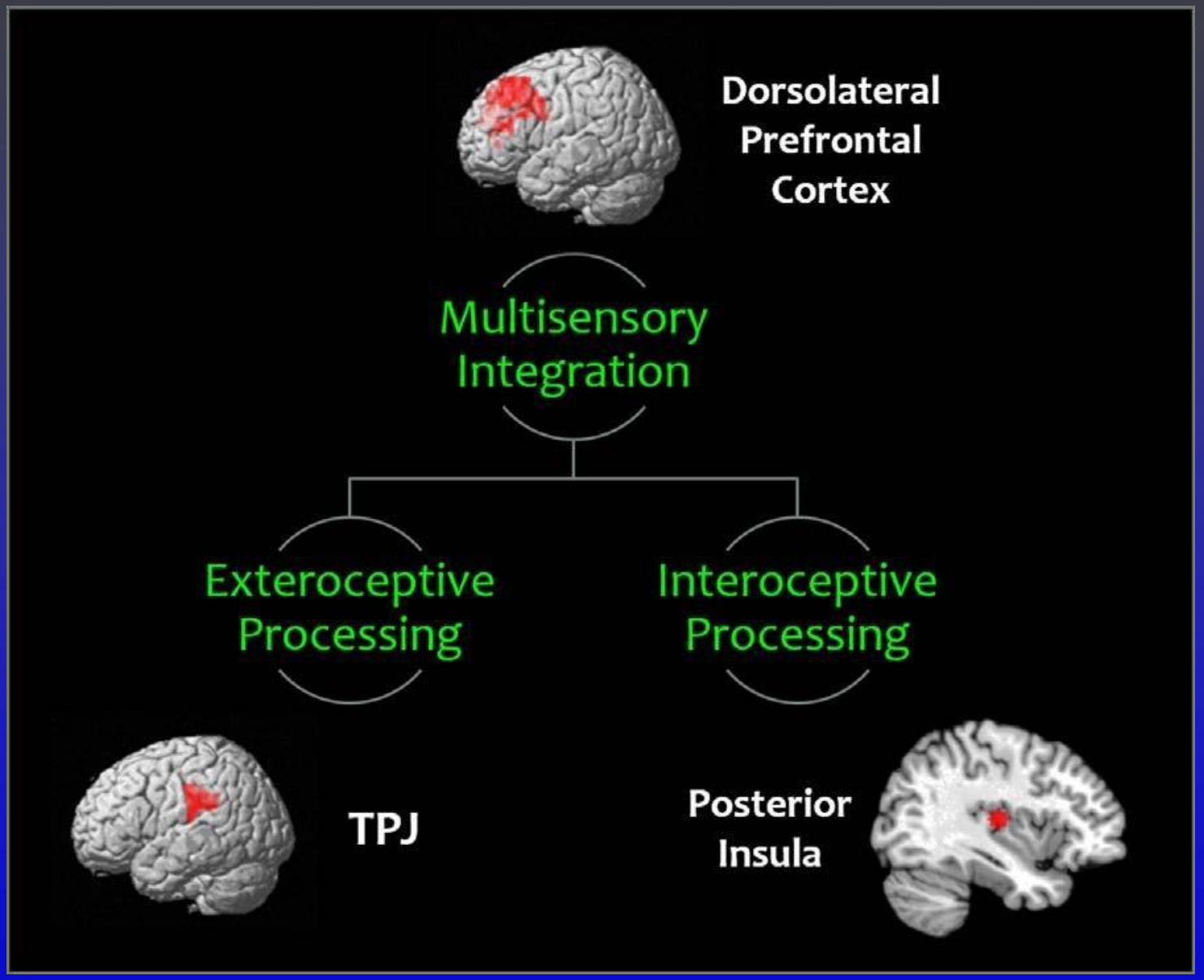
Frewen et al Emotional awareness in PTSD (2016





Hopper, Frewen, van der Kolk & Lanius, 2007

Sensory overload and imbalance: Resting-state vestibular connectivity in PTSD and its dissociative subtype Harricharan, Nicholson, …. Neufeld, Lanius,



The processing of multisensory integration and sensorimotor transformations

"Mr. Osborne, may I be excused?
My brain is full."

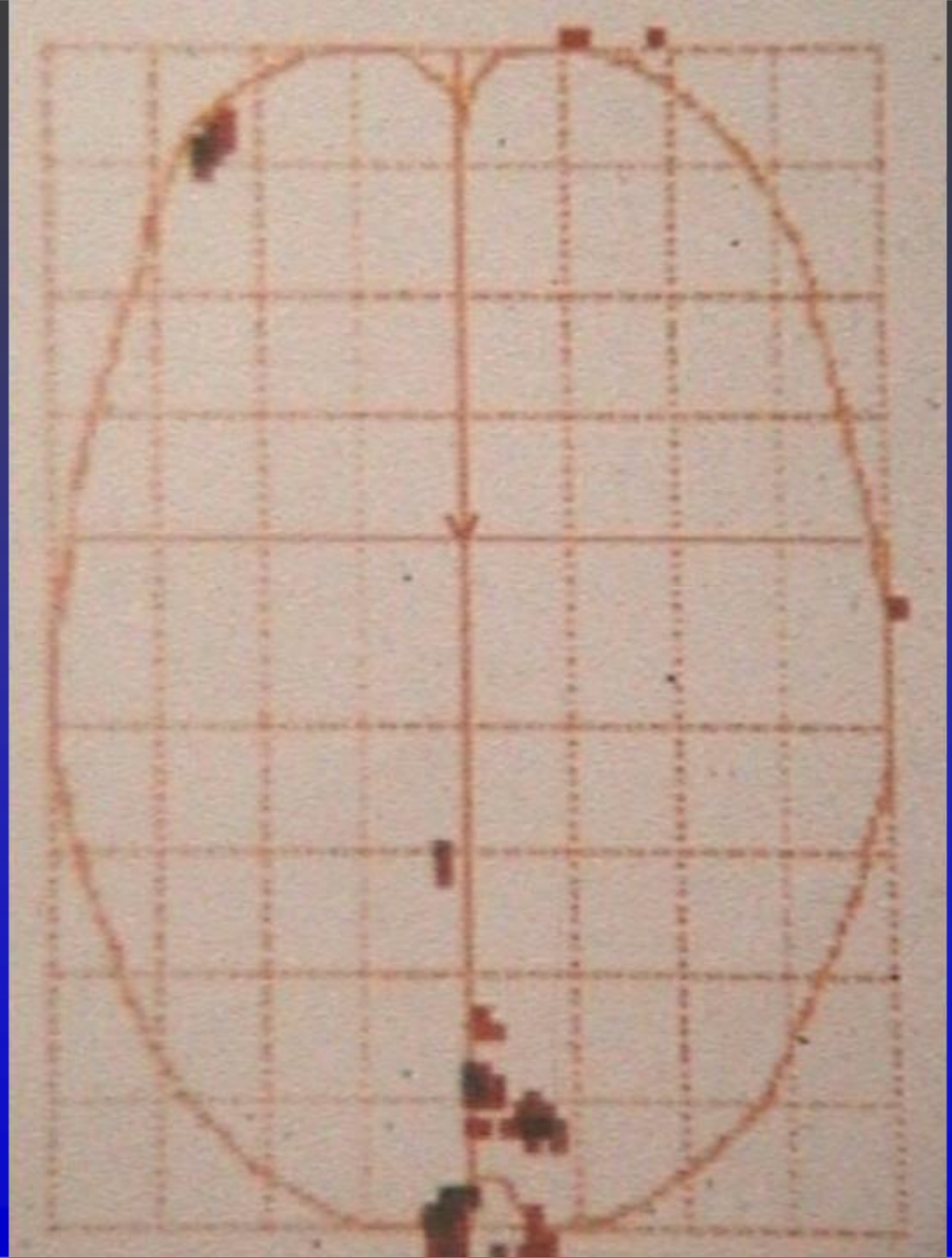
An event becomes traumatic because it overwhelms the brain's capacity to cope.

Rigidly stuck in the past

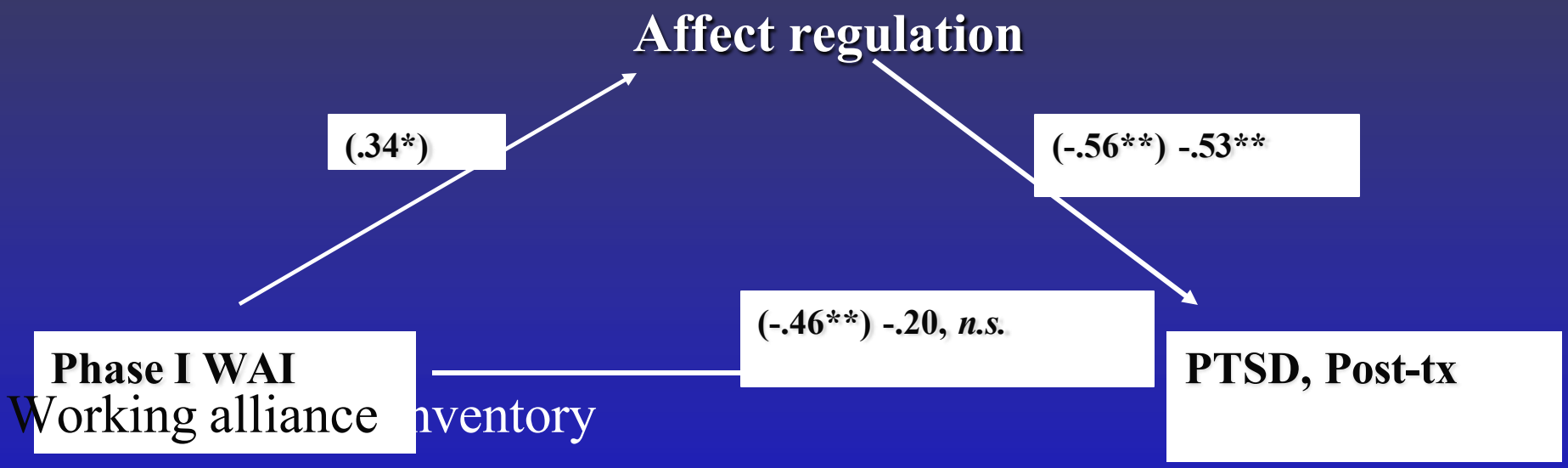
b/c thalamus (sensory integration) & Dorsolateral Prefrontal Cortex (timekeeper) off-line

Lanius
Dissociation

Dissociation/numbing: parasympathetic shutdown

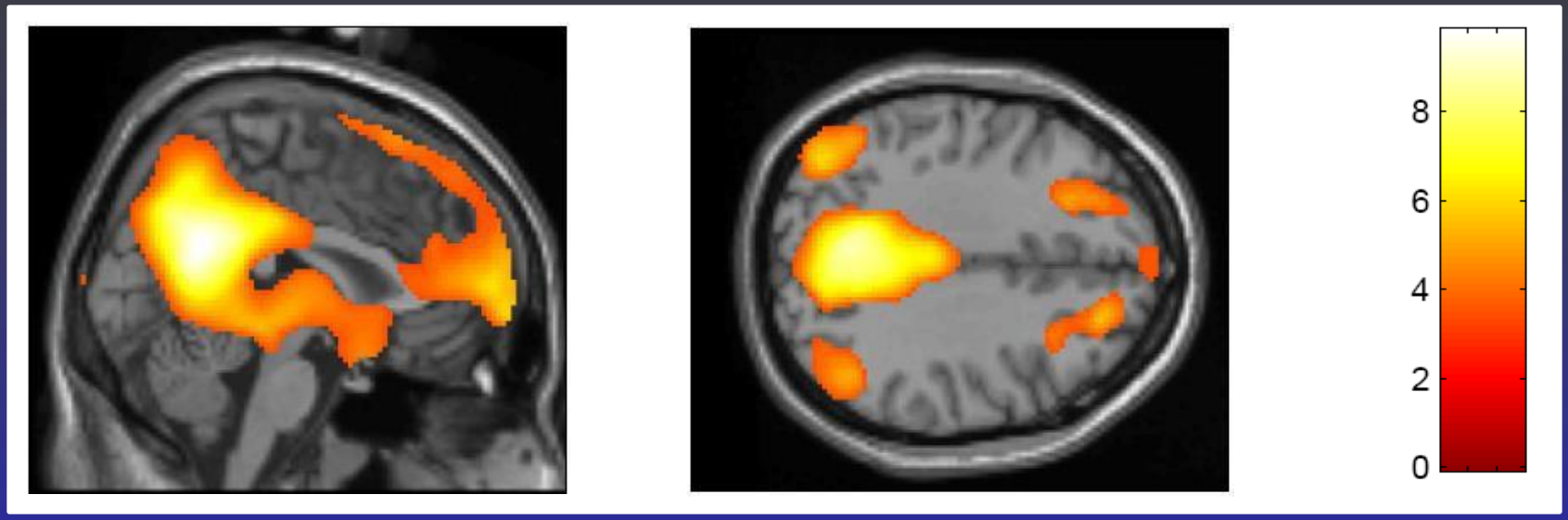


PREDICTORS
OF TREATMENT OUTCOME

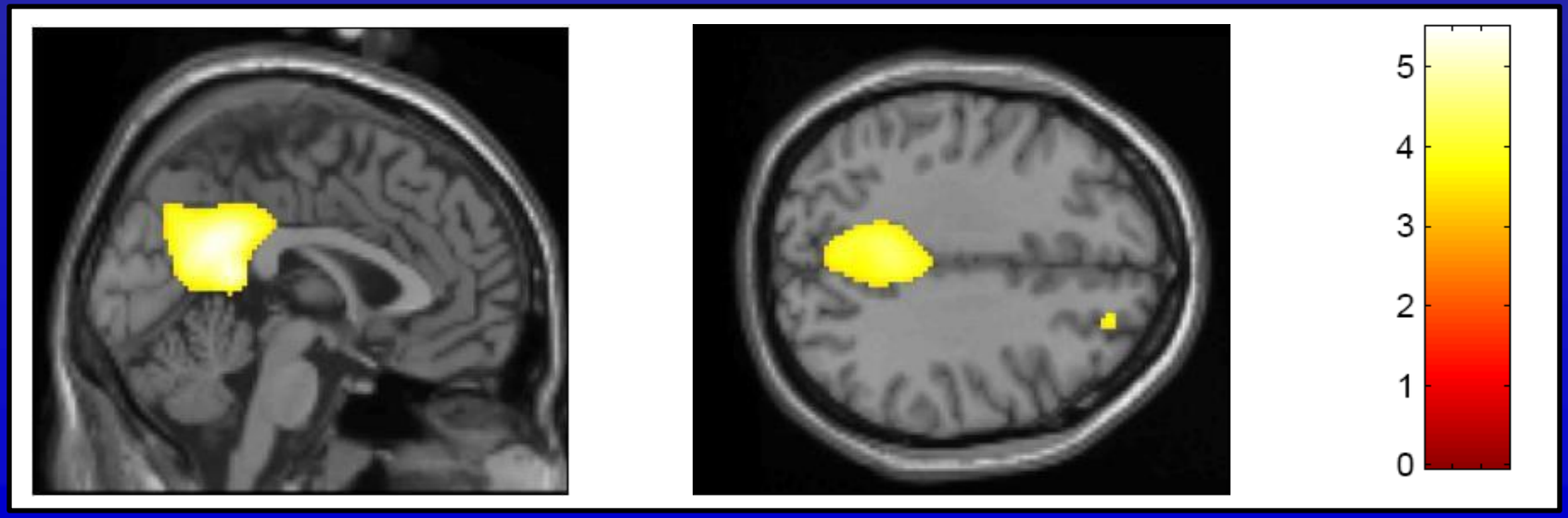


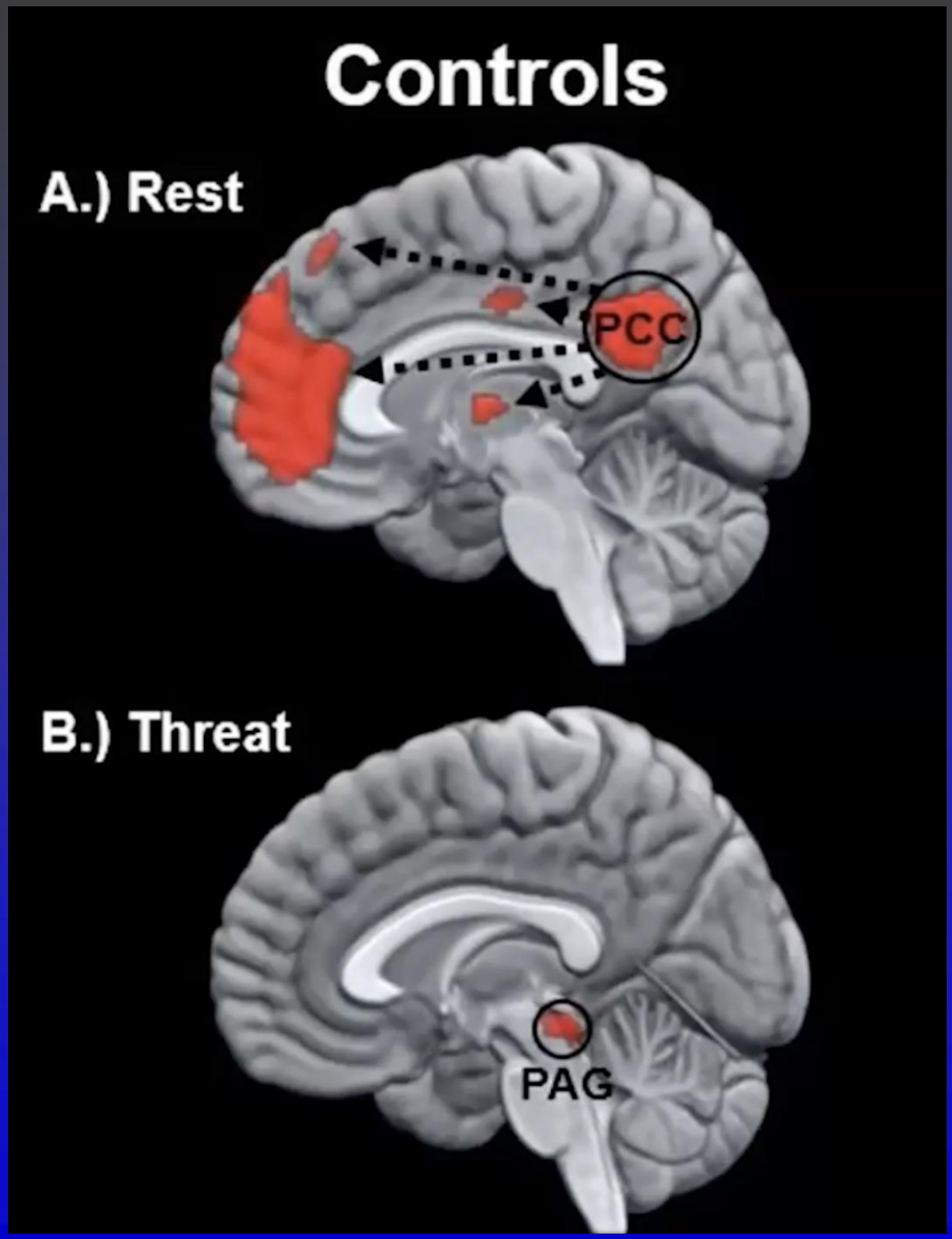
Cloitre et al, 2003

Controls (n=16): Positive Correlation



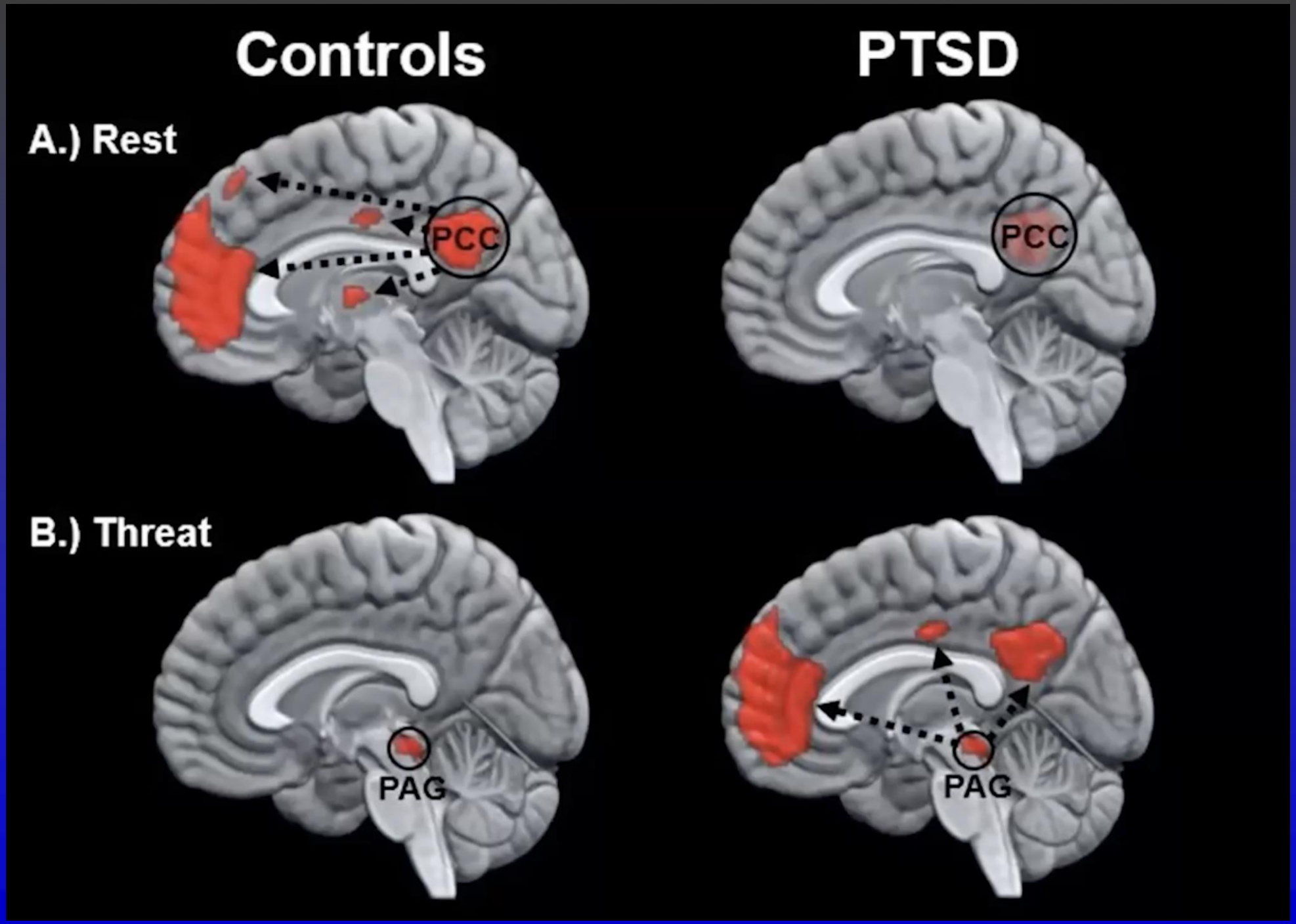
PTSD (n=18): Positive Correlation

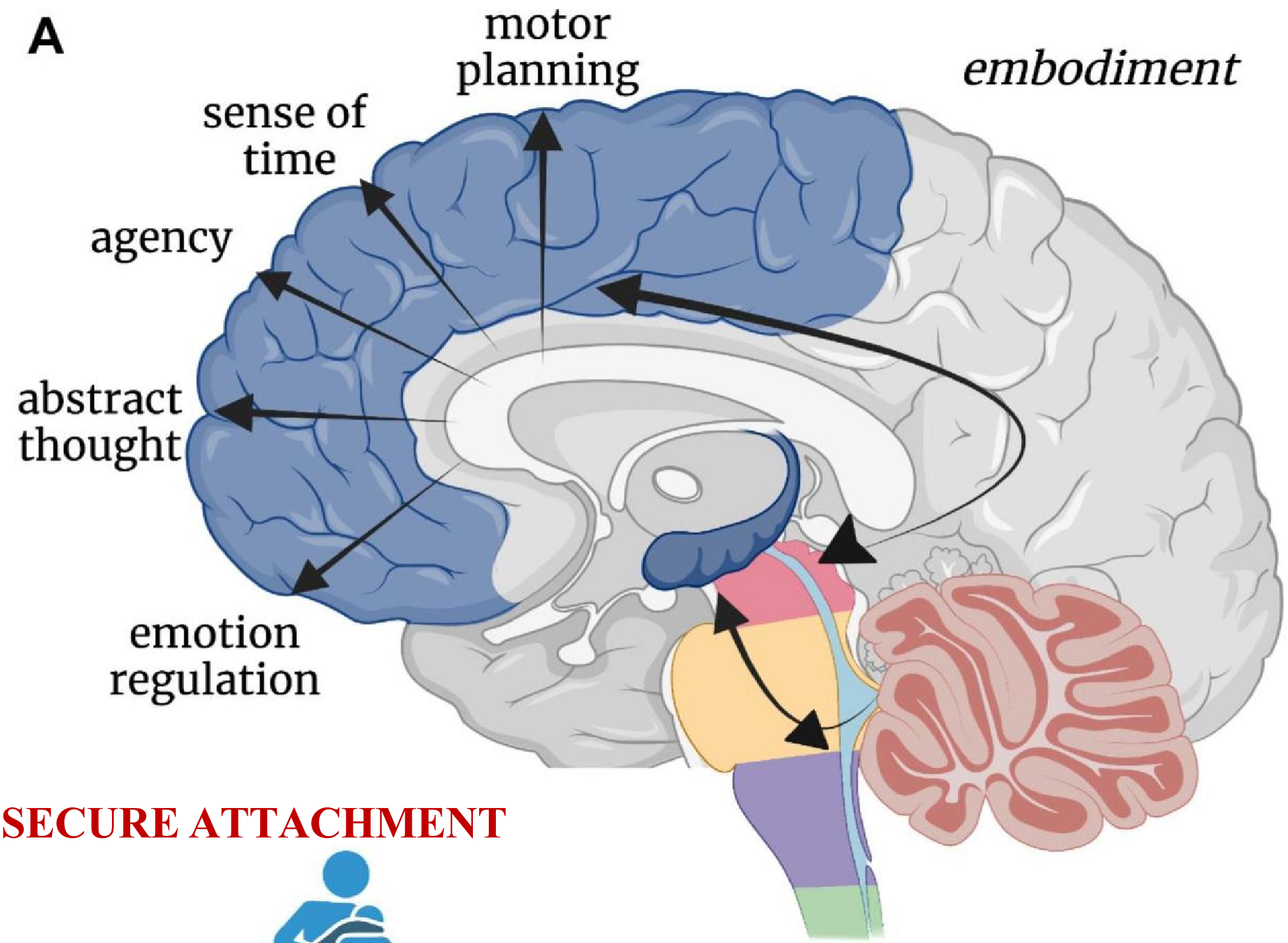




Default Mode Network in people without PTSD

Lanius et al 2020


Controls
PTSD
A.) Rest
PCC
PCC
B.) Threat
PAG
PAG



SECURE ATTACHMENT

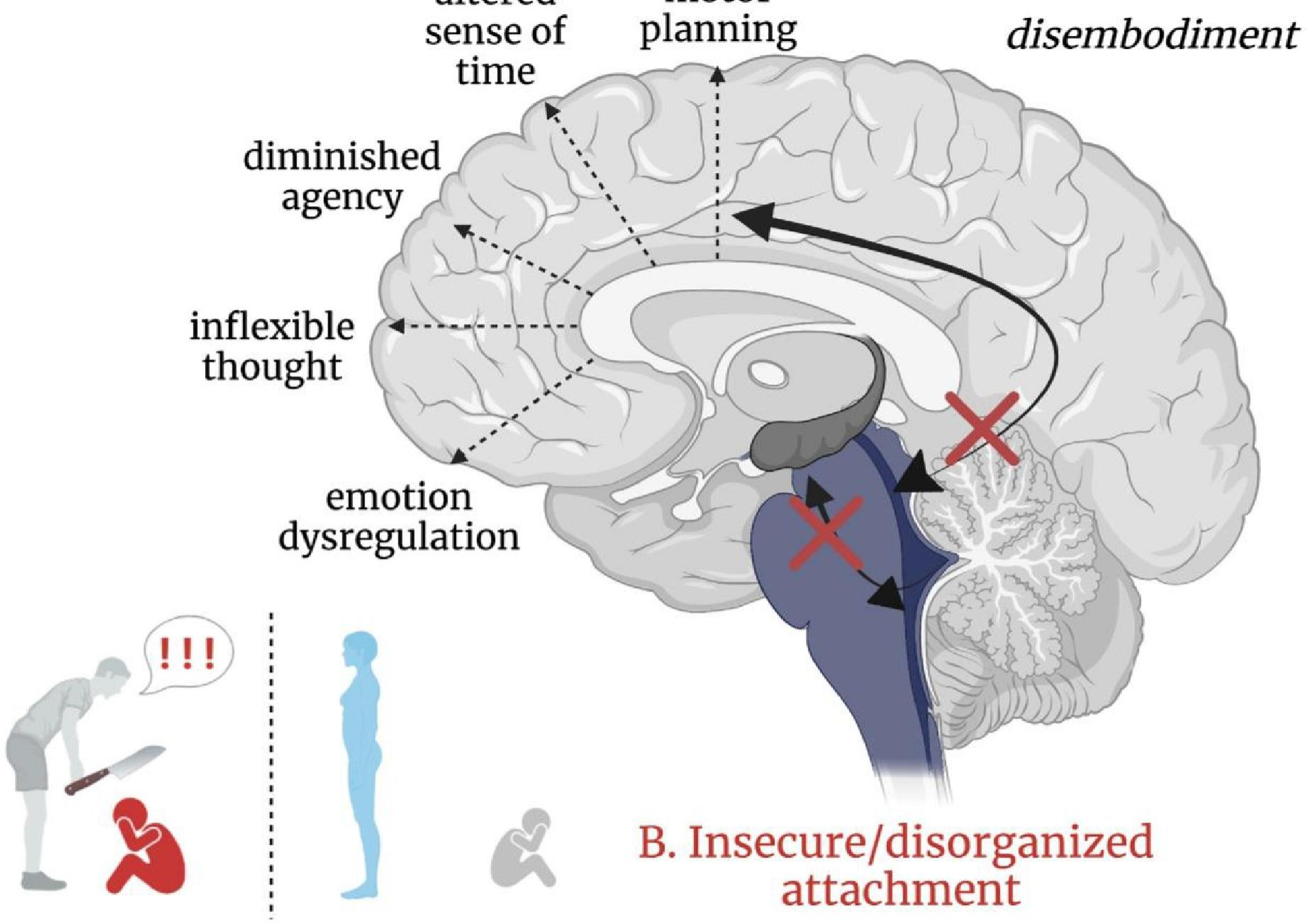
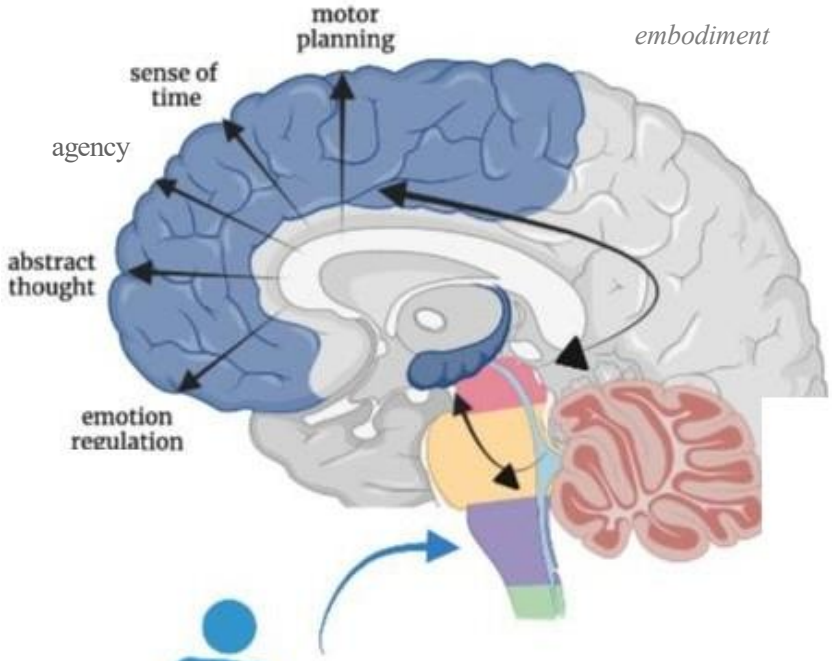
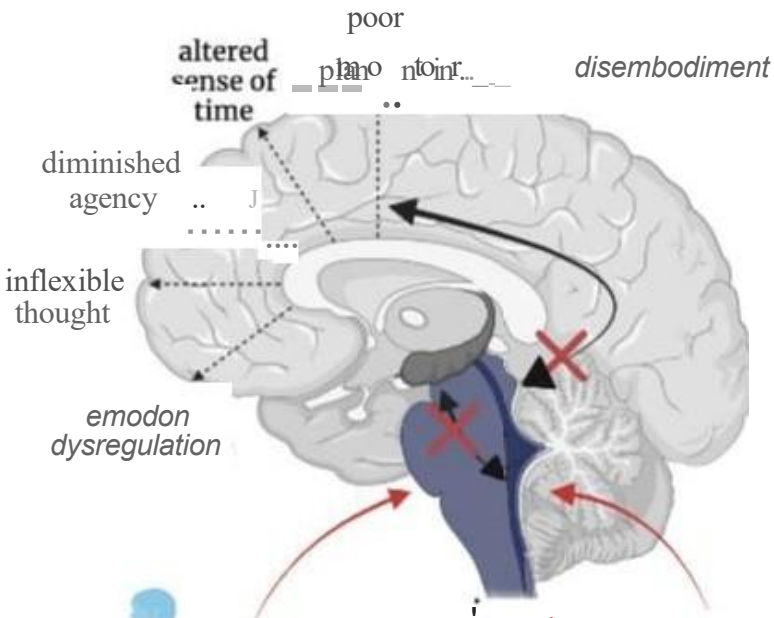

altered
sense of
time
motor
planning
disembodiment
diminished
agency
inflexible
thought
emotion
dysregulation
!!!
B. Insecure/disorganized
attachment

FIGURE 5



embodiment



disembodiment

+ secure attachment

+ neglect

+ abuse

! ! !

somatic sensory integration

somatic sensory . disintegration

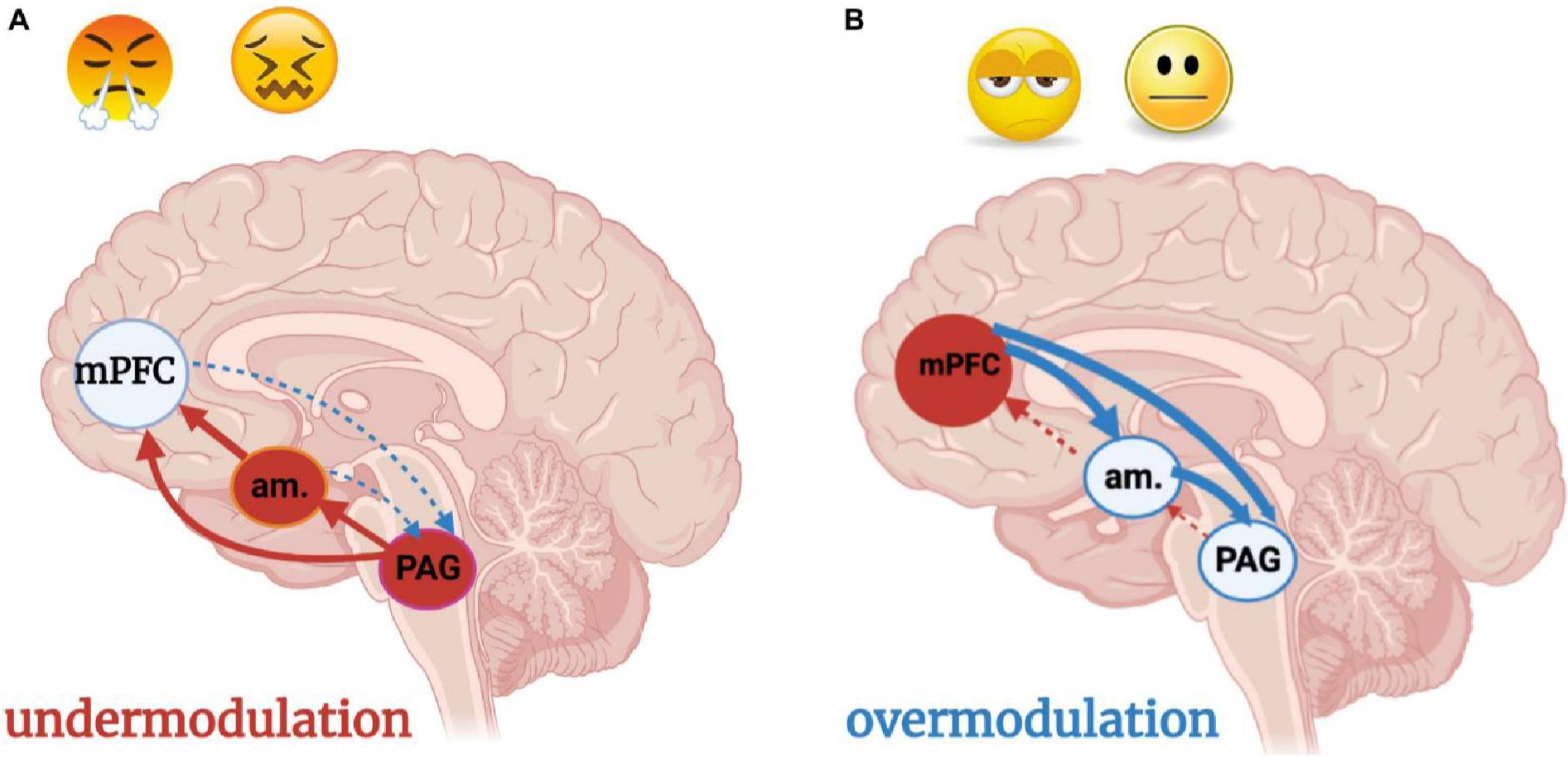


FIGURE 9

(A,B) Under- and over-modulation of emotion and arousal in trauma-related conditions. Image adapted with permission from Nicholson et al. (2017). An individual who encounters a traumatic situation is flooded with negatively valenced sensory stimuli, resulting in hyperactivation of the brainstem and midbrain PAG. An individual who develops a post-traumatic condition experiences persistent over-or under-modulated activity of the PAG and amygdala, resulting in hyper- and hypo- sensory-affective responsivity, respectively, at the level of the PAG.
(A) Under-modulation or bottom-up predominance (solid arrows) results in hyperarousal and weak top-down neocortical modulation (dashed arrows) of sensory input and emotions. Situations incorporating sensory or emotional stimuli similar to the traumatic event, often over-generalized with regard to valence (i.e., every sensation of butterflies in the stomach is labeled as a sign of danger) triggers hyperarousal and a fight/flight response. **(B)** Over-modulation of lower brainstem and midbrain arousal and alarm centers (amygdala, PAG) is driven by frontal neocortical regions including the mPFC. An individual who experiences chronic, repeated traumatization, such as an adolescent who has grown up in a household with domestic violence and physical abuse, adapts to persistent threat through top-down blunting and avoidance. The

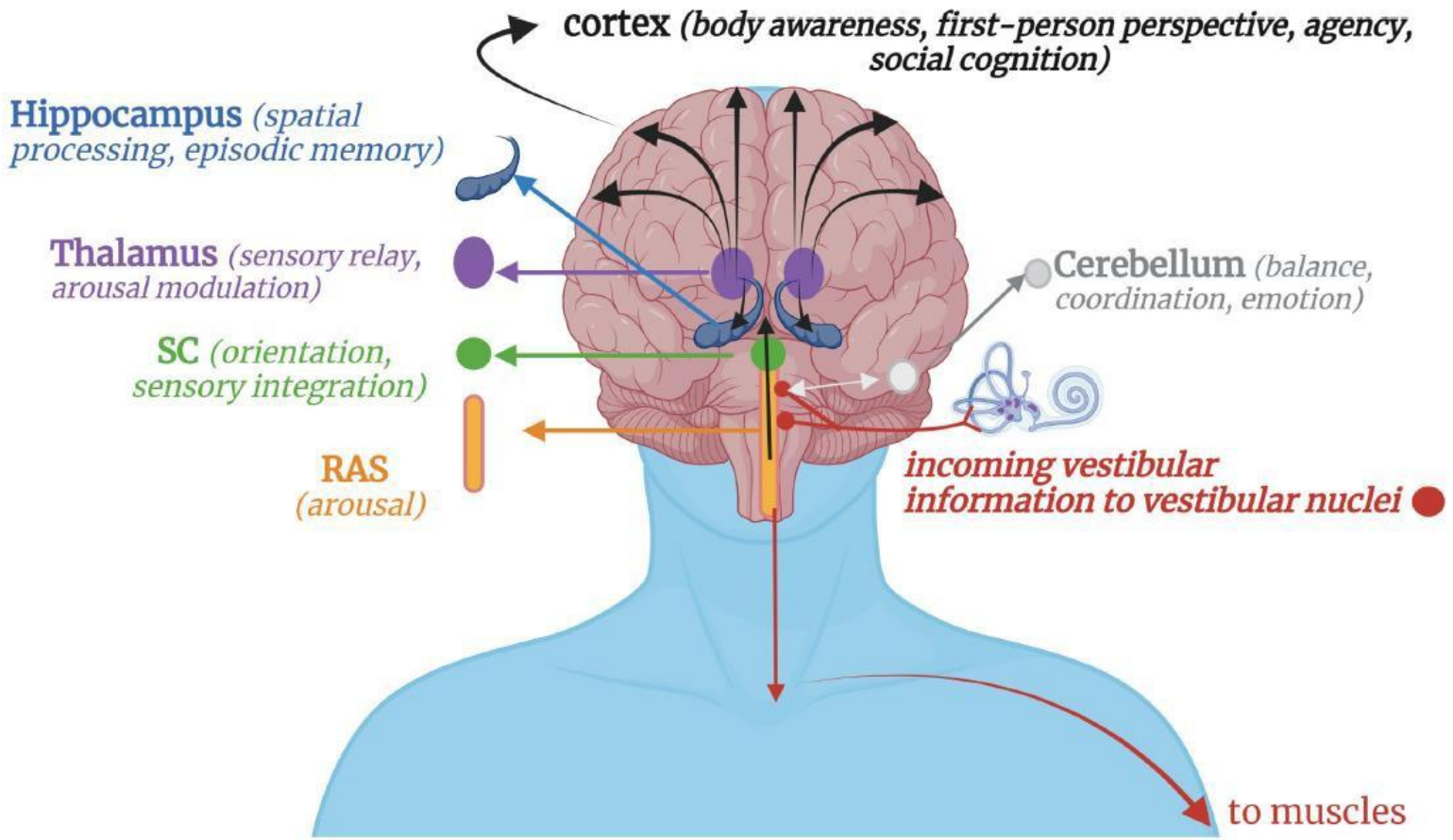
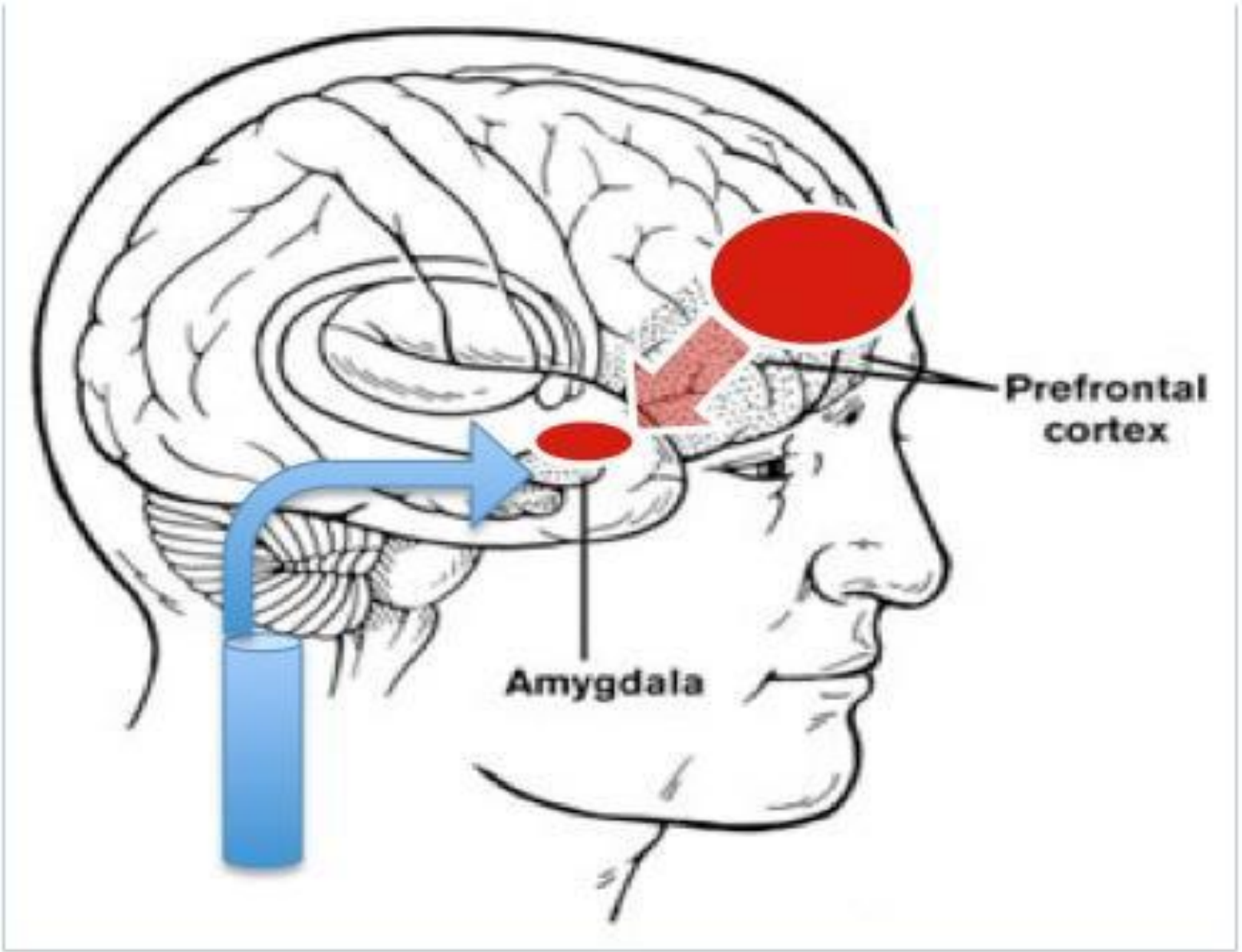


FIGURE 1

A simplified schematic of vestibular projections throughout the nervous system. Afferent input from gravitational forces arrives at the vestibular nuclei, which integrate with somatosensory input via the cerebellum, reticular formation, and spinal afferent tracts. Downward vestibular efferent projections send signals for muscular extension and postural control. Reciprocal connections with the cerebellum, mainly its flocculonodular lobe, allow for feedback-feedforward mechanisms of motor coordination and fluency, with the cerebellum projecting information back to the vestibular nuclei or directly up to the cortex. Ascending vestibular projections integrate with the RAS and SC for arousal modulation and orienting responses before continuing on to higher cortical structures via the thalamus. Vestibular projections to the cortex then contribute to higher-order cognitive processes such as a sense of agency, first-person perspective, social cognition, and bodily self-consciousness. RAS, Reticular activating system; SC, Superior colliculi.


Prefrontal cortex
Amygdala

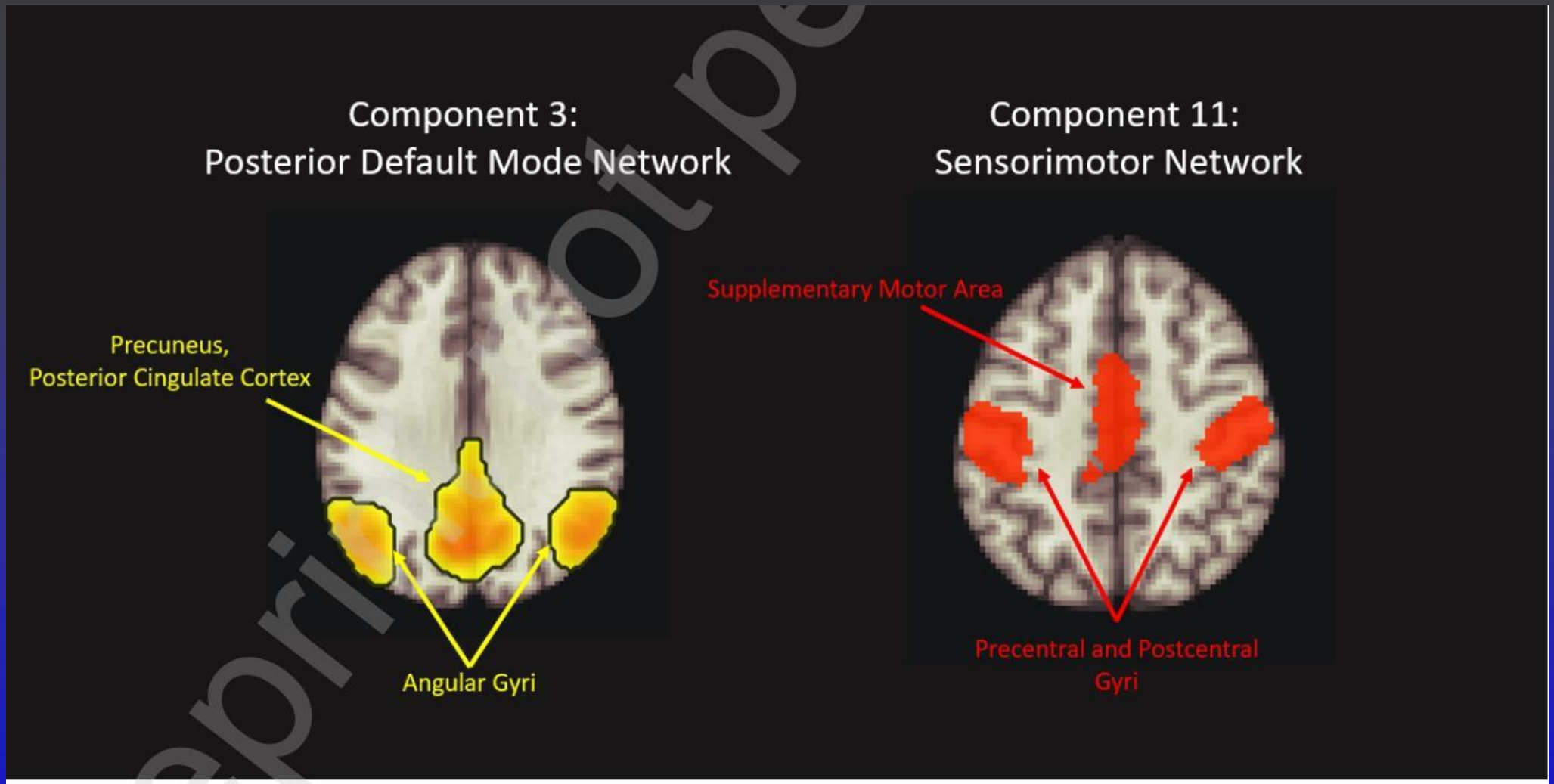


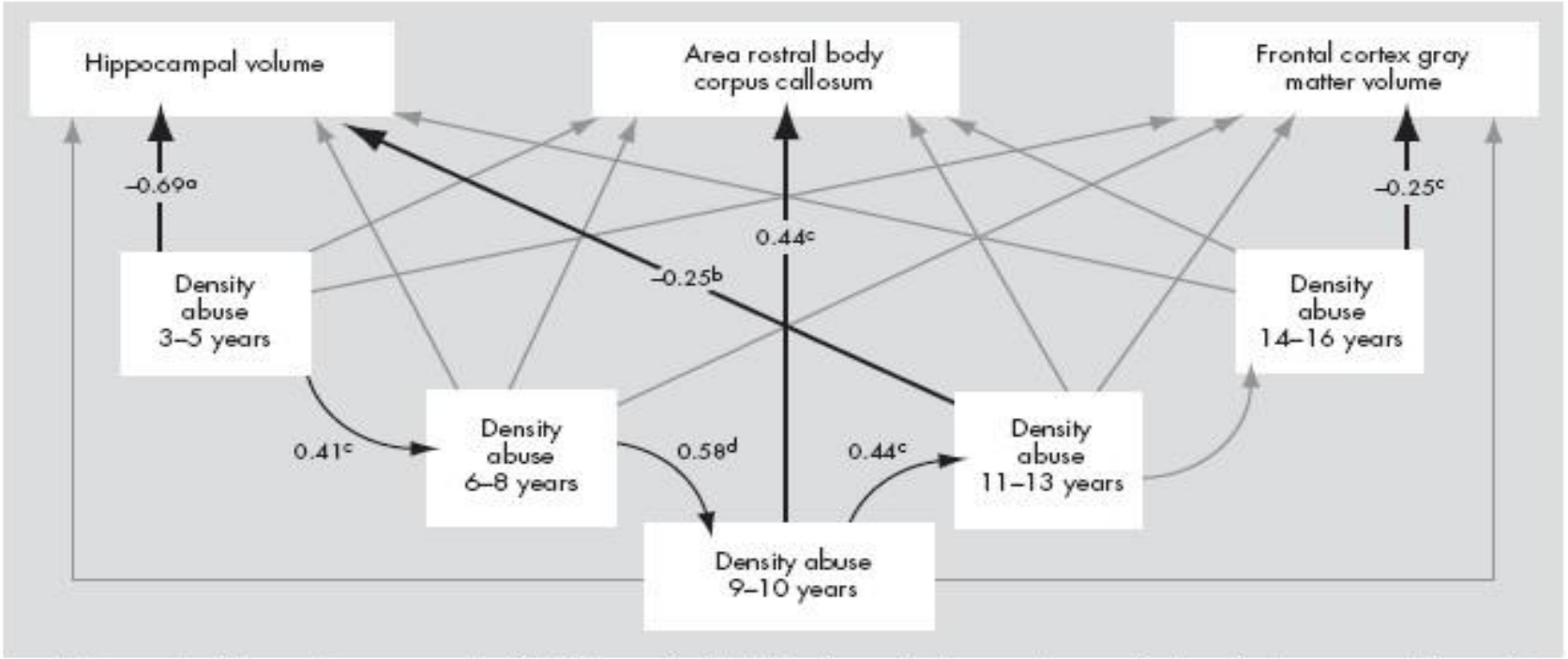
Figure 1: Components 3 and 11 from a group-ICA using 11 components generated in CONN21.a. Whereas component 3 correlated highest with the posterior nodes of the default mode network (r = 0.489), Component 11 correlated highest with the sensorimotor network (r = 0.422). ICA: Independent Component Analysis.

Without a Self there is No Other

Martin Teicher

Abuse at Different Ages Affects Different Brain Areas

FIGURE 1. Path Analysis Indicating Relationships Between Density of Abuse During Different Stages of Development and Measures of Brain Size Derived from Structural Equation Modeling



Path analysis examined two main components. The first was that childhood sexual abuse or absence of abuse during one period would predict childhood sexual abuse (or absence of abuse) during the subsequent period. The second component examined the association between density of childhood sexual abuse during each stage and all morphometric measures. Numerical values represent standardized beta-weights and their associated p values. Light gray lines were evaluated in the model but were not significantly predictive of any relationship between the variables. Morphometric measures for corpus callosum and frontal cortex gray matter volume were covaried by midsagittal area and total gray matter volume, respectively. Hippocampal volume was covaried by intracranial volume and list recall, based on results of the multiple regression analyses (see Table 2).

[a] $p<10^{-7}$
[b] $p<0.05$
[c] $p<0.005$
[d] $p<0.0001$

Andersen, S.L. et al. (2008). Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. *J Neuropsychiatry*, 20, 3, 292-301.

nature REVIEWS NEUROSCIENCE

The effects of childhood maltreatment on brain structure, function and connectivity

Martin H. Teicher, Jacqueline A. Samson, Carl M. Anderson & Kyoko Ohashi

Nature Reviews Neuroscience **17**, 652–666 (2016) | doi:10.1038/nrn.2016.111
Published online 19 September 2016

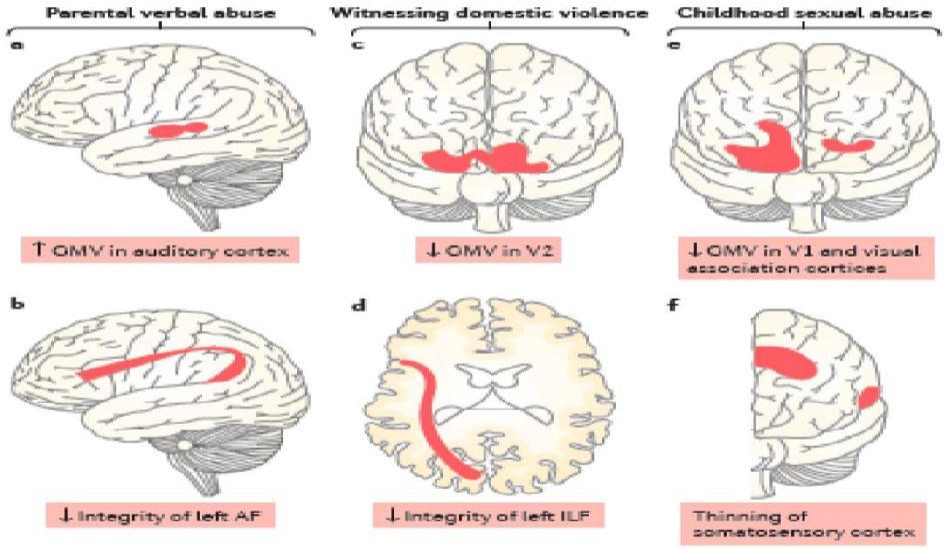
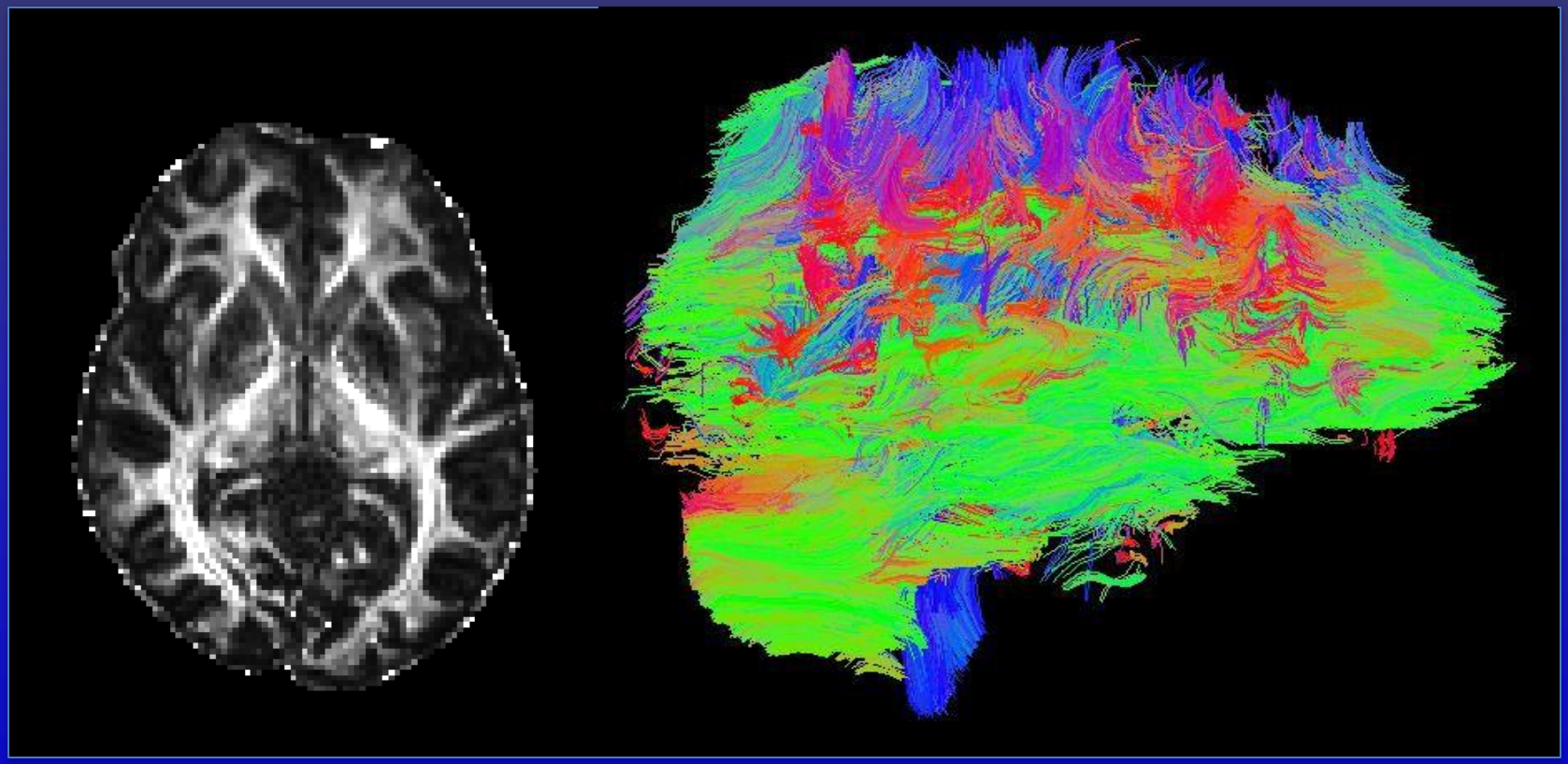


Figure 1 | Abuse type-specific effects on the developing brain. Images depicting the potential effects of exposure to specific types of childhood maltreatment on grey-matter volume (GMV) or thickness and fibre-tract integrity. Exposure to parental verbal abuse was associated with increased GMV in the auditory cortex portion of the left superior temporal gyrus[23] (part **a**) and decreased integrity of the left arcuate fasciculus (AF) interconnecting Wernicke's area and Broca's area[24] (part **b**). Visually witnessing multiple episodes of domestic violence was associated with reduced GMV in right lingual gyrus, left occipital pole and bilateral secondary visual cortex (V2)[27] (part **c**) and decreased integrity of the left inferior longitudinal fasciculus (ILF), which serves as a visual–limbic pathway[28] (part **d**). Adults reporting exposure to multiple episodes of childhood forced-contact sexual abuse were found to have reduced GMV in right and left primary visual cortex (V1) and visual association cortices, as well as reduced thickness in right lingual, left fusiform and left middle occipital gyri[29] (part **e**) and portions of the somatosensory cortex representing the clitoris and surrounding genital area[30] (part **f**). Part **a** is adapted with permission from REF. 25, Elsevier. Part **b** is adapted with permission from REF. 26, Elsevier. Part **c** is adapted from REF. 27. Part **d** is adapted with permission from REF. 28, Elsevier. Part **e** is adapted with permission from REF. 29, Elsevier. Part **f** is adapted from an image courtesy of C. Heim, Charité Universitätsmedizin Berlin, Germany, and J. Pruessner, McGill University, Canada.

- Verbal abuse: higher grey matter volume (GMV) in auditory cortex and lower integrity of left arcuate fasciculus. Diminished arcuate fasciculus integrity associated with lower verbal IQ and comprehension.
- Witness domestic abuse: Lower grey matter density in right lingual gyrus and reduced thickness in portions of visual cortex. Witnessing domestic violence between 11-13 years of age had considerable effect on thickness and volume.
- Sexual abuse: Lower GMV in primary visual cortex and visual association cortices directly correlate with duration of exposure before age of 12 and associated with deficit in visual memory.

Brain Fiber Tract Network

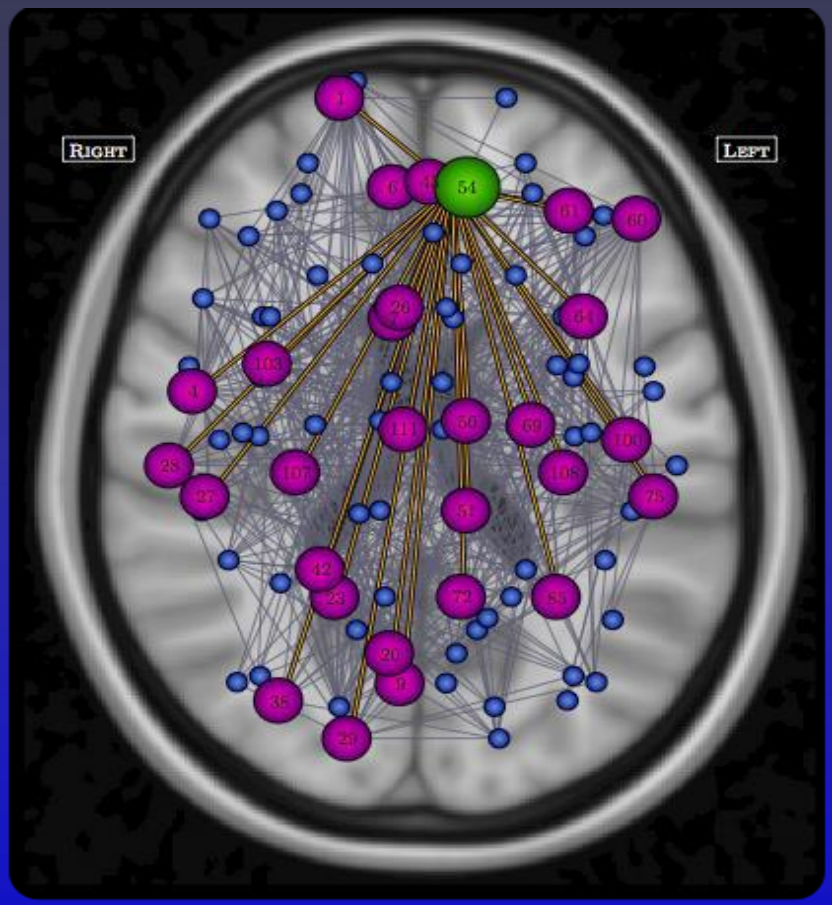
- Edges -> Fiberstreams
  - –Diffusion tensor imaging (DTI)
  - –Tractography



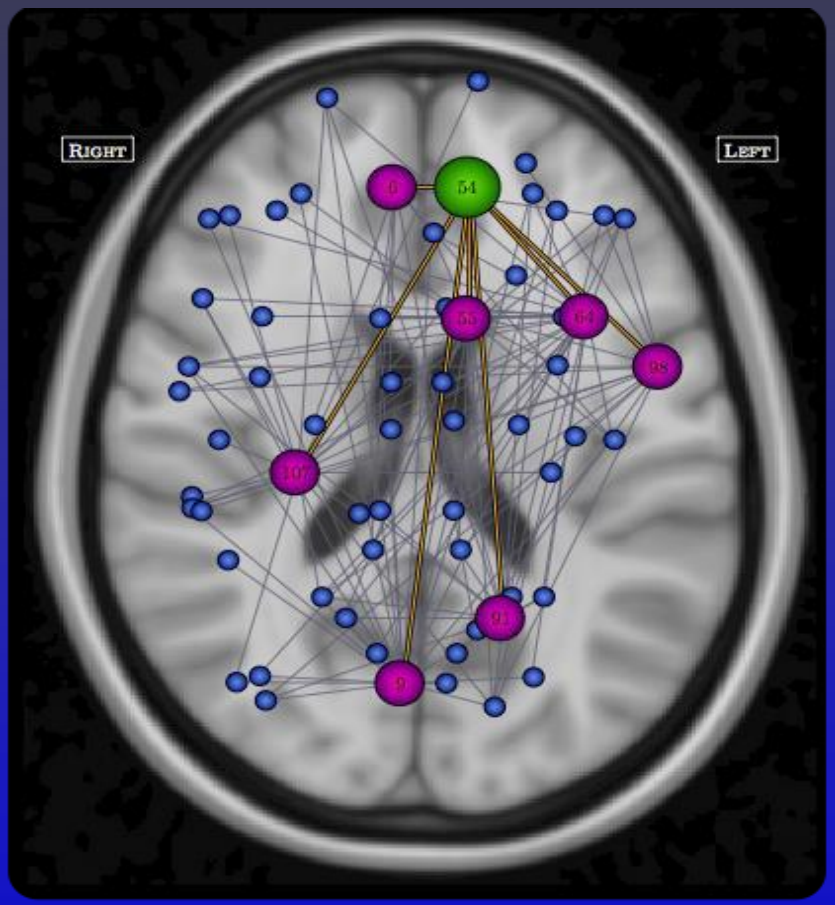
Teicher 2015

Left Anterior Cingulate

Emotion regulation



Unexposed

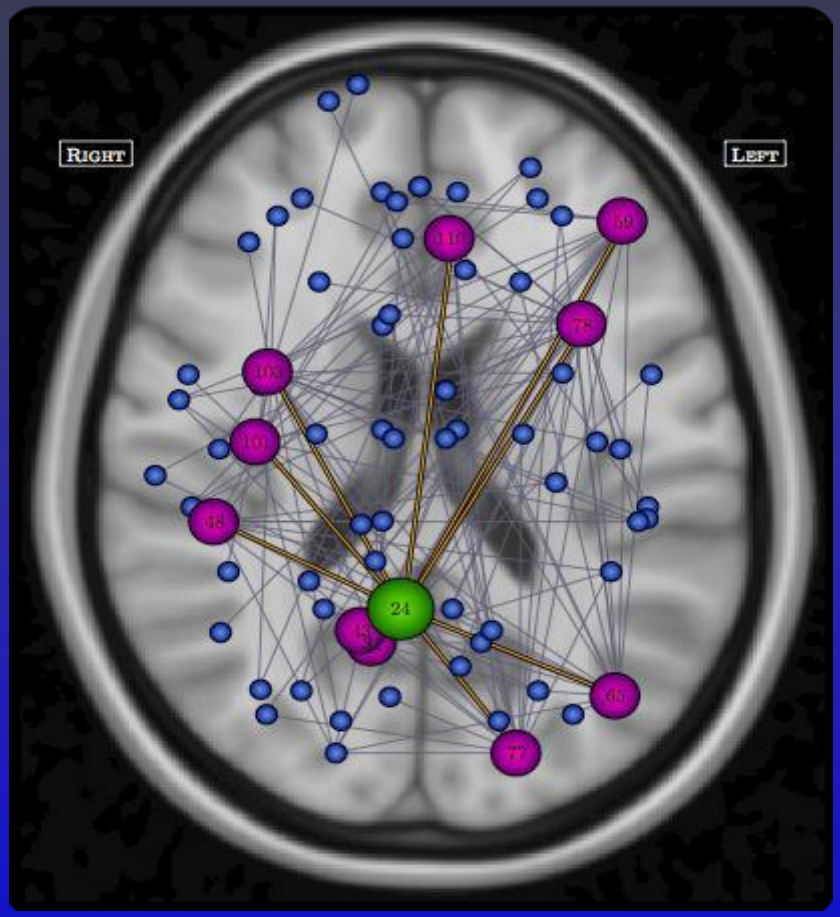


Maltreated

Teicher 2015

Right Precuneus

Self-identity, self-referential, self-centered preoccupation



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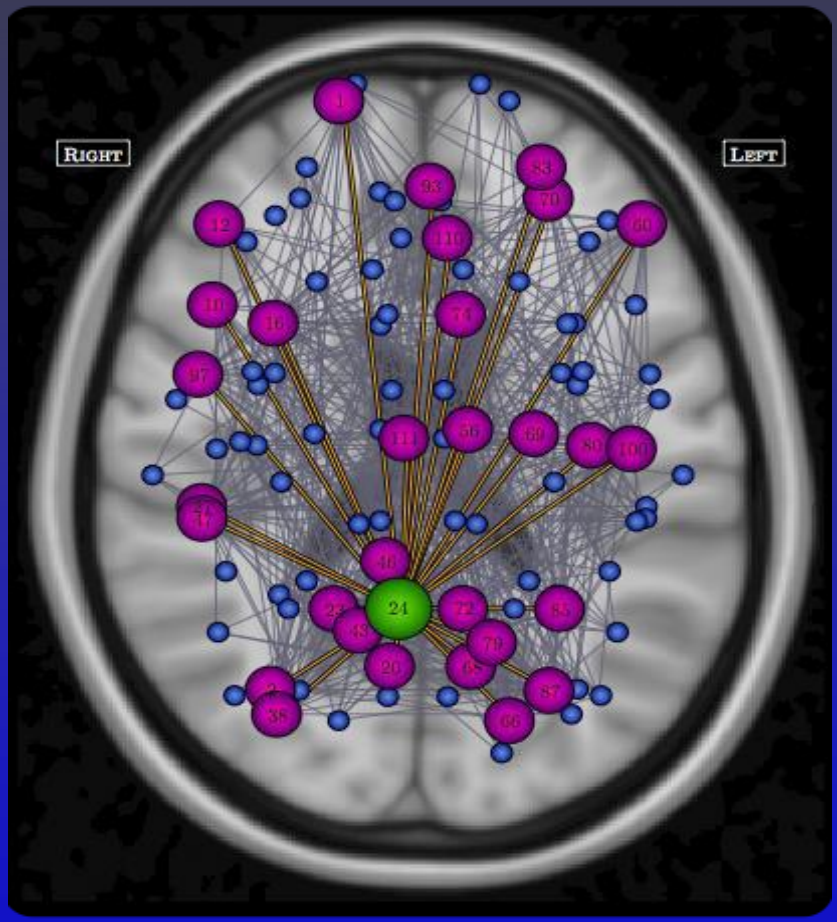
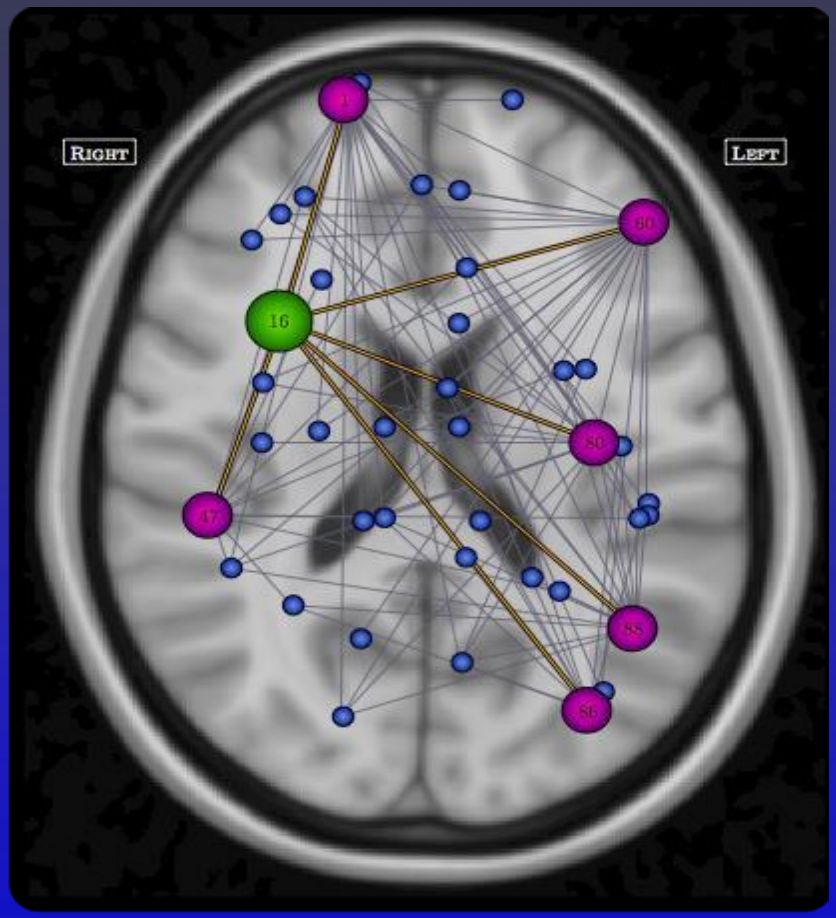


Maltreated

Right Anterior Insula

Interoception, subjective experience of self



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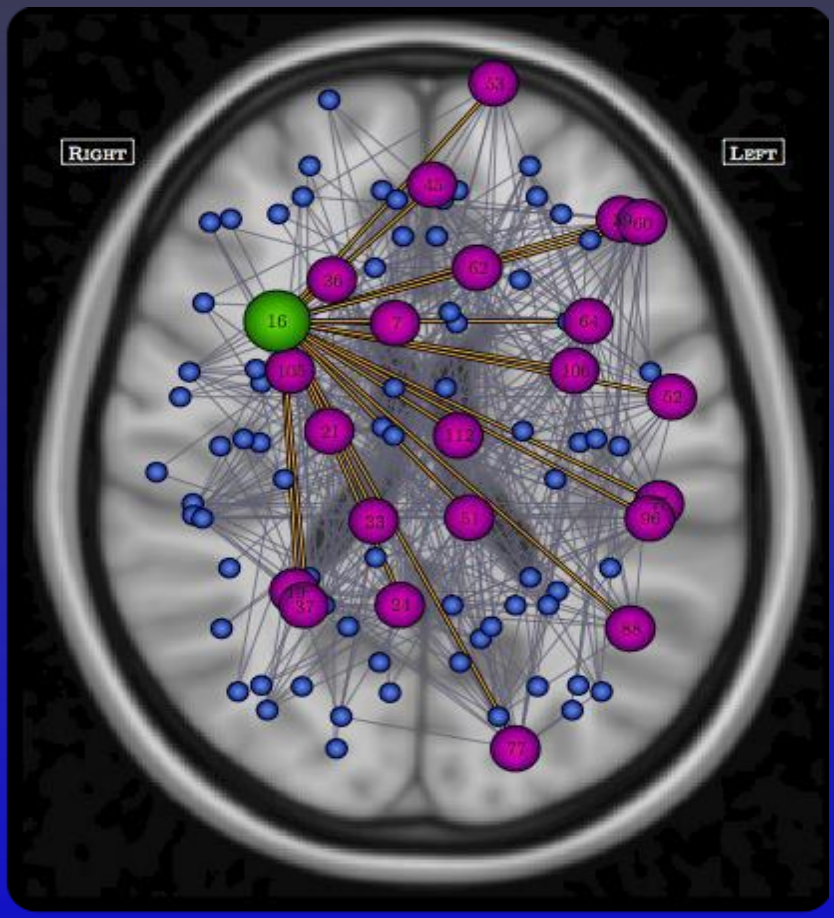


Maltreated

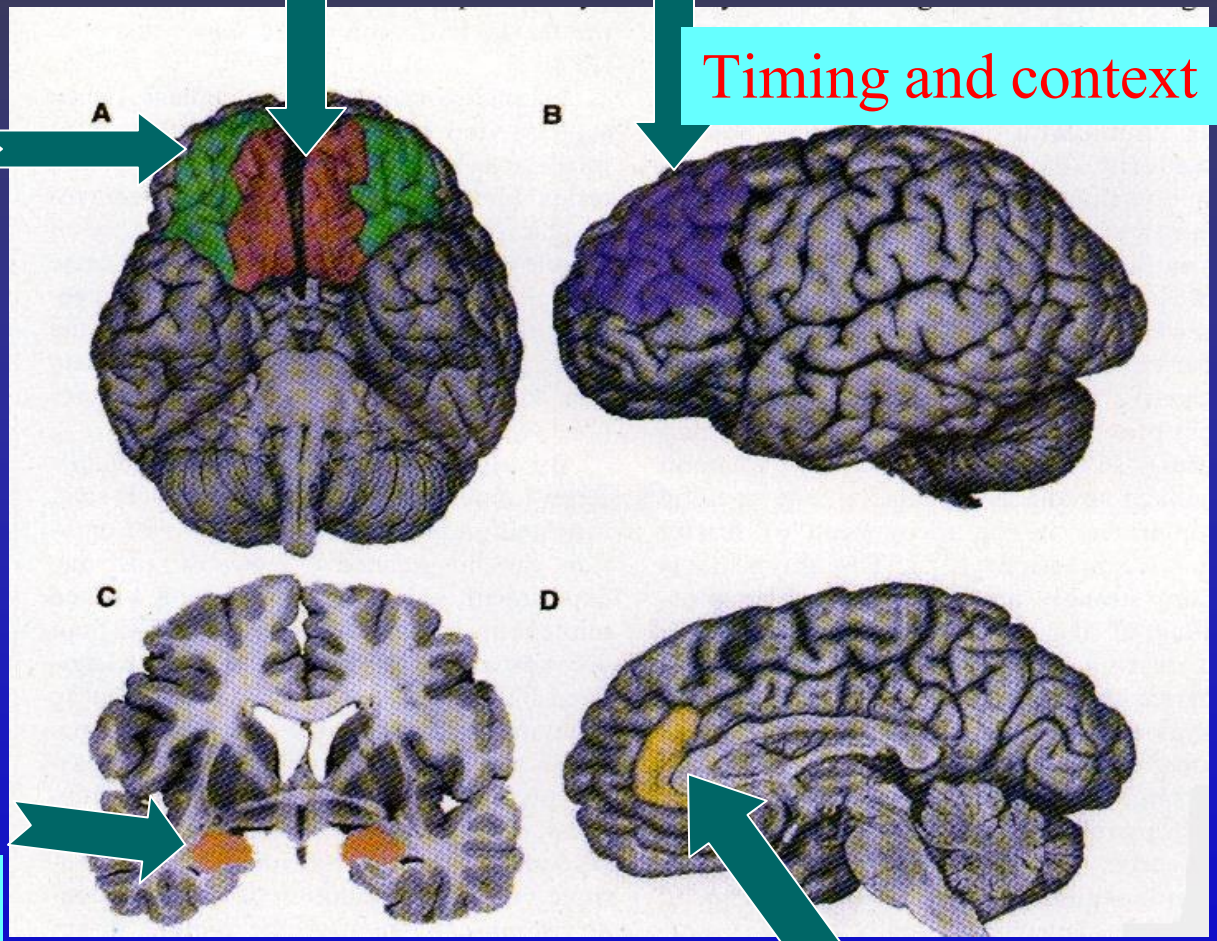
Developmental Trauma Impacts Key Structures Underlying Emotional Regulation

Ventral Prefrontal Cortex

Self-awareness

Dorsolateral Cortex

Timing and context



Orbital Prefrontal Cortex

Inhibition

Amygdala

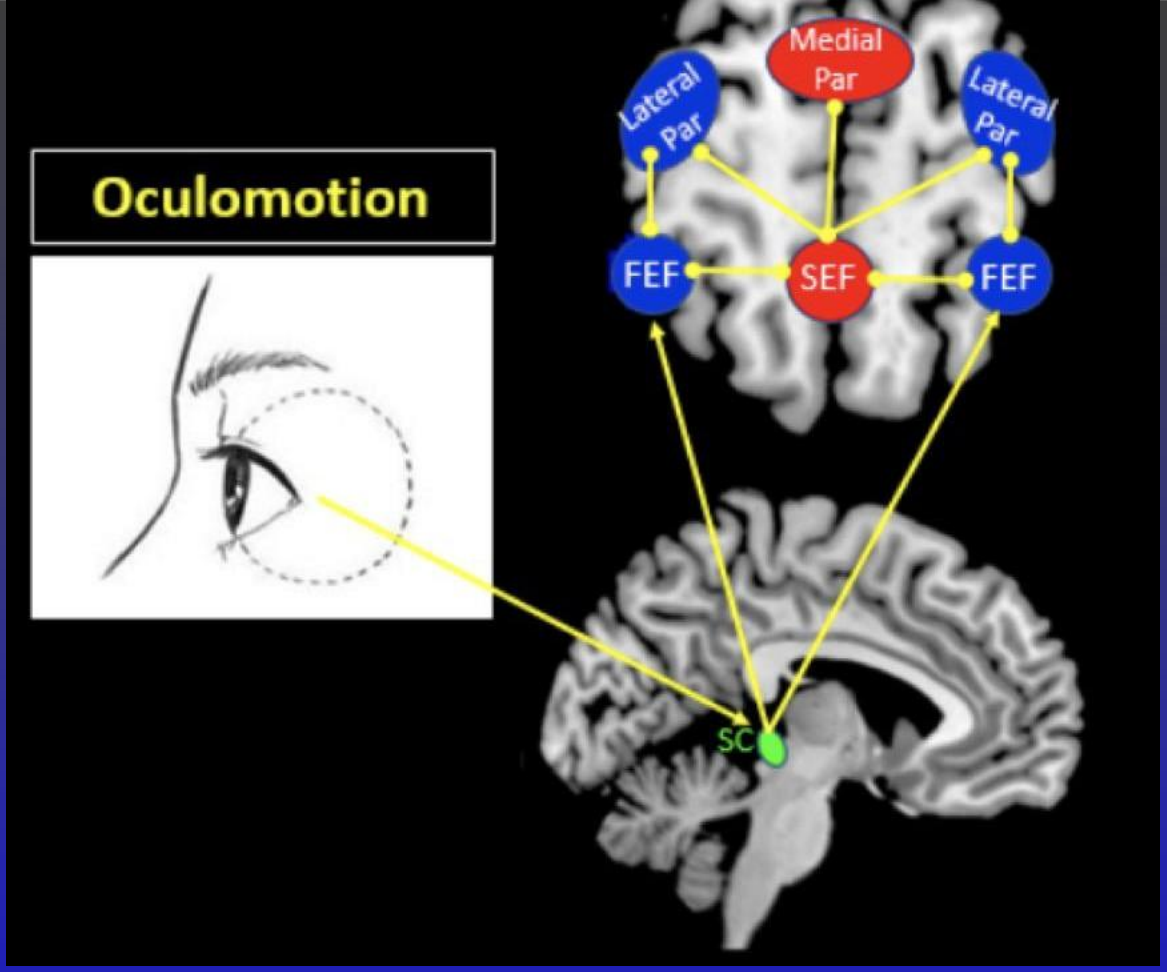
Threat detection

Science Vol 289, p 592

Anterior Cingulate

Filtering what's relevant

So, how does EMDR work?



Visuospatial sensory information Travels to the superior colliculus in the midbrain.

.

The frontal eye field connects with the lateral posterior parietal cortex, which processes details according to one's personal perspective.

The supplementary eye field, through its connections with the temporo-pariental junction, helps a person gain simultaneously a subjective and an objective perspective on the memories and sensations that are being processed.

Harricharran, van der Kolk & Lanius, 2018

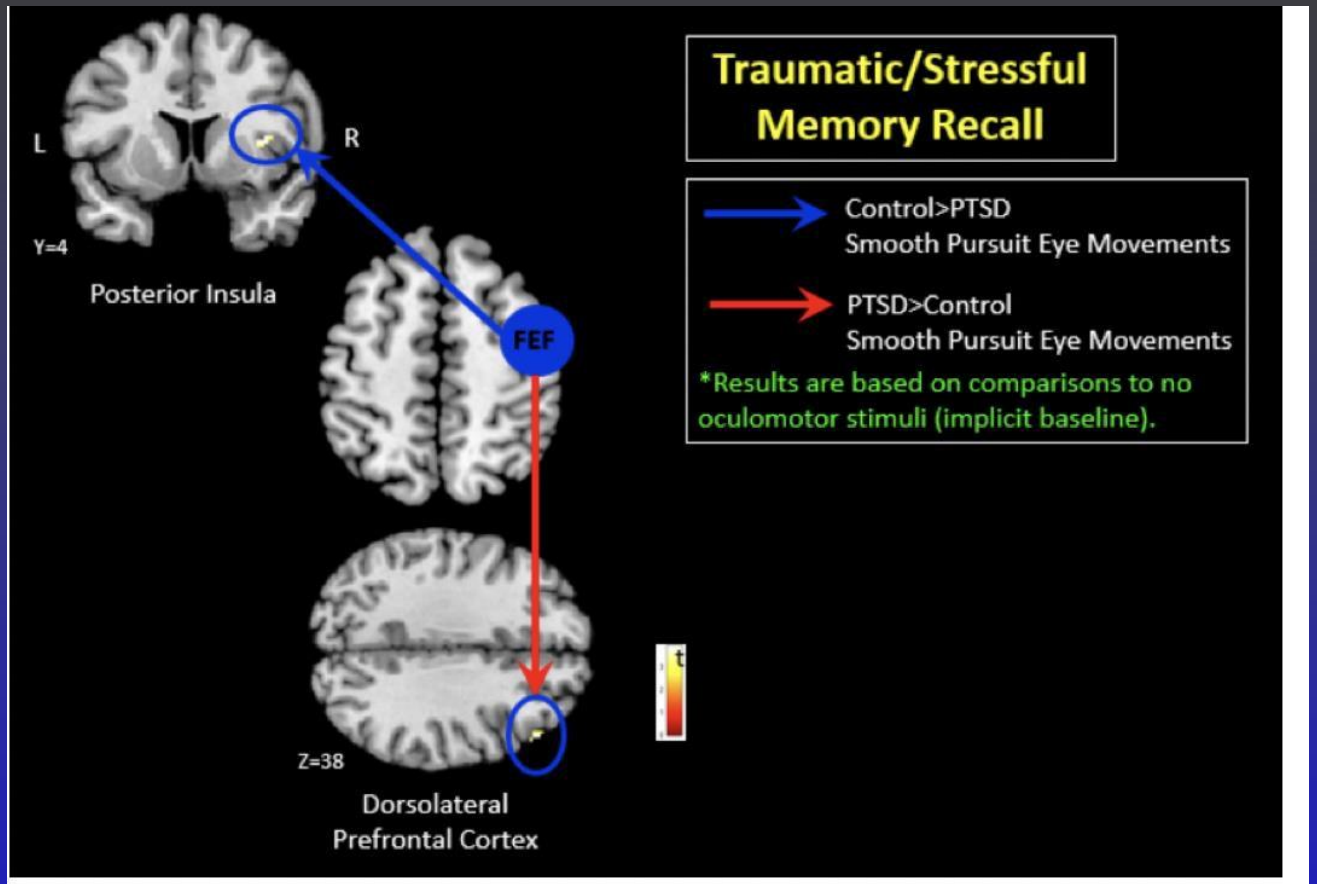
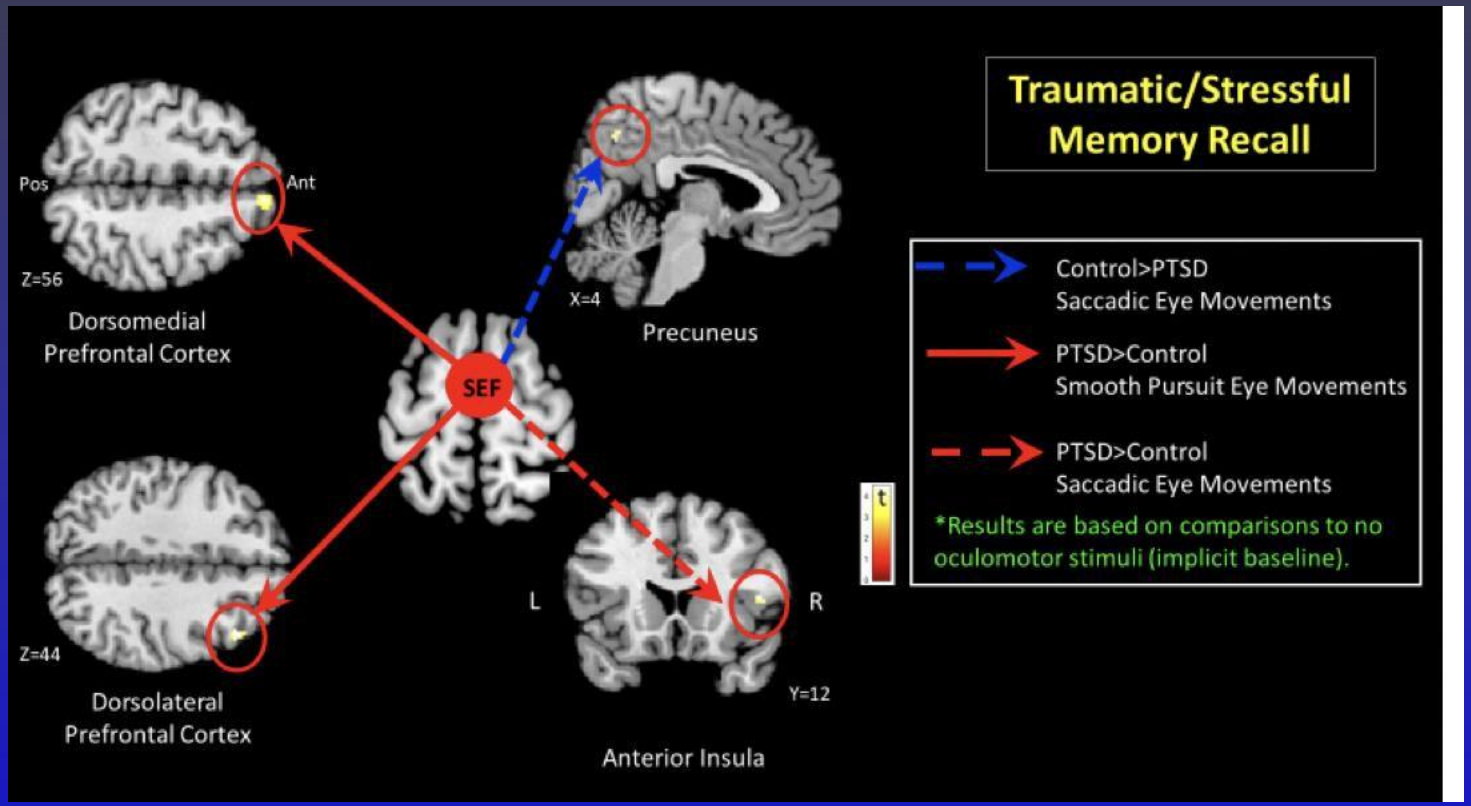


Figure 3. Explorative functional connectivity analyses (psychophysiological interaction) of the right frontal eye field [FEF; (x; 46, y; 0, z; 56)] seed region during the traumatic

During retrieval of a traumatic/stressful memory, healthy controls had increased right FEF connectivity with the right posterior insula with EMDR.

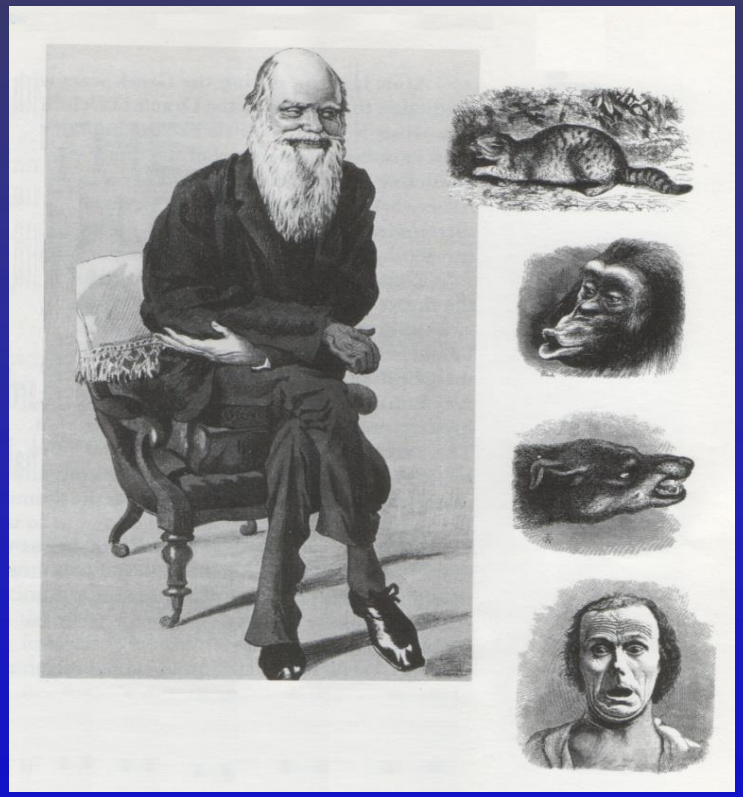
In contrast, PTSD patients had increased **right FEF connectivity with the right DLPFC during retrieval of a traumatic memory during EMDR.**



During retrieval of a traumatic/stressful memory with smooth pursuit eye movements PTSD patients showed increased right SEF connectivity with **the right dorsomedial and the right dorsolateral prefrontal cortices.**

PTSD showed increased right SEF connectivity **with the right anterior insula** during retrieval of a traumatic memory.

Charles Darwin 1809 - 1882



““Man and animals…all have the same senses, intuition, sensation, passions, affections and emotions,;

Behaviors to avoid or escape from danger have clearly evolved to render each organism competitive in terms of survival. But inappropriately prolonged escape or avoidance behavior would put the animal at a disadvantage in that successful species preservation demands reproduction which, in turn, depends upon feeding, shelter and mating activities all of which are reciprocals of avoidance and escape.

Darwin: The goal of emotion

The goal of emotion.. is to effect physical movement and regain a state of physical equilibrium:

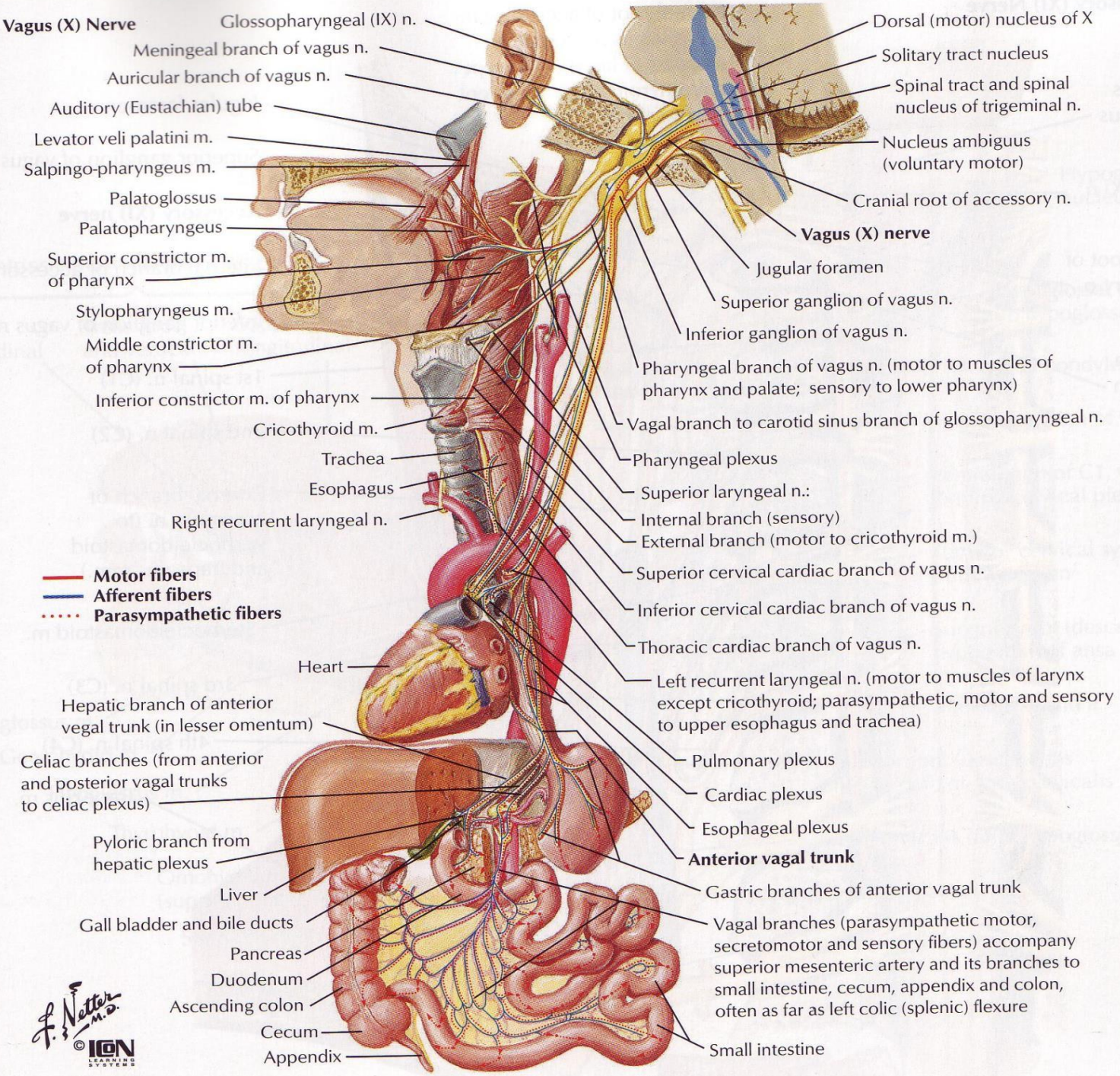
"the …. liberated nerve-force …. produces in us the state we call feeling, [which] *must* expend and liberate itself in intense sensations, active thought, violent movements, or increased activity of the glands.

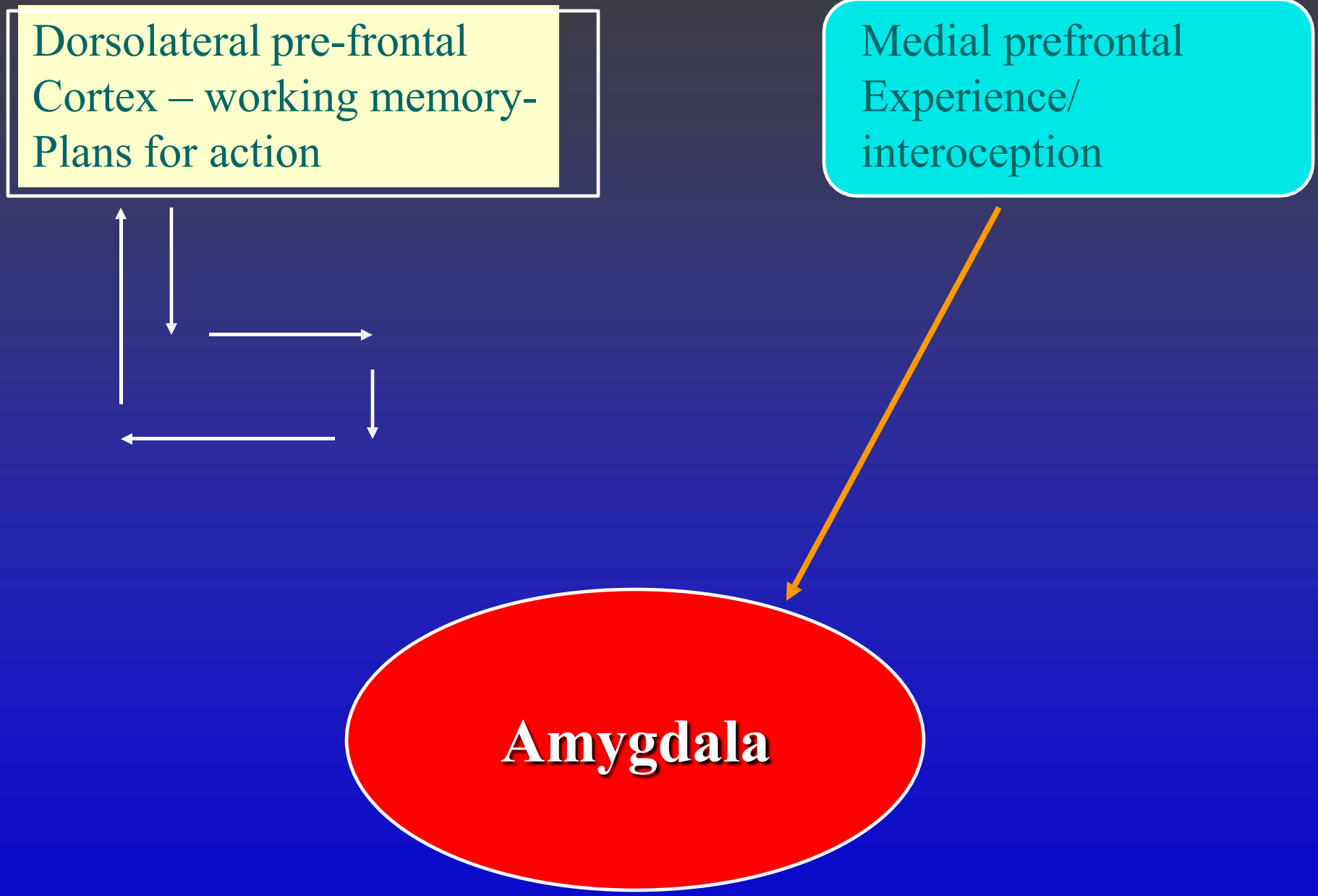
The “pneumogastric nerve”
Vagus – cranial nerve X

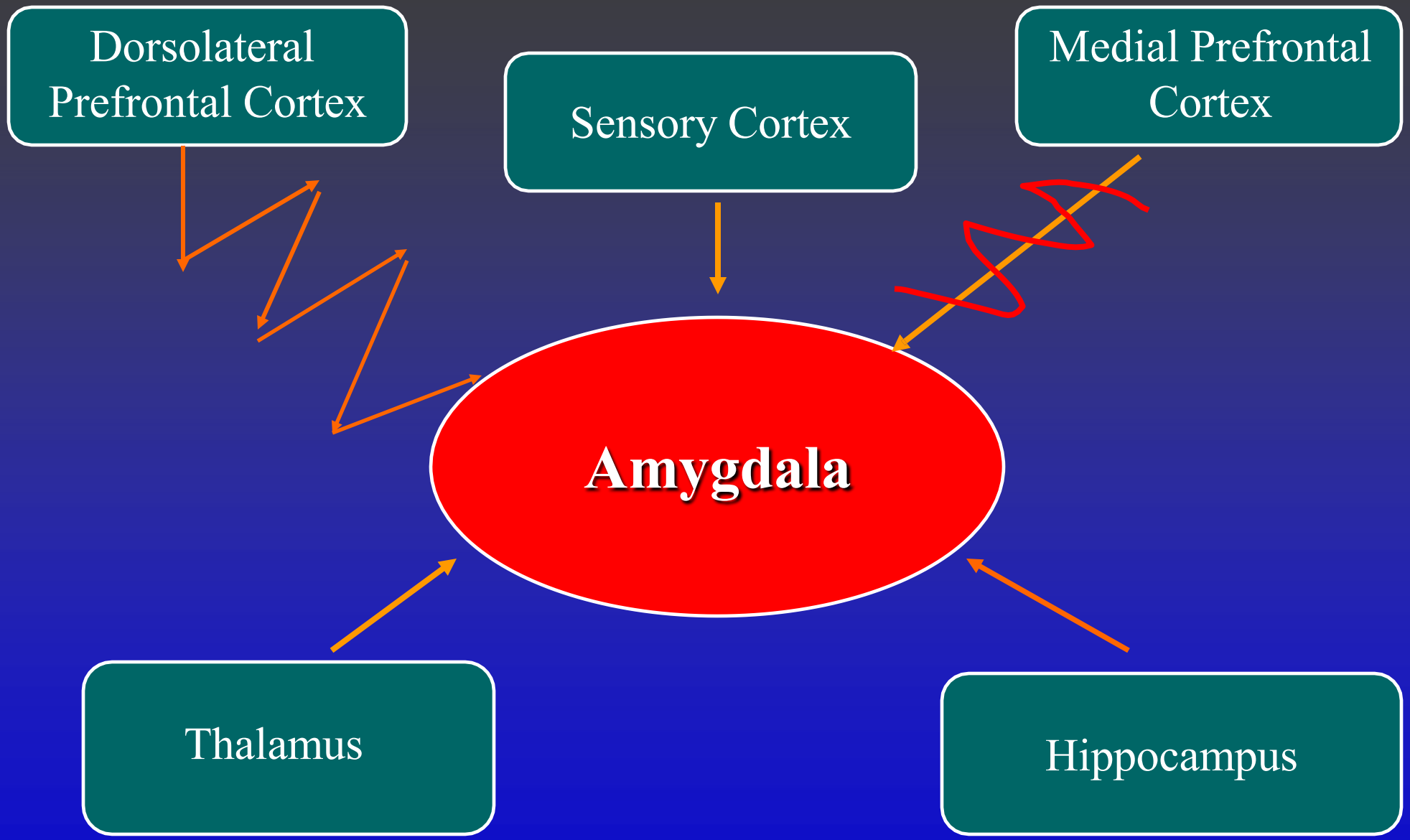
Charles Darwin (1872):

The Expression of Emotions in Man and Animals’

Heart, guts and brain communicate intimately via the "pneumogastric" nerve, the critical nerve involved in the expression and management of emotions in both humans and animals. When the mind is strongly excited, it instantly affects the state of the viscera.


Vagus (X) Nerve
Glossopharyngeal (IX) n.
Meningeal branch of vagus n.
Auricular branch of vagus n.
Auditory (Eustachian) tube
Levator veli palatini m.
Salpingo-pharyngeus m.
Palatoglossus
Palatopharyngeus
Superior constrictor m. of pharynx
Stylopharyngeus m.
Middle constrictor m. of pharynx
Inferior constrictor m. of pharynx
Cricothyroid m.
Trachea
Esophagus
Right recurrent laryngeal n.
Motor fibers
Afferent fibers
Parasympathetic fibers
Heart
Hepatic branch of anterior vegal trunk (in lesser omentum)
Celiac branches (from anterior and posterior vagal trunks to celiac plexus)
Pyloric branch from hepatic plexus
Liver
Gall bladder and bile ducts
Pancreas
Duodenum
Ascending colon
Cecum
Appendix
Dorsal (motor) nucleus of X
Solitary tract nucleus
Spinal tract and spinal nucleus of trigeminal n.
Nucleus ambiguus (voluntary motor)
Cranial root of accessory n.
Vagus (X) nerve
Jugular foramen
Superior ganglion of vagus n.
Inferior ganglion of vagus n.
Pharyngeal branch of vagus n. (motor to muscles of pharynx and palate; sensory to lower pharynx)
Vagal branch to carotid sinus branch of glossopharyngeal n.
Pharyngeal plexus
Superior laryngeal n.:
Internal branch (sensory)
External branch (motor to cricothyroid m.)
Superior cervical cardiac branch of vagus n.
Inferior cervical cardiac branch of vagus n.
Thoracic cardiac branch of vagus n.
Left recurrent laryngeal n. (motor to muscles of larynx except cricothyroid; parasympathetic, motor and sensory to upper esophagus and trachea)
Pulmonary plexus
Cardiac plexus
Esophageal plexus
Anterior vagal trunk
Gastric branches of anterior vagal trunk
Vagal branches (parasympathetic motor, secretomotor and sensory fibers) accompany superior mesenteric artery and its branches to small intestine, cecum, appendix and colon, often as far as left colic (splenic) flexure
Small intestine
F. Netter M.D.
© ICON LEARNING SYSTEMS


Dorsolateral pre-frontal
Cortex – working memory-
Plans for action
Medial prefrontal
Experience/
interoception
Amygdala


Dorsolateral Prefrontal Cortex
Sensory Cortex
Medial Prefrontal Cortex
Amygdala
Thalamus
Hippocampus

Overcoming trauma

1. (re-)establishing community
2. ***Effective action***
3. Dealing with affect regulation
4. Accessing the emotional brain-knowing one's self
5. Dealing with parts
6. Processing traumatic memories
7. Re-wiring neural circuits (neurofeedback)

What cannot be communicated to the (m)other cannot be communicated to the self.

Bowlby (1991)

Need to know and name

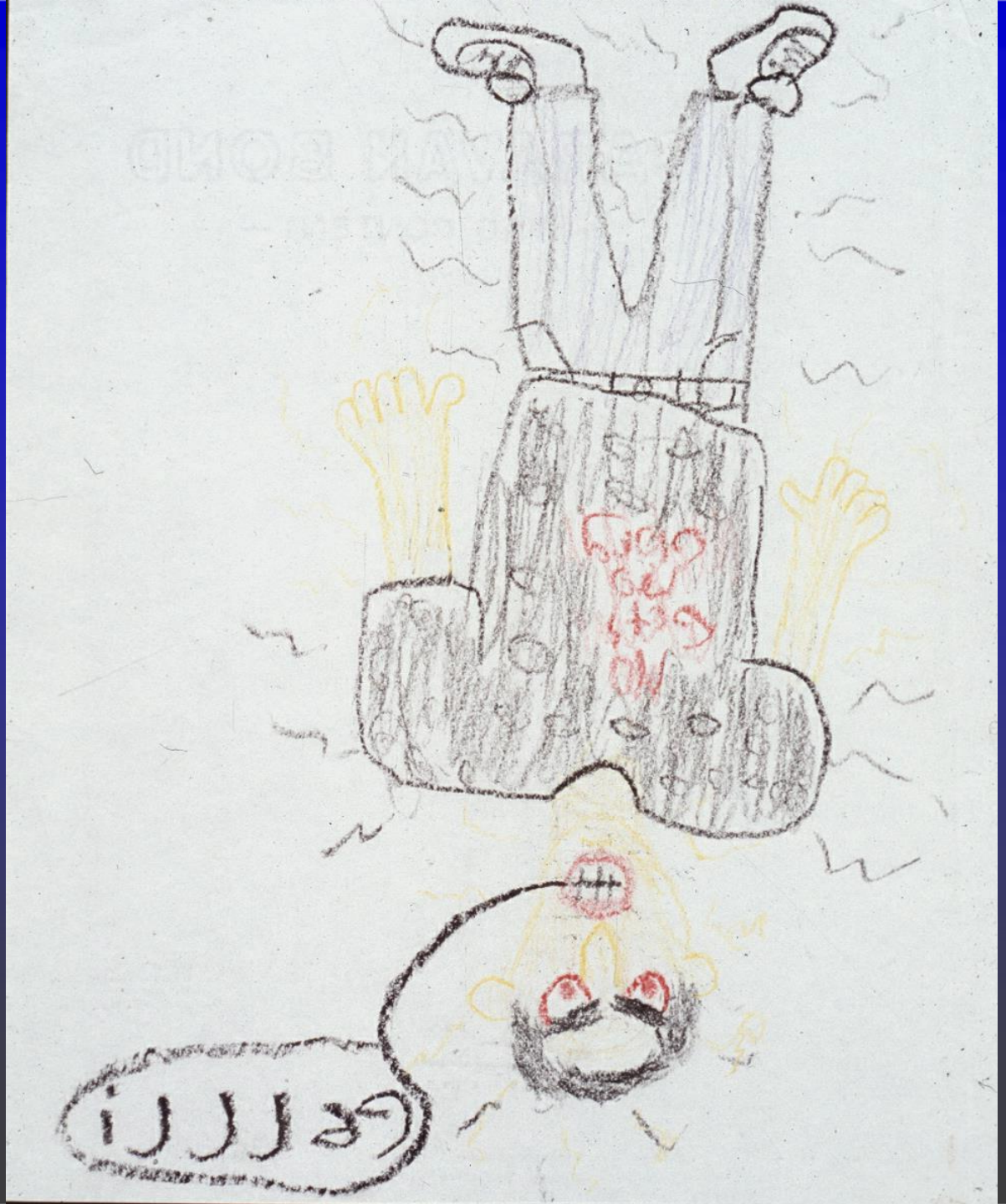
Feeling listened to and understood changes our physiology; being able to articulate a complex feeling, and having our feelings recognized, lights up our limbic brain and creates an "aha moment". In contrast, being met by silence and incomprehension kills the spirit.

•If you hide from yourself that an uncle molested you when you were a kid you are vulnerable to react to triggers like an animal in a thunderstorm: with a full-body response to the hormones that signal "danger".

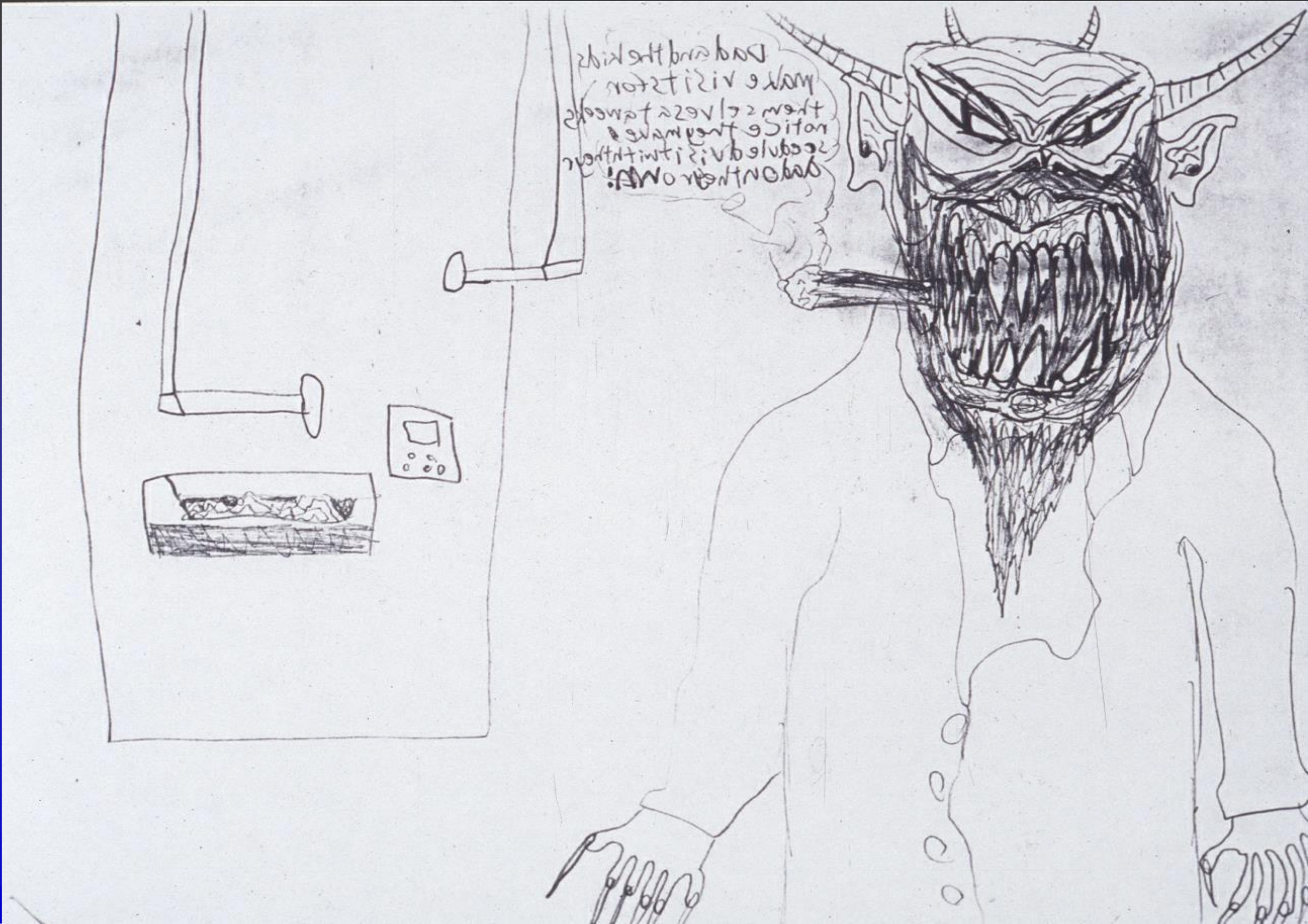
Putting experience in mind

- Without language and context, your awareness may be limited to:“ I’m scared”
- Alternating between being inhibited and uptight or reactive and explosive—all without knowing why.
- Limited life in imagination and symbols

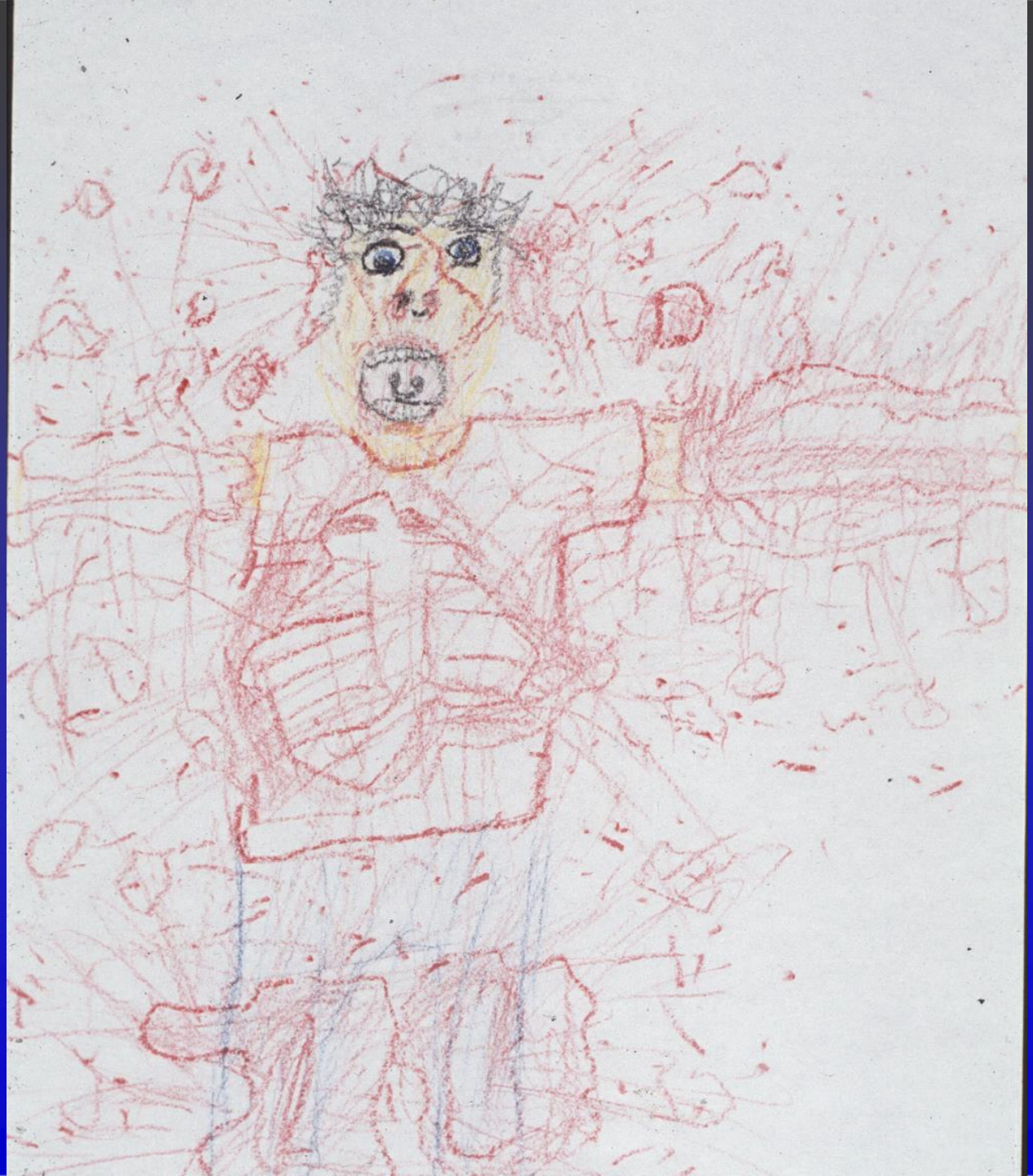

JOHN
Aged 17 months
For nine days
in a residential nursery

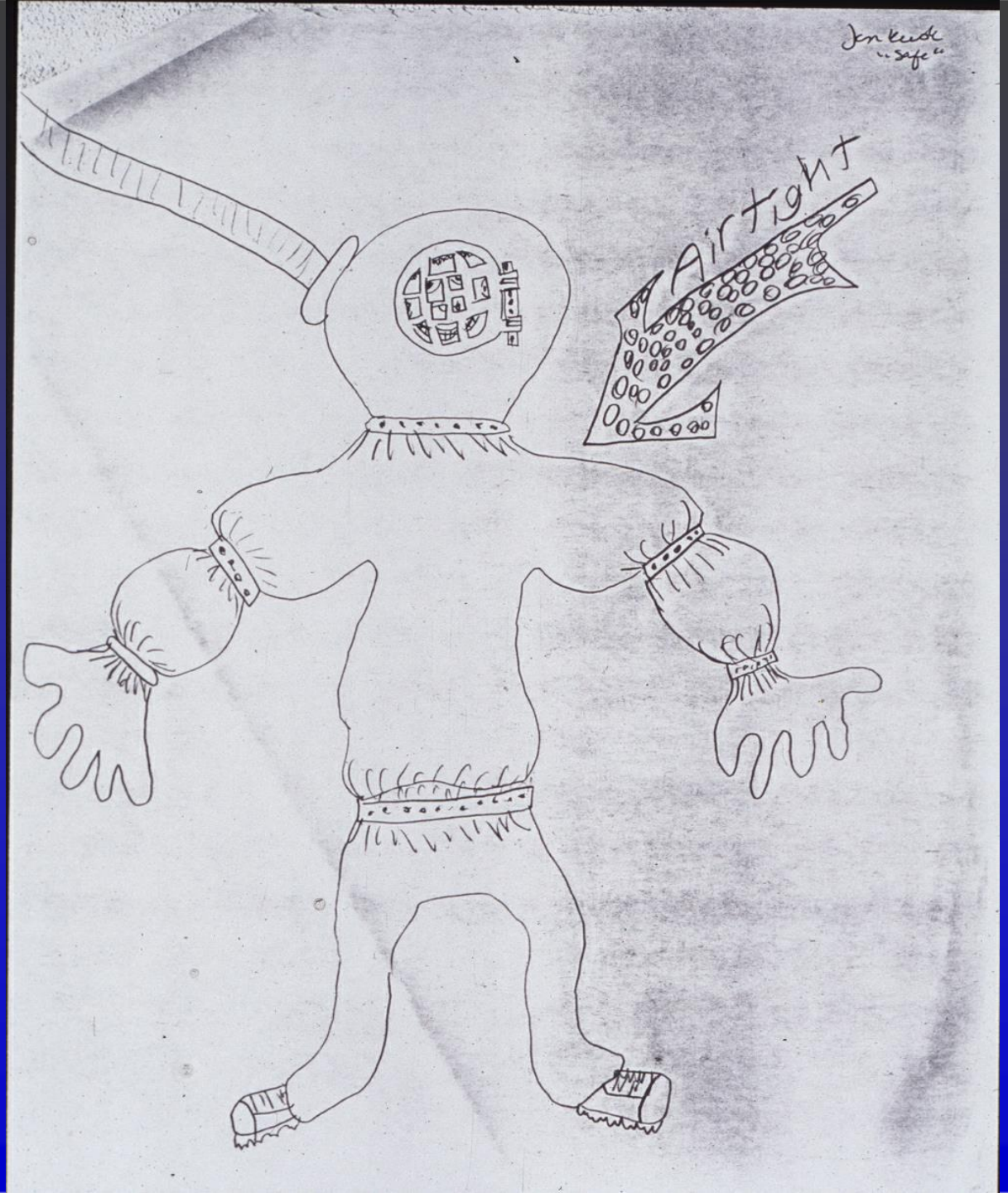


maur

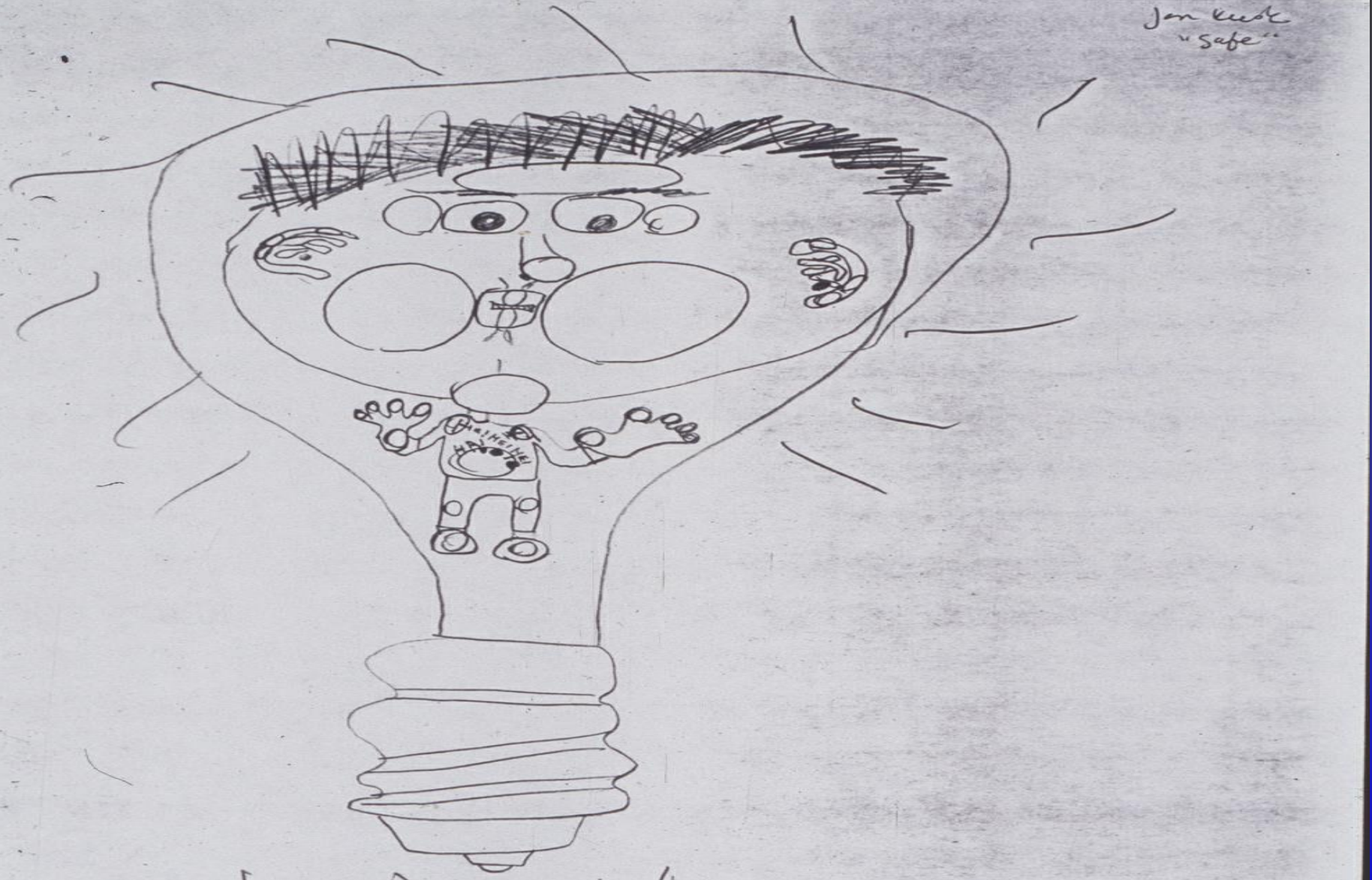

Dad and the kids make visits for themselves 2 weeks notice they make & sceduled visit with their dad on their own!

maureen3

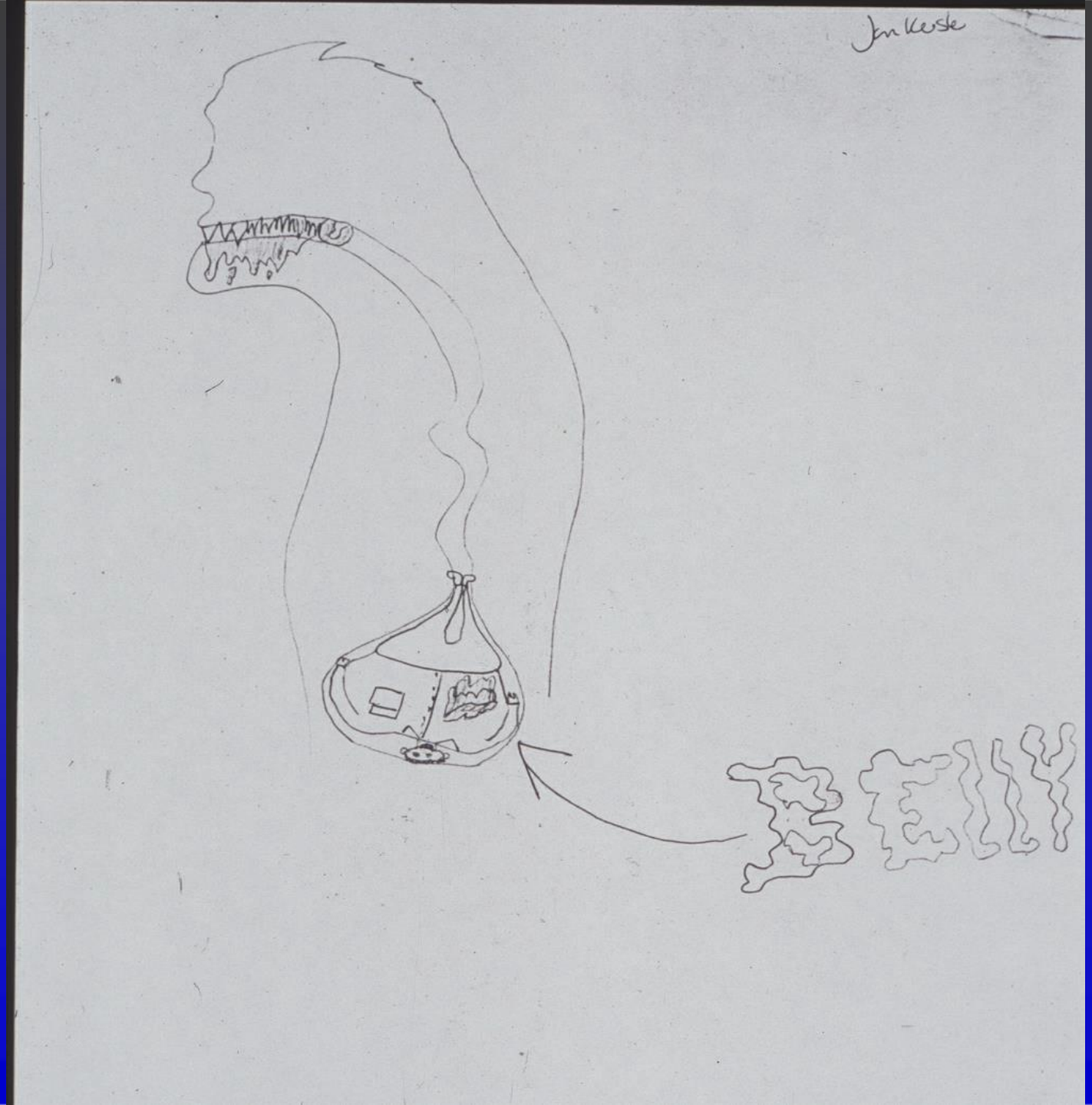



Jen Kuck
"Safe"
Airtight

Jan Kurk
"Safe"



Light bulb



NCTSN The National Child Traumatic Stress Network

Developmental psychopathology

Dante Cicchetti

Developmental Psychology
1989, Vol. 25, No. 4, 516-524

0012-1649/89/$00.75

Effects of Maltreatment on School-Age Children's Socioemotional Development: Assessments in a Day-Camp Setting

Joan Kaufman
Yale University

Dante Cicchetti
University of Rochester and
Mt. Hope Family Center, Rochester, New York

This study assessed the impact of different forms of maltreatment on the socioemotional development of 5- to 11-year-old children in a day-camp setting. Obtained measures of self-esteem and peer relations for 70 neglected, emotionally abused and/or physically abused children, and 67 demographically matched nonmaltreated comparison children. Completed counselor assessments of the children's self-esteem and provided both counselor and peer ratings of the children's prosocial, aggressive, and withdrawn behavior. Found maltreated children to score lower than the comparison children on the self-esteem and prosocial measures and higher on the withdrawn behavior ratings. Found welfare dependency to exert an independent additive negative effect, beyond maltreatment history, on the socioemotional development of the children. Results are discussed in relation to past studies of high-risk children and existing theories of developmental psychopathology.

Recent estimates indicate that over 1 million children are maltreated each year (National Center on Child Abuse and Neglect, 1982). Given the tremendous economic and human costs associated with child abuse and neglect (Dubowitz, 1986), there is great interest in establishing a data base to guide social policy, prevention, and treatment efforts (Aber, Allen, Carlson, & Cicchetti, in press; Cicchetti, Toth, & Bush, 1988). Studies on the effects of maltreatment, however, have important theoretical as well as practical implications. Although they are needed to determine the most effective intervention strategies (Cicchetti, Toth, Bush, & Gillespie, 1988), they can also provide valuable information about the effects of adverse childhood experiences on the development of self, social relations, and psychopathology (Cicchetti, in press a, in press b).

In the past, child maltreatment research was criticized for its isolation from other more developed research areas (Zigler, 1976). It is only within the past 10 years that systematic, theo-

socioemotional development (Aber & Cicchetti, 1984). Many of these studies were guided by the organizational perspective (Cicchetti & Sroufe, 1978; Rieder & Cicchetti, 1989; Sroufe, 1979), which views development as a series of qualitative reorganizations among and within behavioral and biological systems. According to this perspective, healthy development is defined in terms of interrelated social, emotional, cognitive, and representational competencies. Specific issues, such as the establishment of a secure attachment relationship in infancy, the emergence of autonomous functioning in toddlerhood, and the ability to negotiate peer relations in early childhood, are considered most salient during each of the specified age periods (Cicchetti & Schneider-Rosen, 1986; Erikson, 1950; Waters & Sroufe, 1983). Assessments of children's competence with regard to these specific tasks have been shown to have convergent and discriminant validity and to be linked to earlier functioning

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Published online 2009 Dec 29.

doi: 10.1111/j.1469-7610.2009.02202.x

Longitudinal pathways linking child maltreatment, emotion regulation, peer relations, and psychopathology

Jungmeen Kim[1] and Dante Cicchetti[2]

Author information ▶ Copyright and License information ▶

Abstract

Go to:

Background

The aim of this study was to investigate longitudinal relations among child maltreatment, emotion regulation, peer acceptance and rejection, and psychopathology.

Methods

Data were collected on 215 maltreated and 206 nonmaltreated children (ages 6–12 years) from low-income families. Children were evaluated by camp counselors on emotion regulation and internalizing and externalizing symptomatology and were nominated by peers for peer acceptance and rejection.

Results

Development and Psychopathology, **13** (2001), 759–782

Dimensions of child maltreatment and children's adjustment: Contributions of developmental timing and subtype

JODY TODD MANLY, JUNGMEEN E. KIM, FRED A. ROGOSCH, AND DANTE CICCHETTI
Mt. Hope Family Center, University of Rochester

Abstract

This investigation examined the dimensions of developmental timing, subtype, and severity of maltreatment and their relations with child adaptation. The 814 children who participated in a summer day camp, 492 of whom were maltreated and 322 of whom were nonmaltreated comparison children, were assessed by camp counselors on their internalizing and externalizing symptomatology, aggressive, withdrawn, and cooperative behavior, and on personality dimensions of ego resiliency and ego control, and were rated by peers on disruptive, aggressive, and cooperative behavior. The severity within each subtype of maltreatment and the developmental period in which each subtype occurred were examined through hierarchical regression analyses. Additionally, children with similar timing or subtype patterns were grouped to explore diversity in outcomes. Results highlighted the role of severity of emotional maltreatment in the infancy–toddlerhood period and physical abuse during the preschool period in predicting externalizing behavior and aggression. Severity of physical neglect, particularly when it occurred during the preschool period, was associated with internalizing symptomatology and withdrawn behavior. Additionally, maltreatment during the school-age period contributed significant variance after earlier maltreatment was controlled. Chronic maltreatment, especially with onset during infancy–toddlerhood or preschool periods, was linked with more maladaptive outcomes. The implications of measuring multiple dimensions for improving research in child maltreatment are discussed.

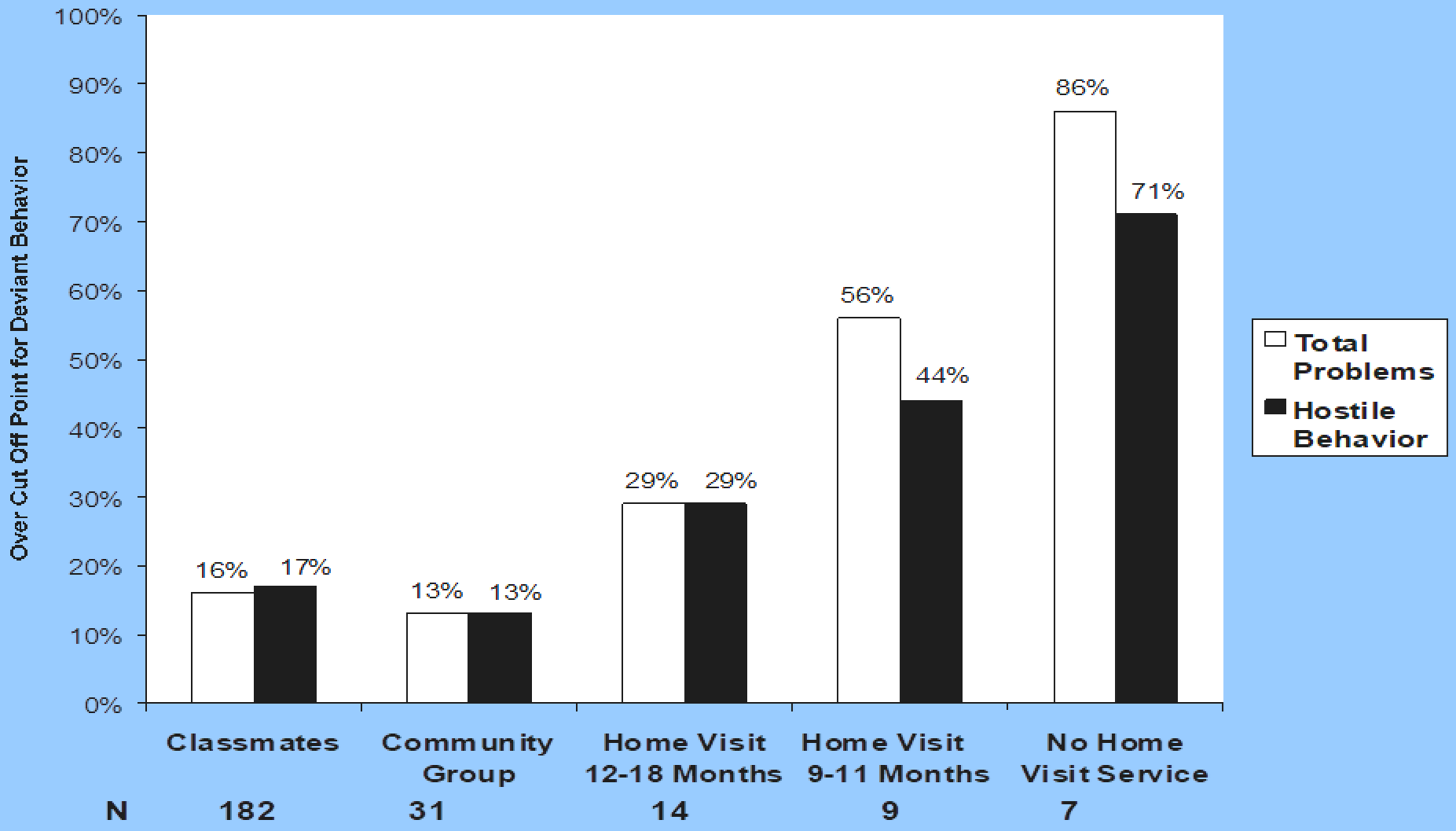
The extant literature on child outcomes of maltreatment has documented mounting evidence of the deleterious consequences of abuse and neglect for child victims (Cicchetti & Carlson, 1989; Cicchetti & Lynch, 1993, 1995; Cicchetti & Toth, 1995; DeBellis, Baum, et al., 1999; DeBellis, Keshavan, et al., 1999; Kaplan, Pelcovitz, & Labruna, 1999; Kendall–Tackett, Williams, & Finkelhor, 1993; Pollak, Cicchetti, Klorman, & Brumaghim, 1997; Trickett & McBride–Chang, 1995; Widom, 1989). Negative sequelae have been found for maltreated children across multiple domains of functioning and across many developmental periods. Consistent findings have emerged that maltreatment increases the risks for maladaptive outcomes and the develop-

We appreciate the cooperation of the Monroe County Department of Social Services. This research was supported by grants from the William T. Grant Foundation, the Office of Child Abuse and Neglect, and the Spunk Fund, Inc. We would like to thank Michael Lynch, Robin Sturm, Peggy Gold, Kurt Olsen, and Enid DeJesus for

Is it Trauma or Disrupted Attachment??

Karlen Lyons-Ruth

Total Problems and Hostile - Aggressive Behavior in Kindergarten by Initial Risk Status and Months of Services Provided



Costs & benefits of early intervention

Perry Preschool Program[b] (Schweinhart, Barnes and Weikart (1993))	$19,162	Weekly home visits with parents; intensive high-quality preschool services for one to two years	2.3 versus 4.6 lifetime arrests by age 27; 7% versus 35% arrested 5 or more times
Syracuse University Family Development (Lally, Mangione and Honig (1988))	$54,483	Weekly home visits for family; day care year round	6% versus 22% had probation files; offenses were less severe

John Hackman, Nobel Prize in Economics 2000.

Response to Threat: Attachment Behavioral System

1. Attachment system is foundational to development, in that it regulates activity in the stress response system (hypothalamic- pituitary-adrenal axis).

2. Preemptive when aroused, in that threat inhibits other motivational and behavioral systems, including exploration.

3. Stress-regulation function, mediated by:

   a. Availability of close physical contact with familiar caregiver.

   b. Caregiver responsiveness to the entire range of infant affective communications.

Wide Range of Behaviors contribute to Insensitive parenting : Maternal Disrupted Affective Communication (AMBIANCE coding system)

Overall rating scale (1-7) assessing five dimensions of interaction:

1. Negative-Intrusive Behavior

   e.g. mocks or teases infant.

2. Role Confusion

   e.g. draws attention to self when infant is in need.

3. Contradictory Affective Communication

   e.g. talks in inviting voice but physically blocks infant's access.

4. Disorientation

   e.g. Shows confused, frightened, or odd affect with infant

5. Withdrawal

   e.g. interacts from a distance; interacts silently; walks around infant.

Caregiving/Role-Confused Behavior

1. Child carries burden of creating interaction.
2. Child structures the interaction.
3. Child diffuses parent's hostility.
4. Child follows into parent's focus of attention
   (rather than vice versa).
5. Child may entertain with overbright affect.
6. Child may encourage and praise parent.

[Parent abdicates parental role.]

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Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Borderline symptoms and suicidality/self-injury in late adolescence: Prospectively observed relationship correlates in infancy and childhood

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[b] School of Psychology, University of Ottawa, Ottawa, Ontario, Canada
[c] School of Life Sciences, Herriot-Watt University, Edinburgh, UK
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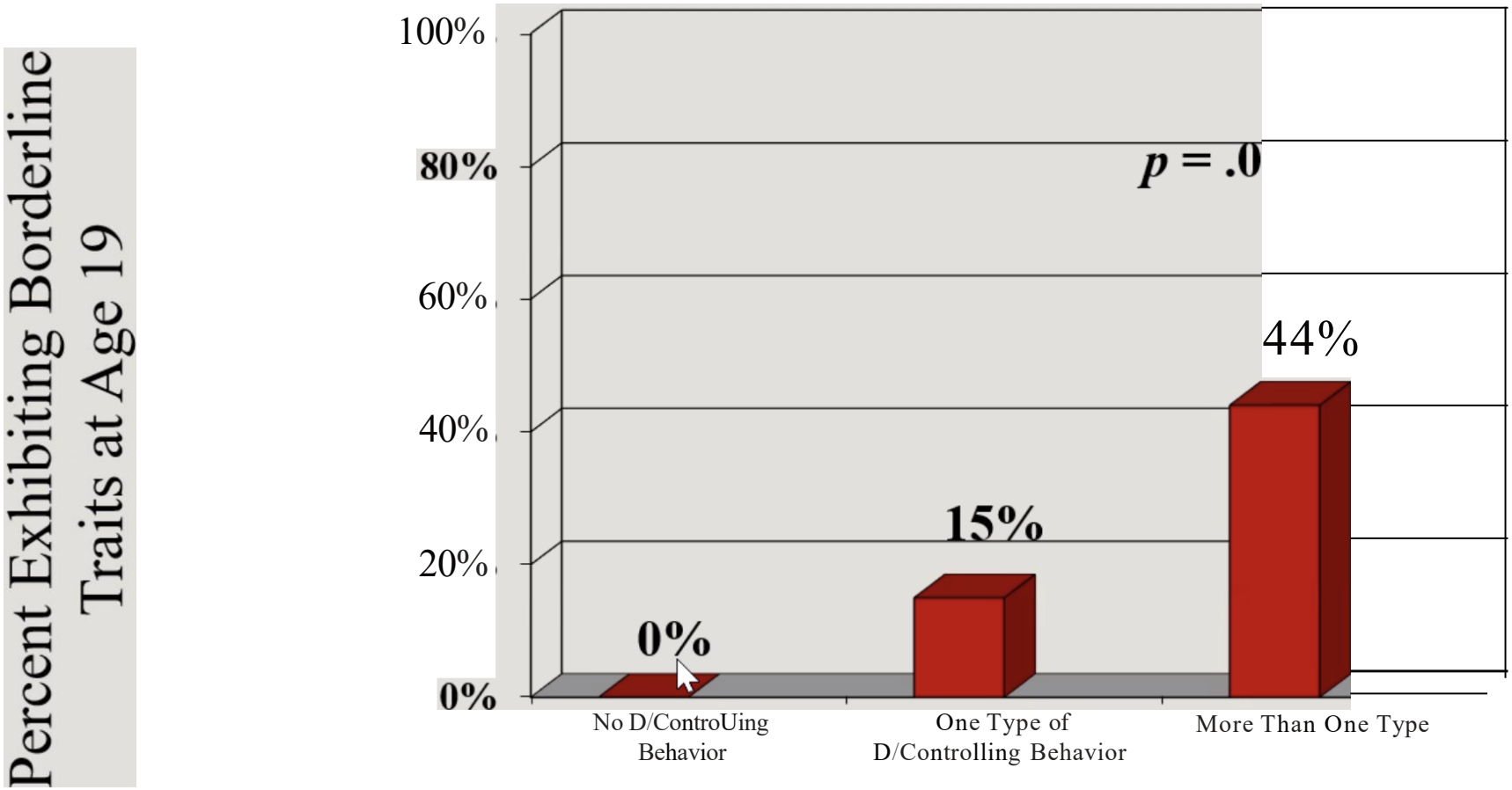
Maltreatment

ABSTRACT

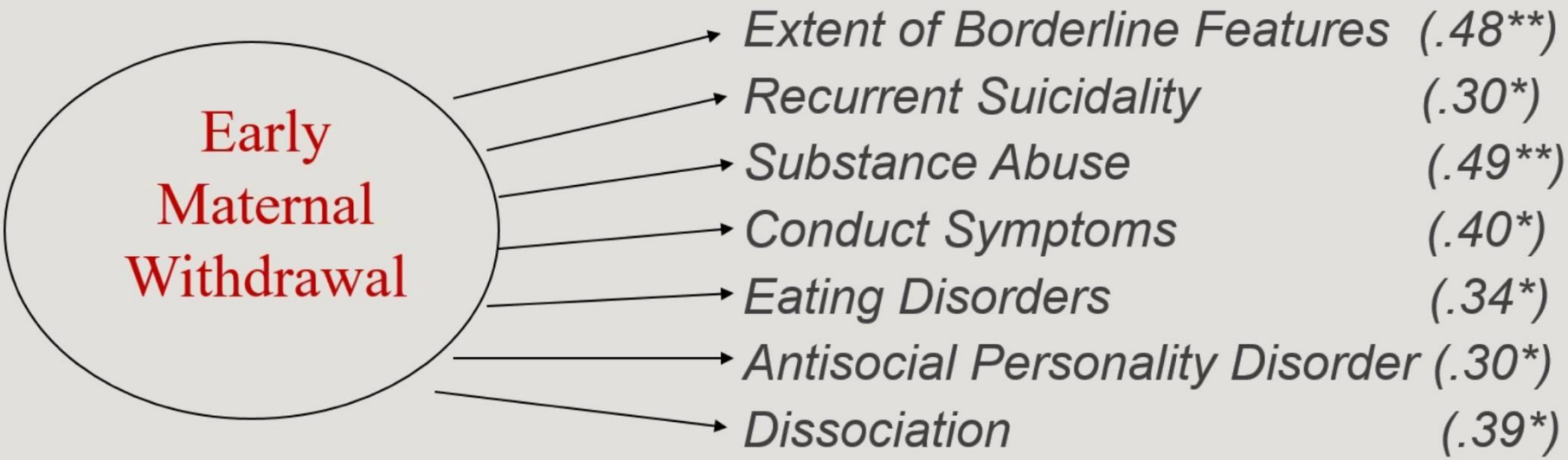
The primary objective was to assess whether prospectively observed quality of parent–child interaction in infancy and middle childhood contributed to the prediction of borderline symptoms and recurrent suicidality/self-injury in late adolescence. Adolescents (mean 19.9 years) from 56 families participating in a longitudinal study since infancy (retention rate 74%) were assessed on the SCID-II for symptoms of borderline personality disorder (BPD), including suicidality/self-injury. Early clinical risk was indexed by clinical referral to parent–infant services. Attachment security and parent–child interaction were assessed from videotape at 18 months and 8 years. Severity of childhood abuse was rated from interview and self-report measures. Maternal withdrawal in infancy was a significant predictor of both borderline symptoms and suicidality/self-injury in late adolescence. Disorganized controlling child behavior at age 8 contributed independently to the prediction of borderline symptoms. The effect of maternal withdrawal was independent of, and additive to, variability explained by severity of childhood abuse. Borderline symptoms and suicidality/self-injury may be preceded developmentally by disturbed interactions as early as 18 months of age. A parent–child transactional model is proposed to account for the findings.

Disorganized/Controlling Behavior at Age 8 Predicts Elevated BPD Traits at Age 19



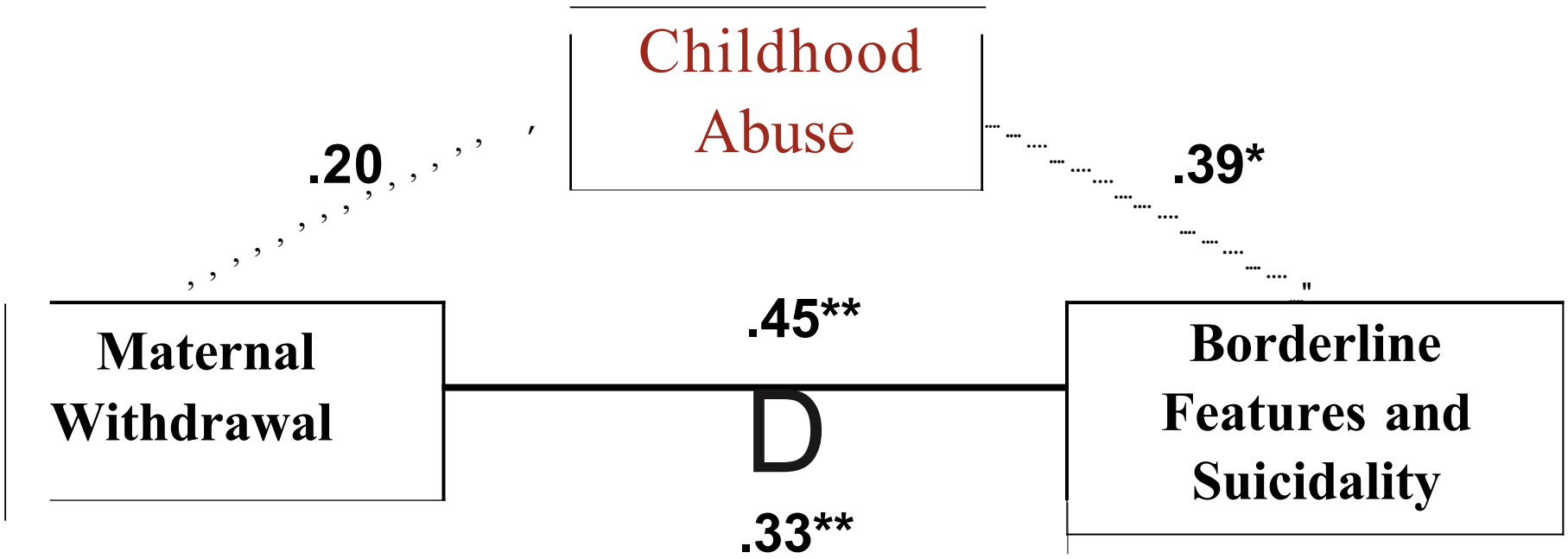
Lyons-Ruth, Bureau, Holmes, Easterbrooks, & Brooks, *Psychiatry Research*, 2013

Maternal Withdrawal and Adolescent Outcomes on the SCID in Late Adolescence



Pechtel et al., *Int. J. Cog. Ther.*, 2012
Shi et al., *Inf. Mental Health J.*, 2011
Lyons-Ruth et al. *Psychiat. Res.*, 2013
Dutra et al., *J. Nerv. Ment. Dis., 2009*
Lyons-Ruth et al., *Att. & HD,* 2014

Does Later Childhood Abuse Account for the Effect of Early Maternal Withdrawal on Borderline Features?



NO. Early care and later abuse have independent effects on borderline features.

Bootstrapping test for mediation not significant. (Same results for suicidality.)

Lyons-Ruth, Bureau, Holmes, Easterbrooks, & Brooks, *Psychiatry Research*, 2013

Frank W Putnam

Psychobiological Effects of Sexual Abuse: 20 Years Later

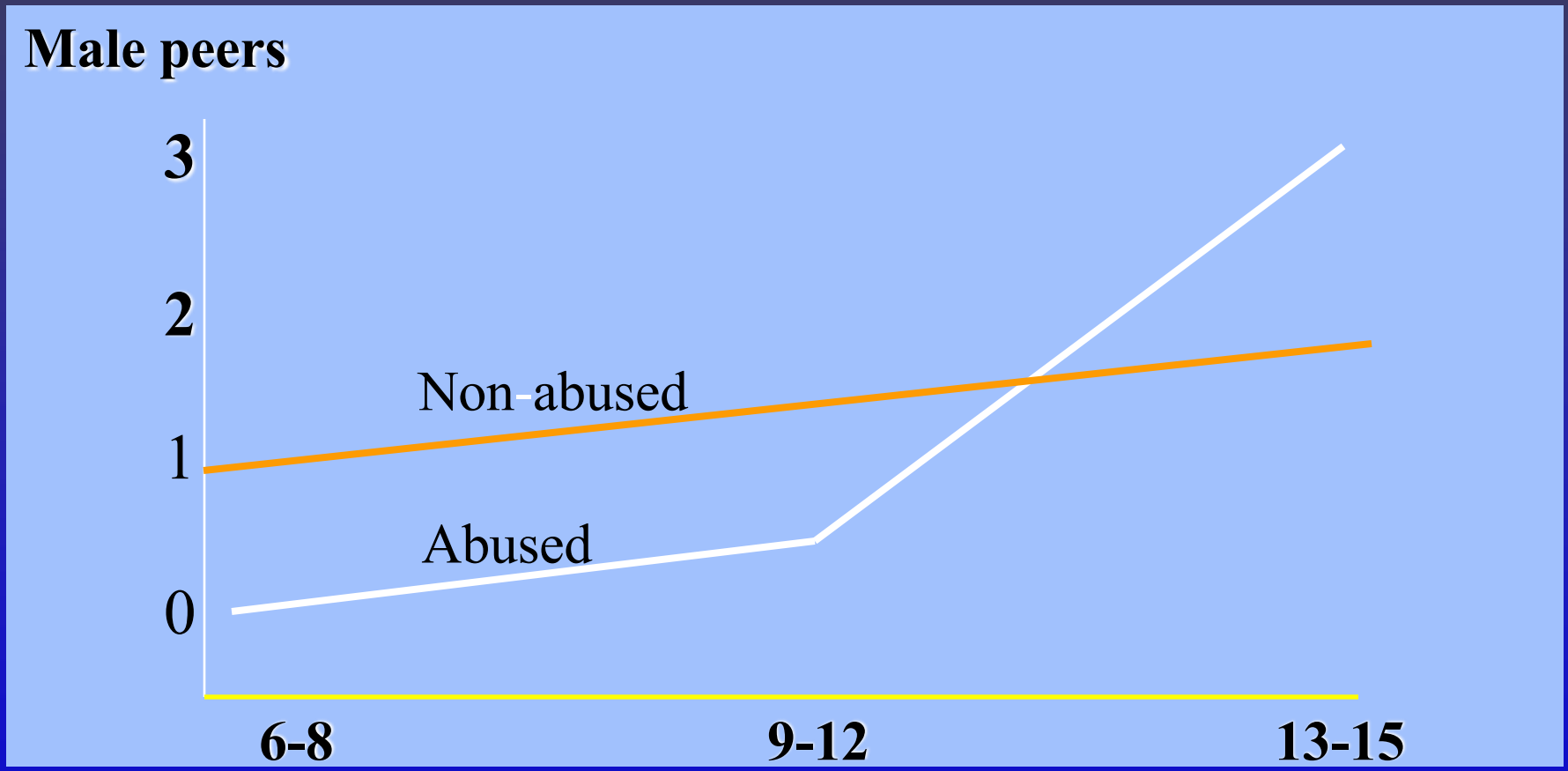
Frank W. Putnam, MD
Professor of Pediatrics and Psychiatry
Cincinnati Children's Hospital Medical Center

Summary of Longitudinal Study

- Serious disorders and high comorbidity (affective, anxiety, suicide, risk taking, self-mutilation, somatization, dissociation, conduct problems, attention, impulse problems, hyperactivity)
- Biological Dysregulation (HPA axis, sympathetic nervous system, obesity, pubertal development?)
- Dysfunctional relationships & sexuality (earlier voluntary intercourse, earlier childbearing, more partners, dysfunctional relationships, more DV, more abused children)

Biology: alteration in HPA feedback loop:

Testosterone	28 (A)	5 (C)
Androstendione	120 (A)	48 (C)



Increased # pregnancies, drug abuse, sexually provocative

Ten-Year Research Update Review: Child Sexual Abuse

FRANK W. PUTNAM, M.D.

ABSTRACT

Objective: To provide clinicians with current information on prevalence, risk factors, outcomes, treatment, and prevention of child sexual abuse (CSA). To examine the best-documented examples of psychopathology attributable to CSA. **Method:** Computer literature searches of *Medline* and *PSYCInfo* for key words. All English-language articles published after 1989 containing empirical data pertaining to CSA were reviewed. **Results:** CSA constitutes approximately 10% of officially substantiated child maltreatment cases, numbering approximately 88,000 in 2000. Adjusted prevalence rates are 16.8% and 7.9% for adult women and men, respectively. Risk factors include gender, age, disabilities, and parental dysfunction. A range of symptoms and disorders has been associated with CSA, but depression in adults and sexualized behaviors in children are the best-documented outcomes. To date, cognitive-behavioral therapy (CBT) of the child and a nonoffending parent is the most effective treatment. Prevention efforts have focused on child education to increase awareness and home visitation to decrease risk factors. **Conclusions:** CSA is a significant risk factor for psychopathology, especially depression and substance abuse. Preliminary research indicates that CBT is effective for some symptoms, but longitudinal follow-up and large-scale "effectiveness" studies are needed. Prevention programs have promise, but evaluations to date are limited. *J. Am. Acad. Child Adolesc. Psychiatry*, 2003, 42(3):269–278. **Key Words:** sexual abuse, child abuse, prevention, depression, sexualized behavior.

Childhood sexual abuse is a complex life experience, not a diagnosis or a disorder. An array of sexual activities is covered by the term *child sexual abuse* (CSA). These include intercourse, attempted intercourse, oral-genital contact, fondling of genitals directly or through clothing, exhibitionism or exposing children to adult sexual activity or pornography, and the use of the child for prostitution or pornography. This diversity alone ensures that there will be a range of outcomes. In addition, the age and gender of the child, the age and gender of the perpetrator, the nature of the relationship between the child and perpetrator, and the number, frequency, and duration of the abuse experiences all appear to influence some outcomes. Thus sexually abused children constitute a very heterogeneous group with many degrees of abuse about whom few simple generalizations hold. The outcomes summarized in this review are based on studies in which the majority of subjects experienced more severe forms of sexual abuse, generally including some form of child or adult genital contact.

Accepted October 2, 2002.

From Children's Hospital Medical Center, Cincinnati.

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0890-8567/03/4203–0269©2003 by the American Academy of Child and Adolescent Psychiatry.

DOI: 10.1097/01.CHI.0000037029.04952.72

EPIDEMIOLOGY OF CSA

Before the late 1970s, CSA was regarded as rare. In the following decades, the incidence—based on official statistics—increased dramatically (Finkelhor, 1984; U.S. Department of Health and Human Services, 1998). Although much of this apparent increase probably reflected a growing awareness among the public and professionals, some studies suggest that the overall incidence of child abuse and neglect increased. Using as official observers a variety of professionals who routinely came in contact with children, counting both reported and nonreported cases, the series of National Incidence Studies found a 67% increase (from 931,000 to 1,553,800 children) in all forms of child abuse from 1986 to 1993 (U.S. Department of Health and Human Services, 1996). Officially reported cases of CSA, however, declined during this same period (Atabaki and Paradise, 1999; Jones and Finkelhor, 2001). There is little agreement on reasons for this decline or whether it represents a decline in actual cases (Jones et al., 2001). In 2000 (most recent data available) CSA constituted approximately 10% of all officially reported child abuse cases and numbered approximately 88,000 substantiated or indicated

Is it disrupted attachment or is it trauma (or both)?

NCTSN The National Child Traumatic Stress Network

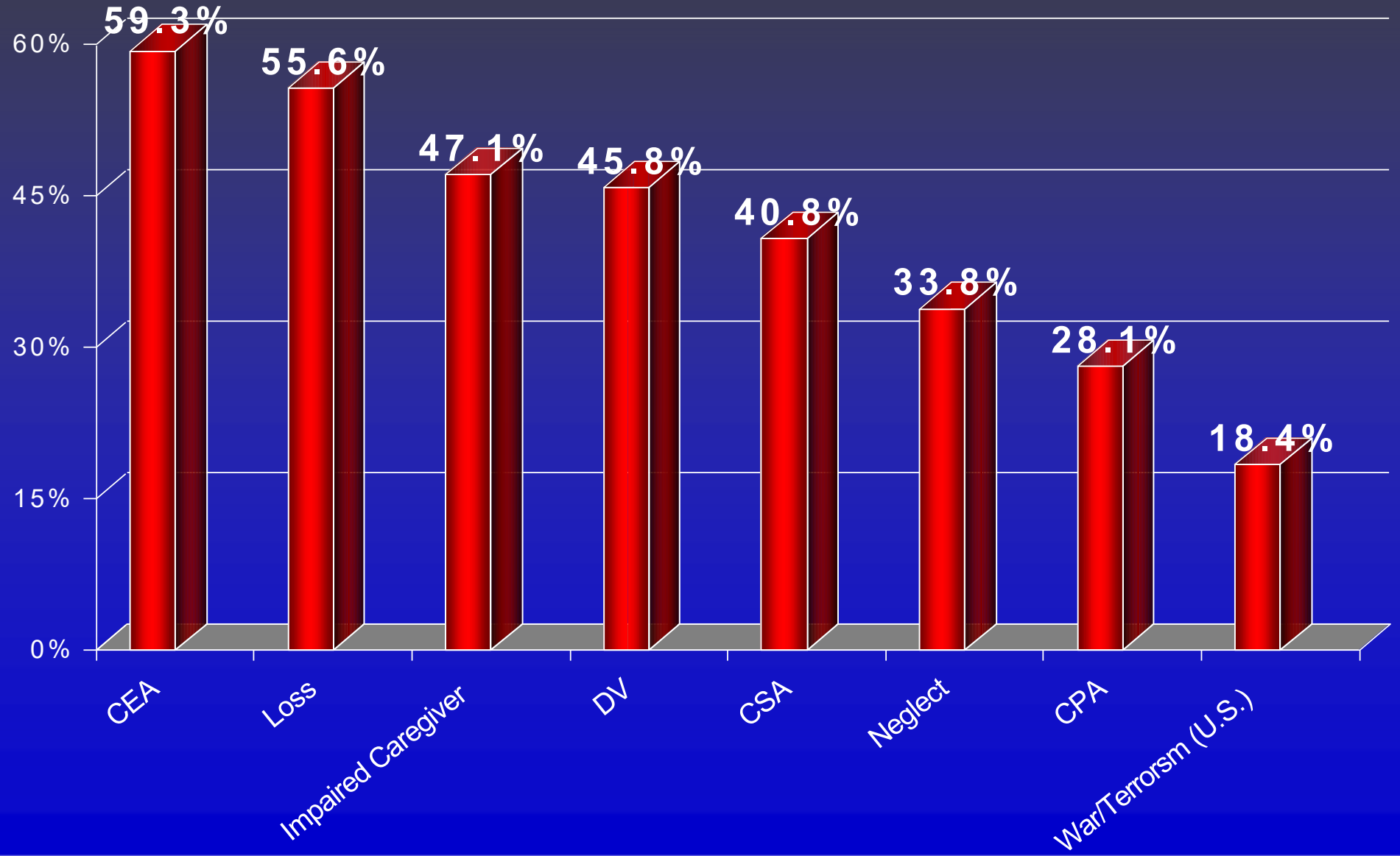
NCTSN The National Child Traumatic Stress Network

Complex Trauma in the National Child Traumatic Stress Network

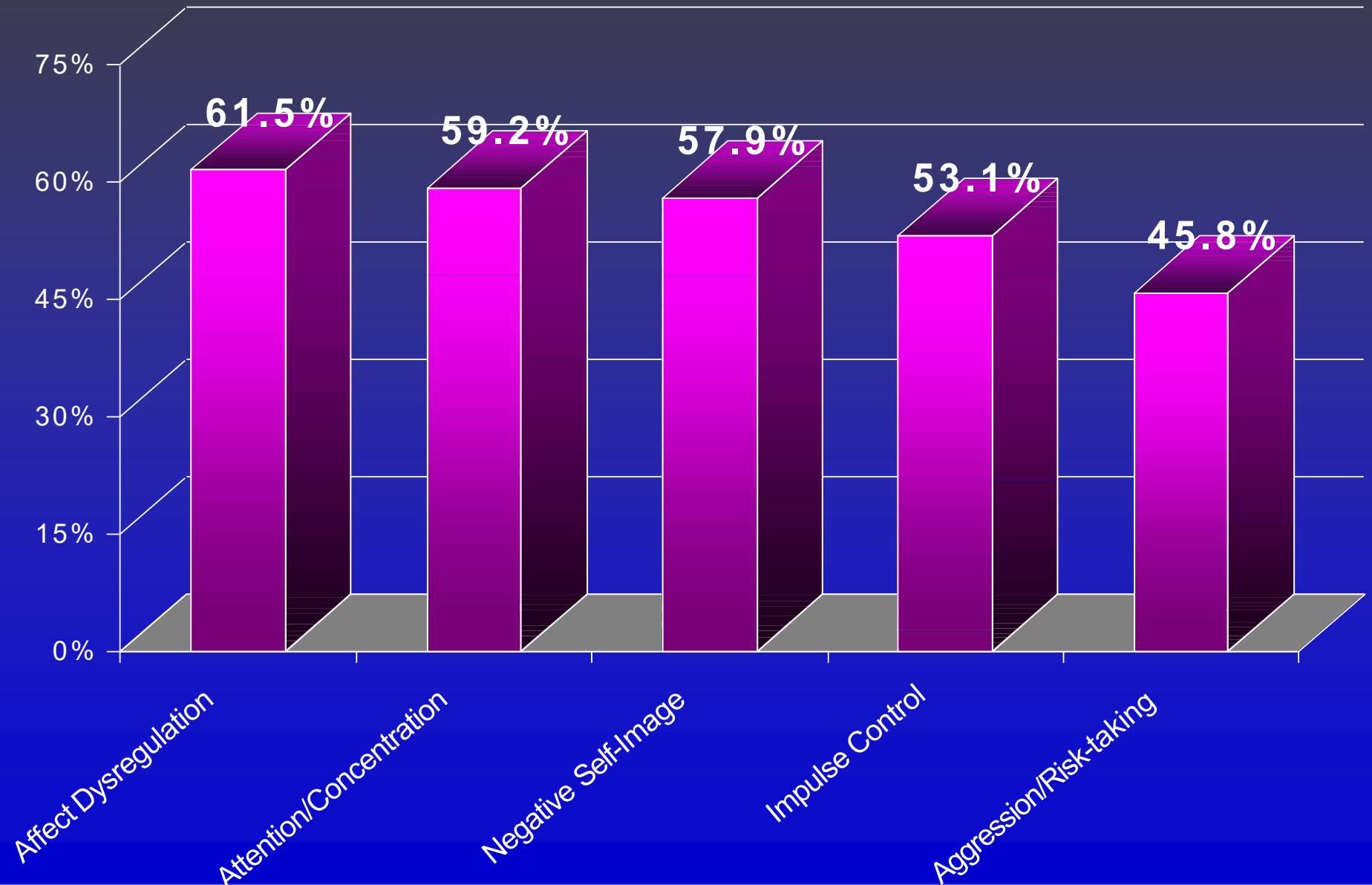
Joseph Spinazzola, Ph.D., Julian Ford, Ph.D., Margaret Blaustein, Ph.D., Melissa Brymer, Psy.D., Laura Gardner, BsPH, Susan Silva, Ph.D., Stephanie Smith, Ph.D.

Bessel van der Kolk, M.D.,

Child Trauma History: Most Frequent Exposure Types



Complex Posttraumatic Sequelae: Most Frequent Difficulties



Proposal to include Developmental Trauma Disorder in the DSM V

Bessel A. van der Kolk MD

Robert Pynoos MD

Dante Cicchetti PhD
Marylene Cloitre PhD
Wendy D'Andrea PhD
Julian Ford PhD
Alicia Lieberman MD
Frank Putnam MD
Glenn Saxe MD
Joseph Spinazzola PhD
Bradley Stolbach PhD
Martin Teicher MD PhD

Developmental Trauma Disorder

- ***Lifetime Exposure***
  - Primary caregiver attachment disruptions, neglect
  - Witness to DV, exposure to high risk
- ***Affective & Somatic Dysregulation***
  - Impaired recovery of negative affect states
  - Aversion to touch, sound
  - Physical anesthesia (not processing pain)
    Impaired ability to recognize somatic feelings
- ***Attentional & Behavioral Dysregulation***
  - Impaired self-protection, recklessness
  - Maladaptive self-soothing
  - Inability to sustain goal-directed behavior
- ***Relational or Self-dysregulation***
  - Self as defective
  - Attachment insecurity or disorganization
  - Reactive physical aggression

Ford, Spinazzola, & van der Kolk, 2019

Table 1. Data Sources

N=20,000

Dataset	Contributors	N	Sample Source
NCTSN Survey	Spinazzola, J., Ford, J.D., Zucker, M., van der Kolk, B.A., Silva, S., Smith, S.F., and Blaustein, M.	1699	Clients at NCTSN sites
NCTSN Core Data Set	Pynoos, R.S., Ostrowski, S., Fairbank, J.A., Briggs-King, E.C., Steinberg, A., Layne, C., and Stolbach, B.	4435	Clients at NCTSN sites
CANS Dataset	McClelland, G., Fehrenbach, T., Griffin, E., Burkman, K., and Kisiel, C.	7668	All Illinois Foster Care system
CCTC Dataset	Stolbach, B.C., Dominguez, R.Z., and Rompala, V.	172	All PTSD criterion A-exposed; none have risk to self or others
Western Michigan Dataset	Richardson, M., Henry, J., Black-Pond, C., and Sloane, M.	209	Foster care
Ford (In press, Journal of Clinical Psychiatry)	Ford, J.D., O'Connor, D.F., and Hawke, J.	397	Child psychiatry inpatients
NSA re-analysis	Ford, J. D., Elhai, J. D., Connor, D. F., and Frueh, B. C.	4023	National random
Juvenile Justice	Ford, J. D., Hawke, J., and Chapman, J.	1825	Juvenile Detention Centers
Ghosh Ippen and Lieberman	Ghosh Ippen, C.G., Harris, W.W., Van Horn, P.J., and Lieberman, A.F.	89	Preschoolers exposed to domestic violence

NCTSN Core Data Set

Core Data Set Symptom Measure	**Mean for DTD+[a] Children**	**Mean for DTD-[b] Children**	***t* =**	***P* =**	**Controlling for PTSD *P* =**
Indicators of Severity (Scale 0-2)					
Academic Difficulties	.8185	.8078	-.419	.675	NS
Alcohol Abuse	.1062	.0500	-5.823	.000	.000
Behavior Problems at Home	.9514	.7741	-7.187	.000	.000
Criminality	.1270	.0661	-5.669	.000	.000
Attachment Problems	.7766	.4345	-15.139	.000	.000
Behavior Problems at School	.7136	.6748	-1.539	.124	NS
Other Medical Problems	.3431	.1806	-8.786	.000	.000
Prostitution	.0090	.0055	-1.135	.256	NS
Running Away	.1064	.0508	-5.660	.000	.000
Substance Abuse	.1425	.0676	-6.367	.000	.000
Self-injurious Behaviors	.2197	.1322	-6.150	.000	.009
Skipping School	.2034	.1723	-1.922	.055	
Suicidality	.2663	.1595	-6.982	.000	.000
Inappropriate Sexualized Behaviors	.2885	.1667	-7.609	.000	.000

The DSM 5 taskforce response to proposal to include DTD in the DSM5

"The consensus was that there is just too little evidence, at this time, to include DTD in the DSM-5"

"The notion that early childhood adverse experiences lead to substantial developmental disruptions is more clinical intuition than a research based fact. This statement is commonly made but cannot be backed up with prospective studies".

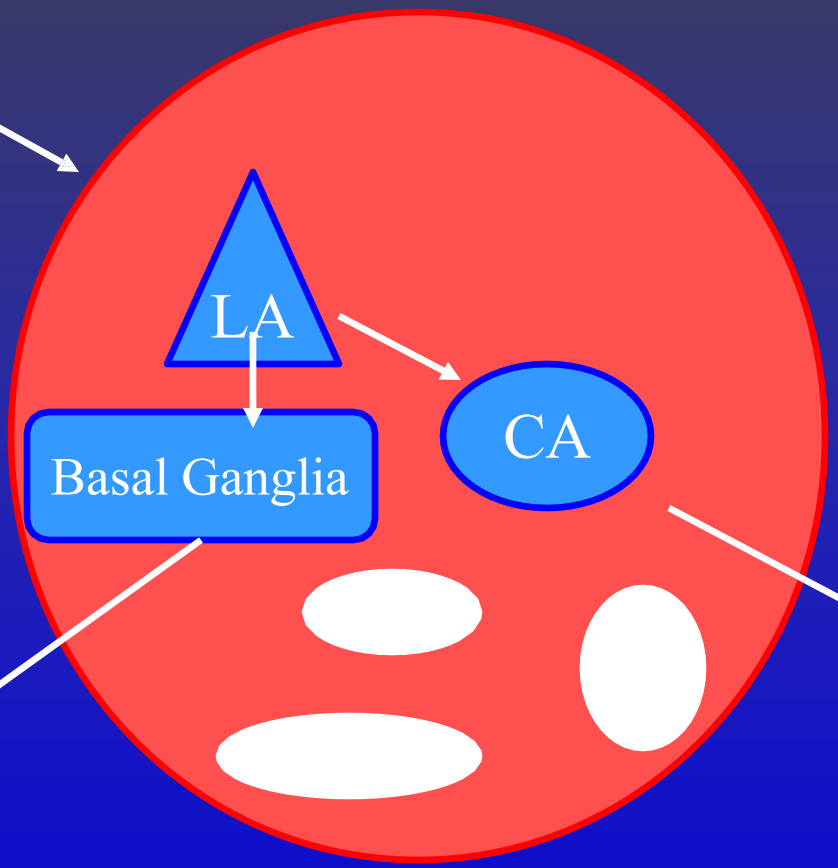
DSM5 – a veritable smorgasbord of random trauma-related "diagnoses"

PTSD
Disruptive mood dysregulation disorder
Reactive Attachment Disorder
Dissociative Identity Disorder
Non-suicidal self-injury
Intermittent Explosive Disorder
Disinhibted Social Engagement Disorder
Oppositional Defiant Disorder
Conduct Disorder
Borderline Personality Disorder


PATRICK MAKUAKANE

How the brain "gets on with life"
(LeDoux, 2003)

Threat



Active coping
- Planning
- Action

Passive coping
- Freezing
- Despondency

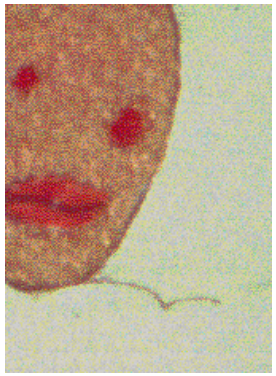
Chronic stress arousal programs the immune system

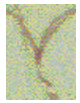
Produce inflammatory cytokines— turning inflammation on— and less effective at producing anti-inflammatory cytokines— turning inflammation off.

Continued release of inflammatory cytokines long after the toxin exposure or injury is gone.

May manifest in chronic pain, fibromyalgia, chronic fatigue syndrome, chronic headaches and migraines, arthritis, back pain, eczema, psoriasis, cardiovascular disease, asthma, allergies, irritable bowel syndrome, and insulin resistance, a precursor to type II diabetes.

In fact, following trauma somatic symptoms more prevalent than PTSD symptoms





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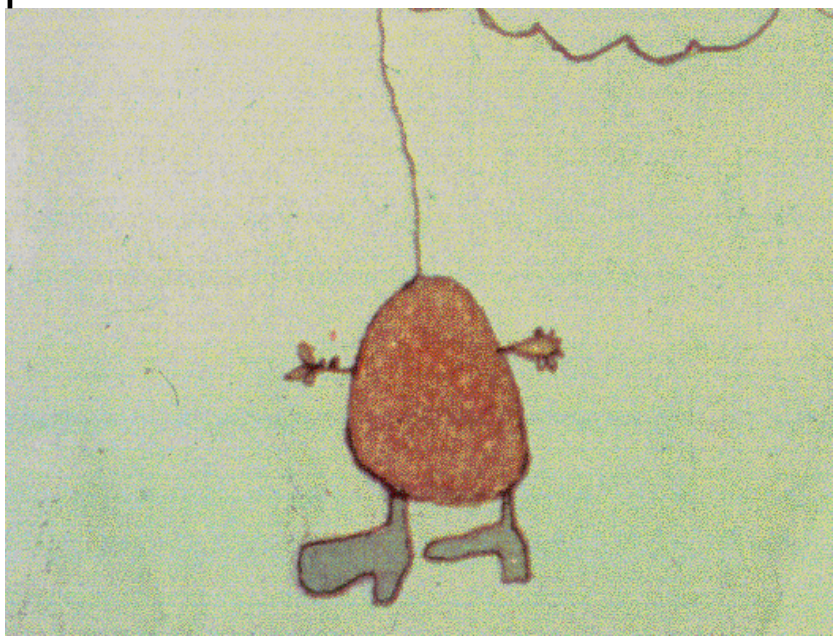
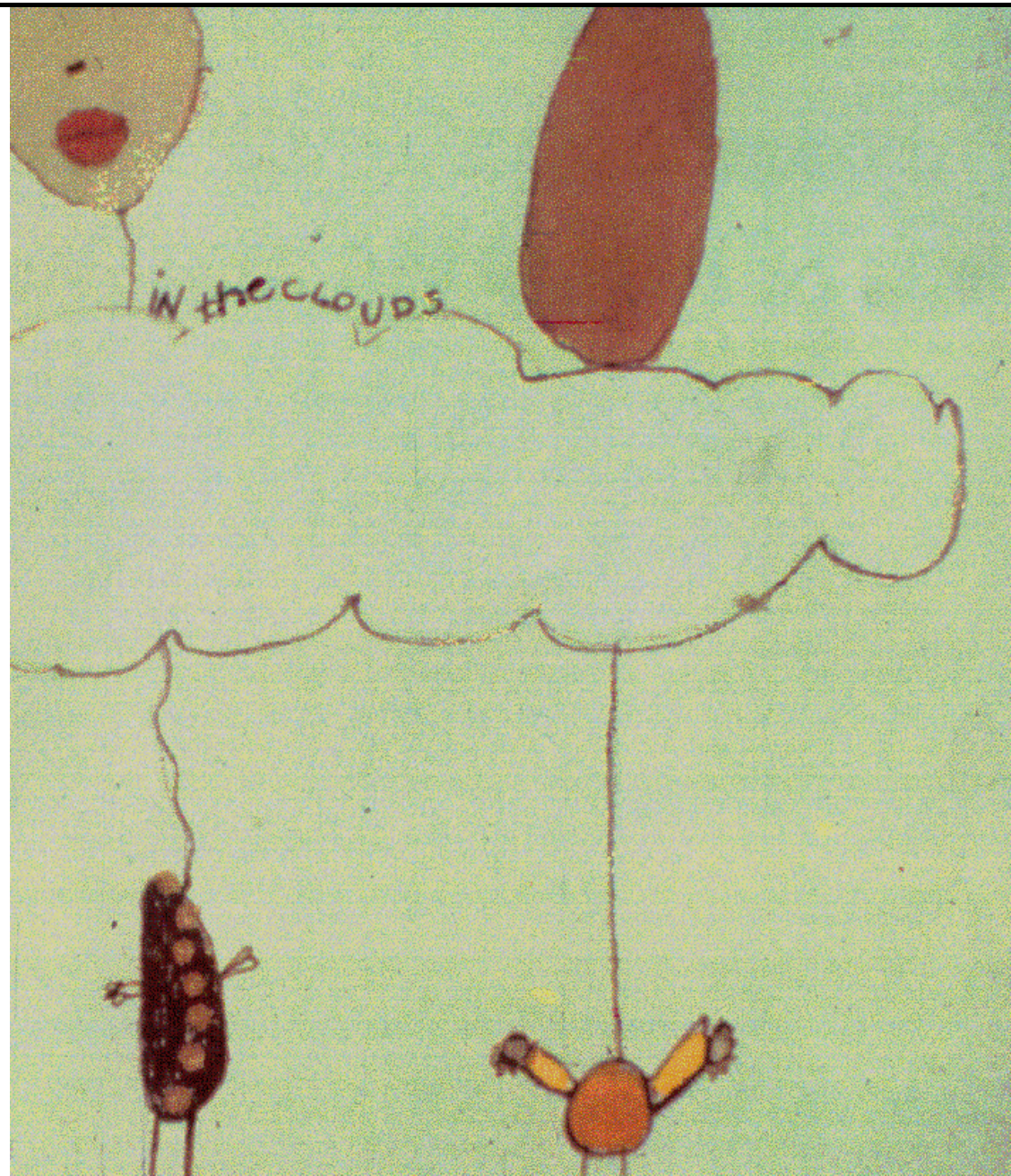




www.traumaresearchfoundation.org

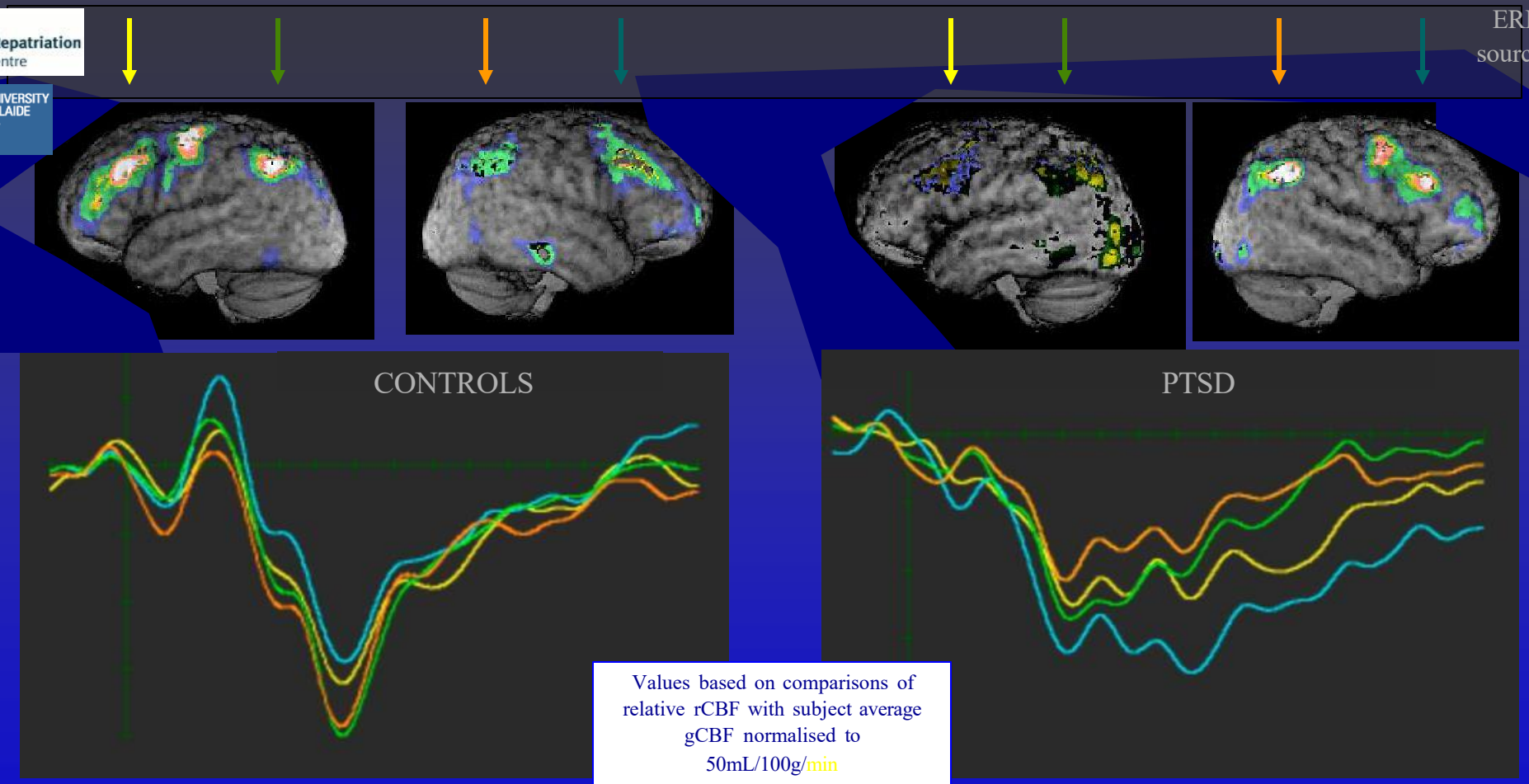
Sensory integration


I'm really happy today.

Breakdown in cortical timing in PTSD

Austin & Repatriation Medical Centre

THE UNIVERSITY OF ADELAIDE AUSTRALIA

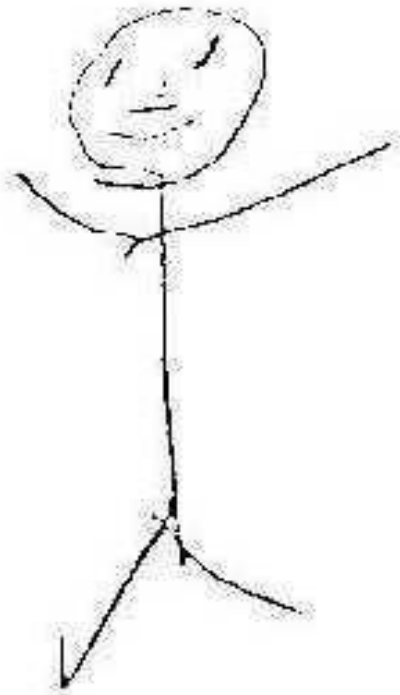


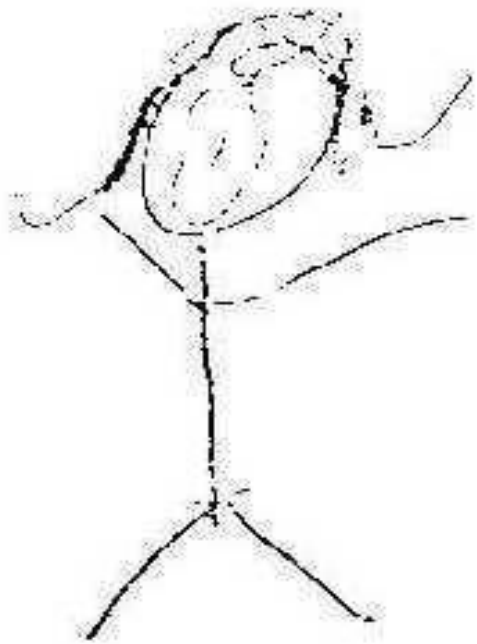
Values based on comparisons of relative rCBF with subject average gCBF normalised to 50mL/100g/min

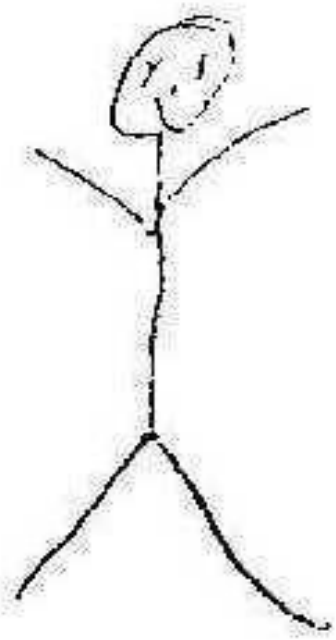
Clark, Egan, McFarlane, Morris, Weber, Sonkkilla, Marcina, Tochon-Danguy. (2000) Human Brain Mapping. 9(1): 42-54

Clark,McFarlane,Morris,Weber,Sonkkilla, Marcina, Egan (in submission)

Child's Family Drawing at Beginning of NF - 8/3/94

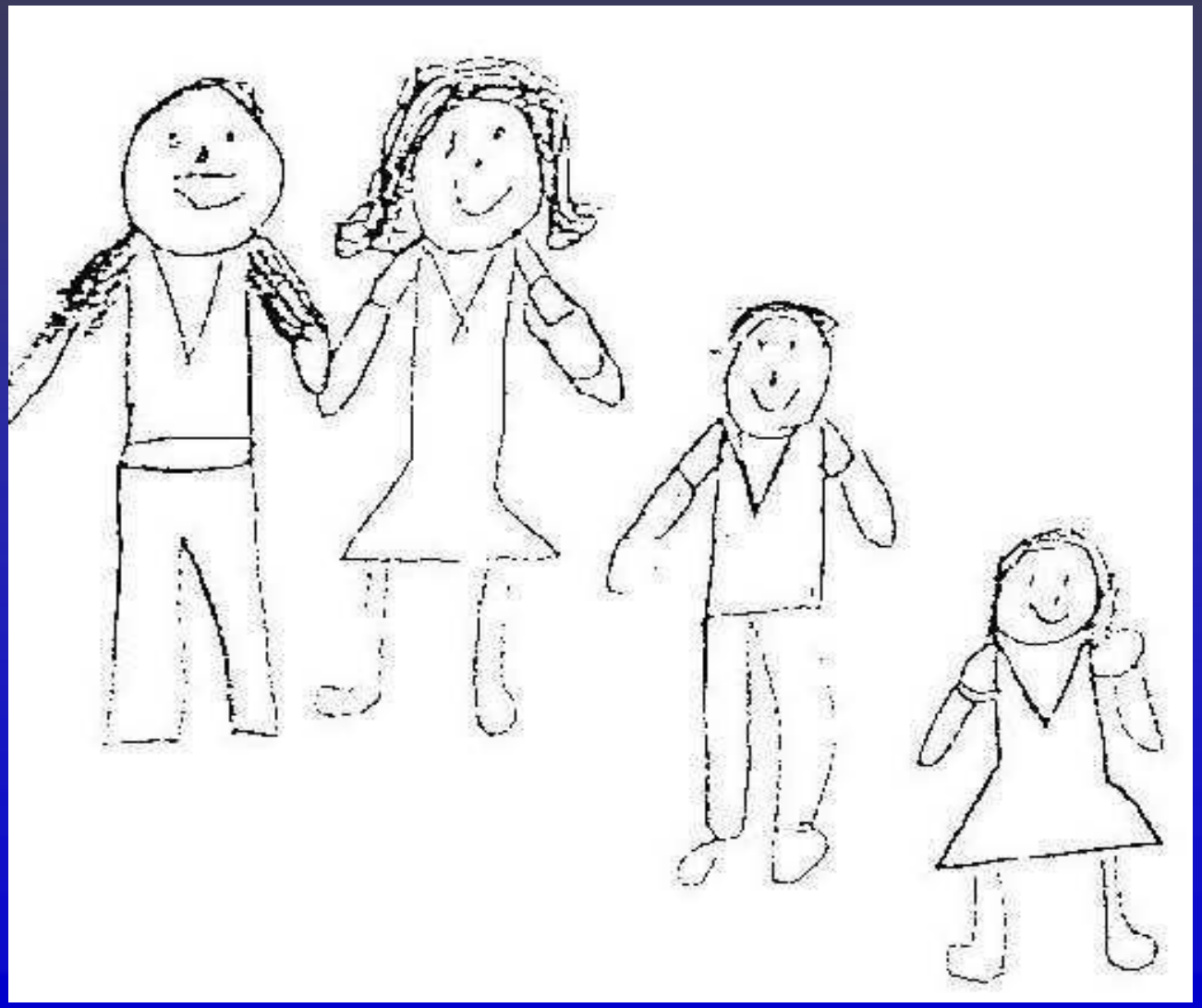






Drawing after Twenty Sessions - 9/8/94

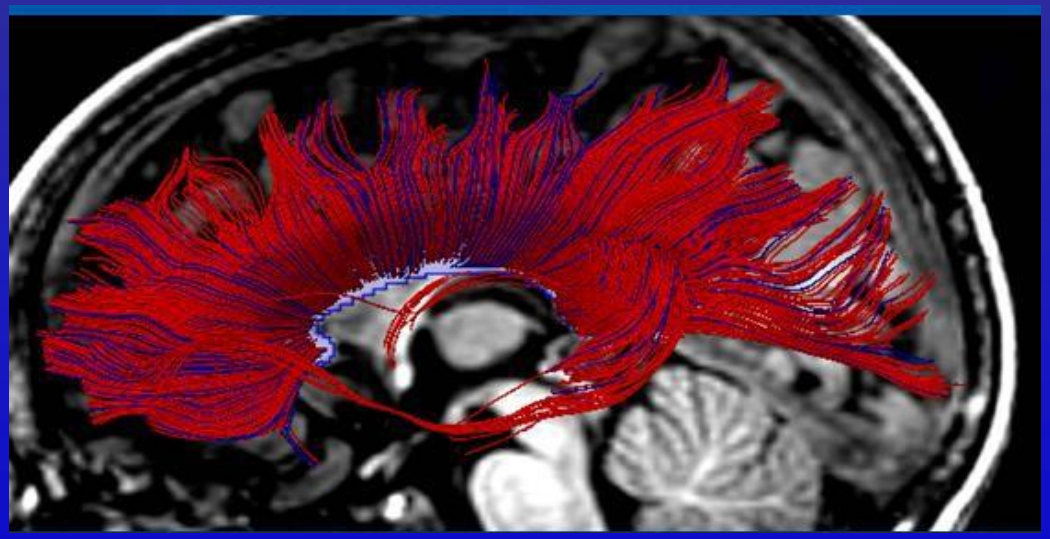
Drawing after forty sessions - 11/25/94

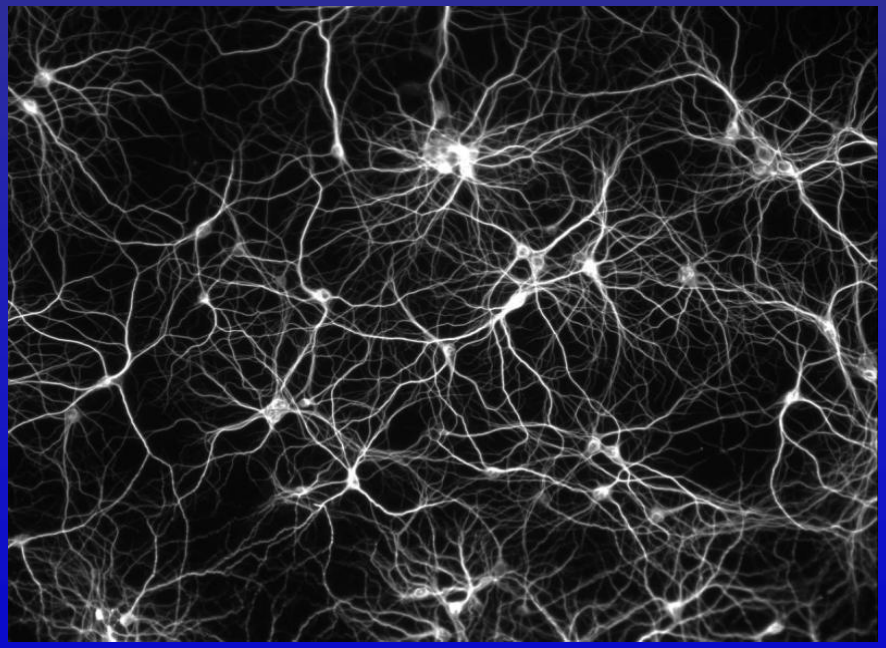


In adult centers the nerve paths are something fixed, ended, immutable. Everything may die, nothing may be regenerated.
It is for the science of the future to change, if possible, this harsh decree.

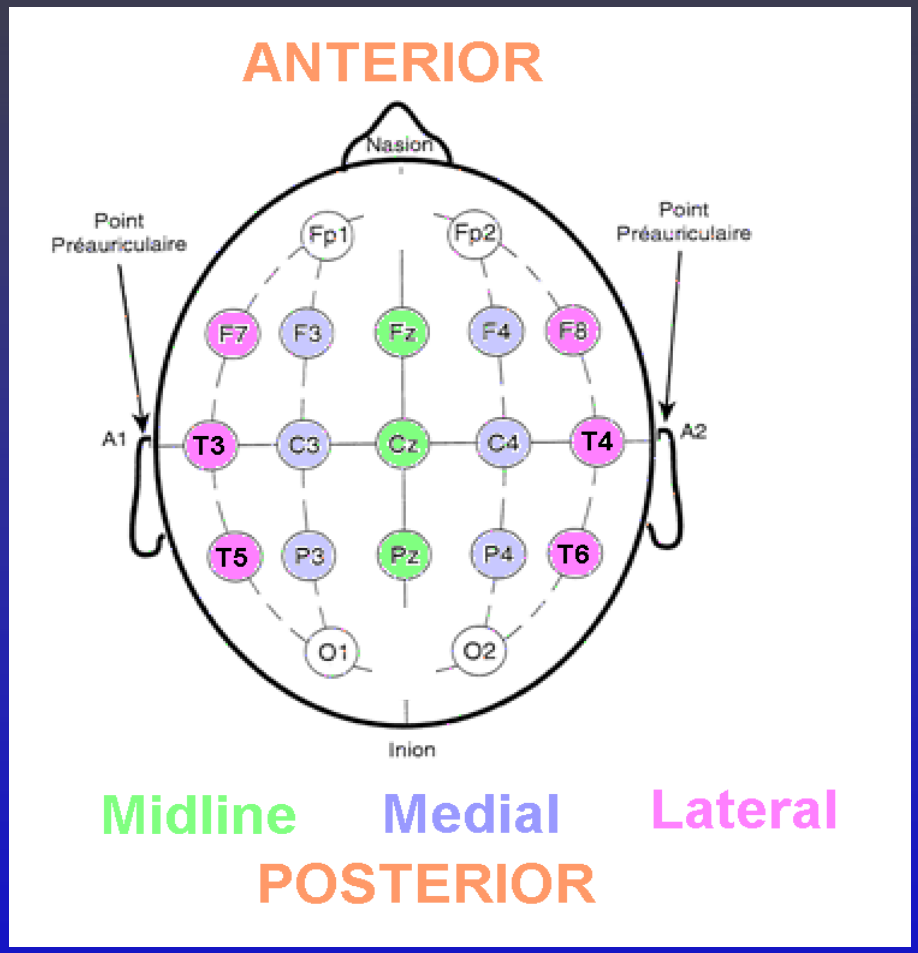
-Santiago Ramon y Cajal, 1928,
founder of modern neuroanatomy

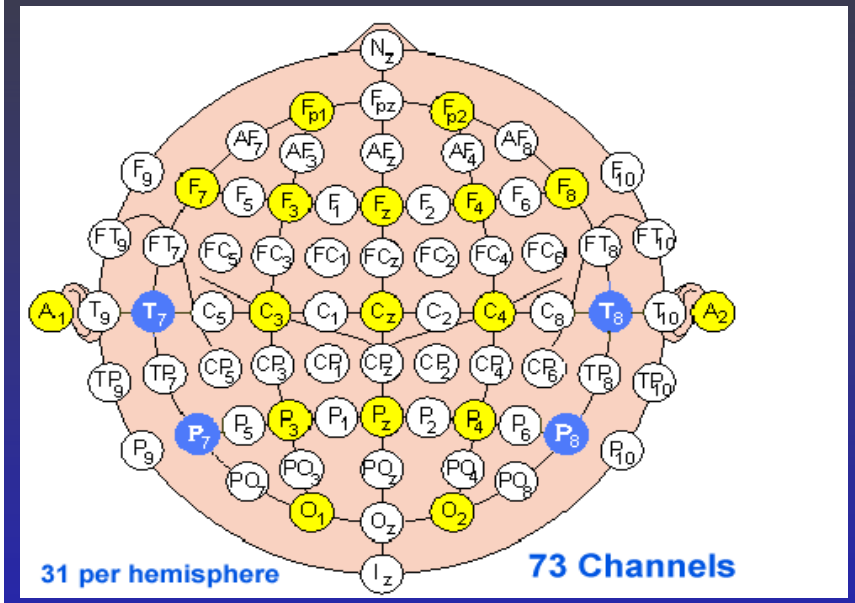
Anatomy is destiny – *Freud*





International System of Electrode Placement (1958; 1974)






SKY news

Many conditions result from problems with regulation of arousal

The RATE of BRAINWAVE FIRING is related to our state of arousal.

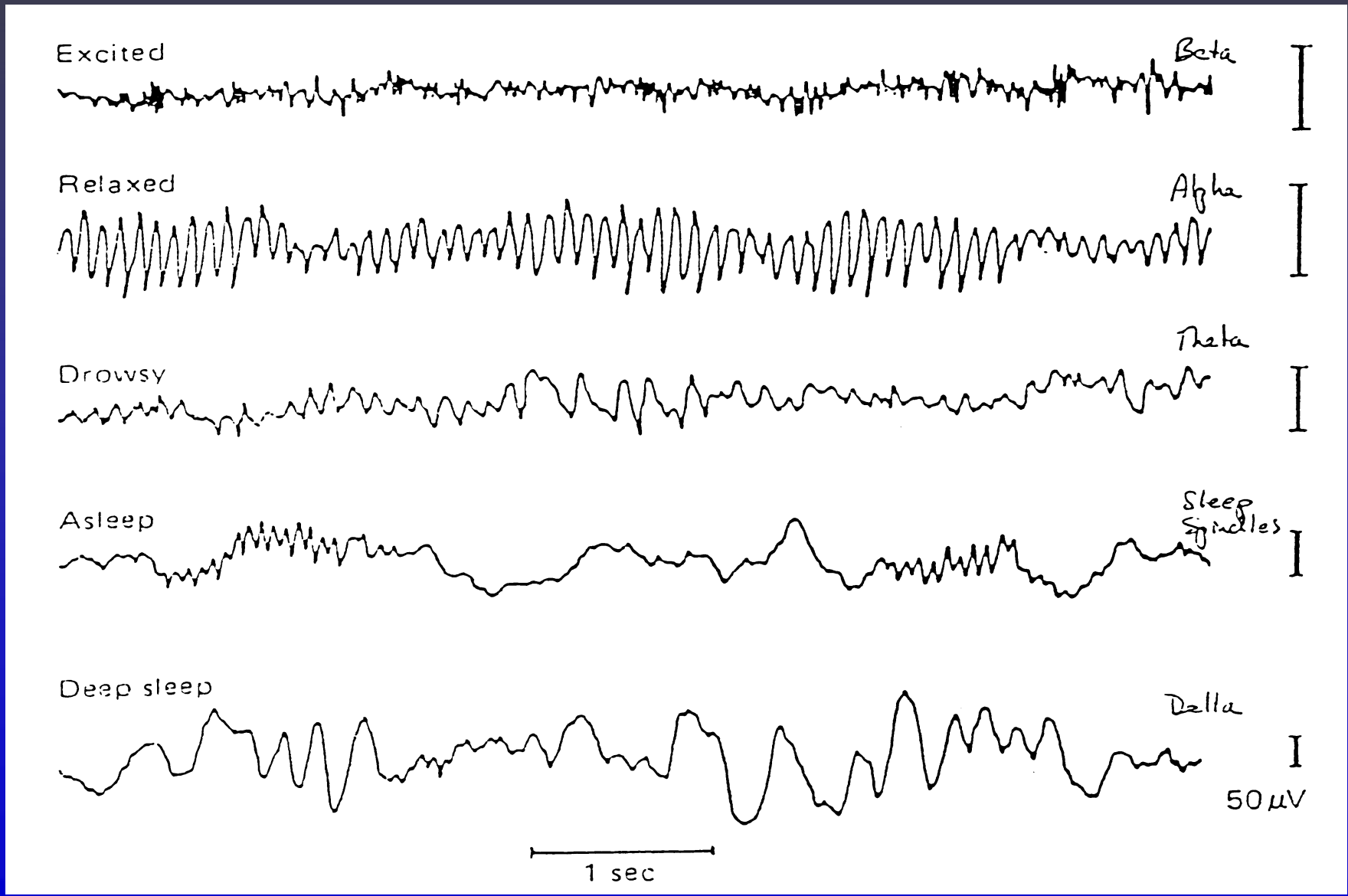
cps = cycles per second, or Hertz

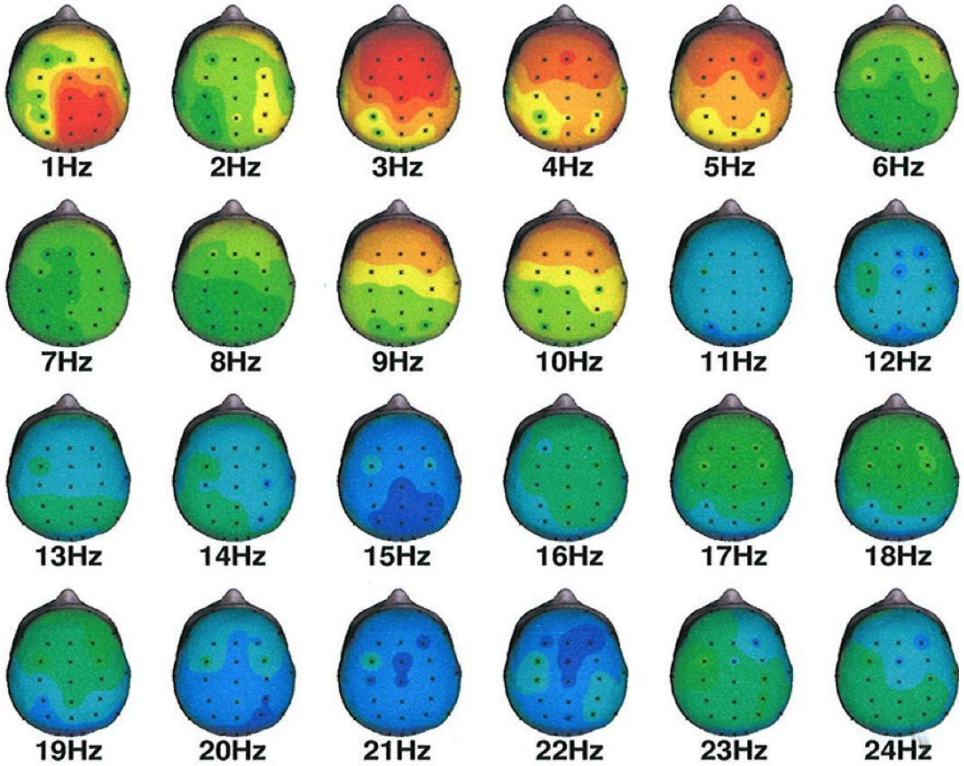
DELTA Less than 4 cps	THETA 4–8 cps	ALPHA 8–12 cps	SMR 12–15 cps	BETA 15–18 cps	HIGH BETA more than 19 cps
Sleep	Drowsy	Relaxed Focus	Relaxed Thought	Active Thinking	Excited
					

Depression, ADD, and seizure activity in this range.

We train the brain to move into this range to modify symptoms of depression, ADD, and improve seizure activity.

State of Arousal and EEG Wave Patterns

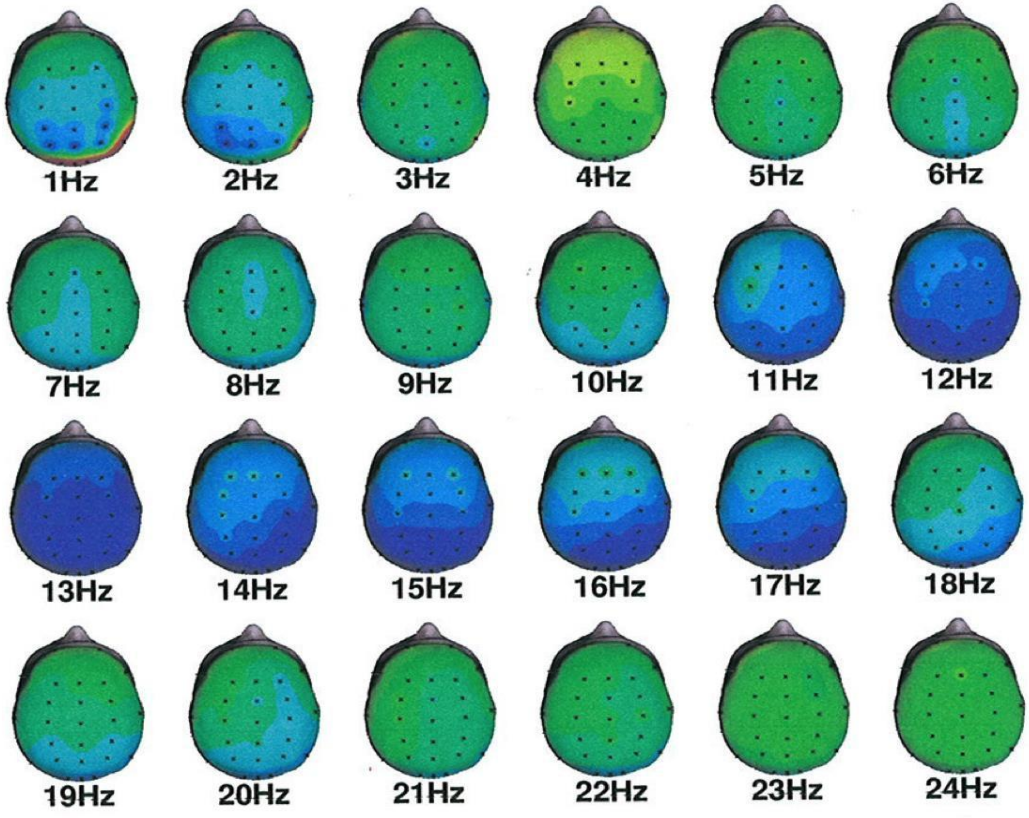


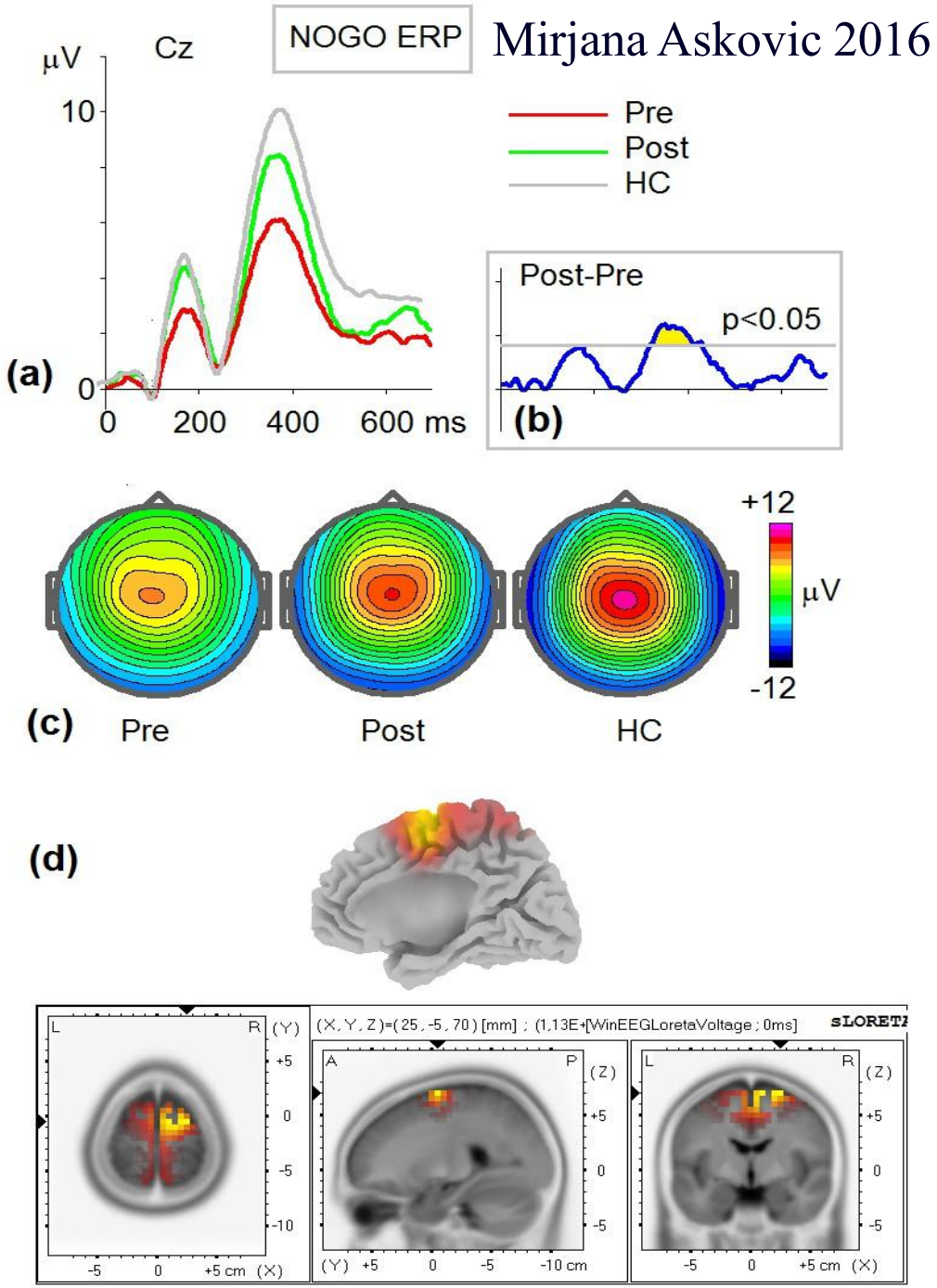


20 weeks of F3-F4 down training of frontal Δ, resulting in good adjustment

12 Year old Somali refugee boy with
serious impulse control and concentration problems, making classroom attendance impossible.

.





ERPs in the cued GO/NOGO task In PTSD (N=13) pr) and after post 25 sessions of neurofeedback . Grand average ERPs at Cz for NOGO stimuli in the group of PTSD patients before (red) and after (green) neurofeedback sessions in comparison to healthy subjects, same age (N=49). Post-Pre difference wave with the confidence level of statistical significance at $p<0.05$. Maps computed at maximums of P300 for Pre, Post and healthy control (HC) subjects sLORETA images of the Post-Pre difference waves.

PLOS ONE

RESEARCH ARTICLE

A Randomized Controlled Study of Neurofeedback for Chronic PTSD

Bessel A. van der Kolk[1,2,3]*, Hilary Hodgdon[1,3], Mark Gapen[1], Regina Musicaro[1,4], Michael K. Suvak[1,4], Ed Hamlin[5,6], Joseph Spinazzola[1,3,4]

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* besselvanderkolk@gmail.com

Abstract

Introduction

Brain/Computer Interaction (BCI) devices are designed to alter neural signals and, thereby, mental activity. This study was a randomized, waitlist (TAU) controlled trial of a BCI, EEG neurofeedback training (NF), in patients with chronic PTSD to explore the capacity of NF to reduce PTSD symptoms and increase affect regulation capacities.

Study Design

52 individuals with chronic PTSD were randomized to either NF (n = 28) or waitlist (WL) (n = 24). They completed four evaluations, at baseline (T1), after week 6 (T2), at post-treatment (T3), and at one month follow up (T4). Assessment measures were:1. Traumatic Events Screening Inventory (T1); 2. the Clinician Administered PTSD Scale (CAPS; T1, T3, T4); 3. the Davidson Trauma Scale (DTS; T1-T4) and 4. the Inventory of Altered Self-Capacities (IASC; T1-T4). NF training occurred two times per week for 12 weeks and involved a sequential placement with T4 as the active site, P4 as the reference site.

Results

Participants had experienced an average of 9.29 (*SD* = 2.90) different traumatic events. Post-treatment a significantly smaller proportion of NF (6/22, 27.3%) met criteria for PTSD than the WL condition (15/22, 68.2%), $\chi 2$ ($n = 44$, $df = 1$) = 7.38, $p = .007$. There was a significant treatment condition x time interaction ($b = -10.45$, $t = -5.10$, $p < .001$). Measures of tension reduction activities, affect dysregulation, and affect instability exhibited a significant Time x Condition interaction. The effect sizes of NF ($d = -2.33$ within, d = - 1.71 between groups) are comparable to those reported for the most effective evidence based treatments for PTSD.

Discussion

Compared with the control group NF produced significant PTSD symptom improvement in individuals with chronic PTSD, as well as in affect regulation capacities. NF deserves further

OPEN ACCESS

Citation: van der Kolk BA, Hodgdon H, Gapen M, Musicaro R, Suvak MK, Hamlin E, et al. (2016) A Randomized Controlled Study of Neurofeedback for Chronic PTSD. PLoS ONE 11(12): e0166752. doi:10.1371/journal.pone.0166752

Editor: Yutaka J. Matsuoka, National Cancer Center, JAPAN

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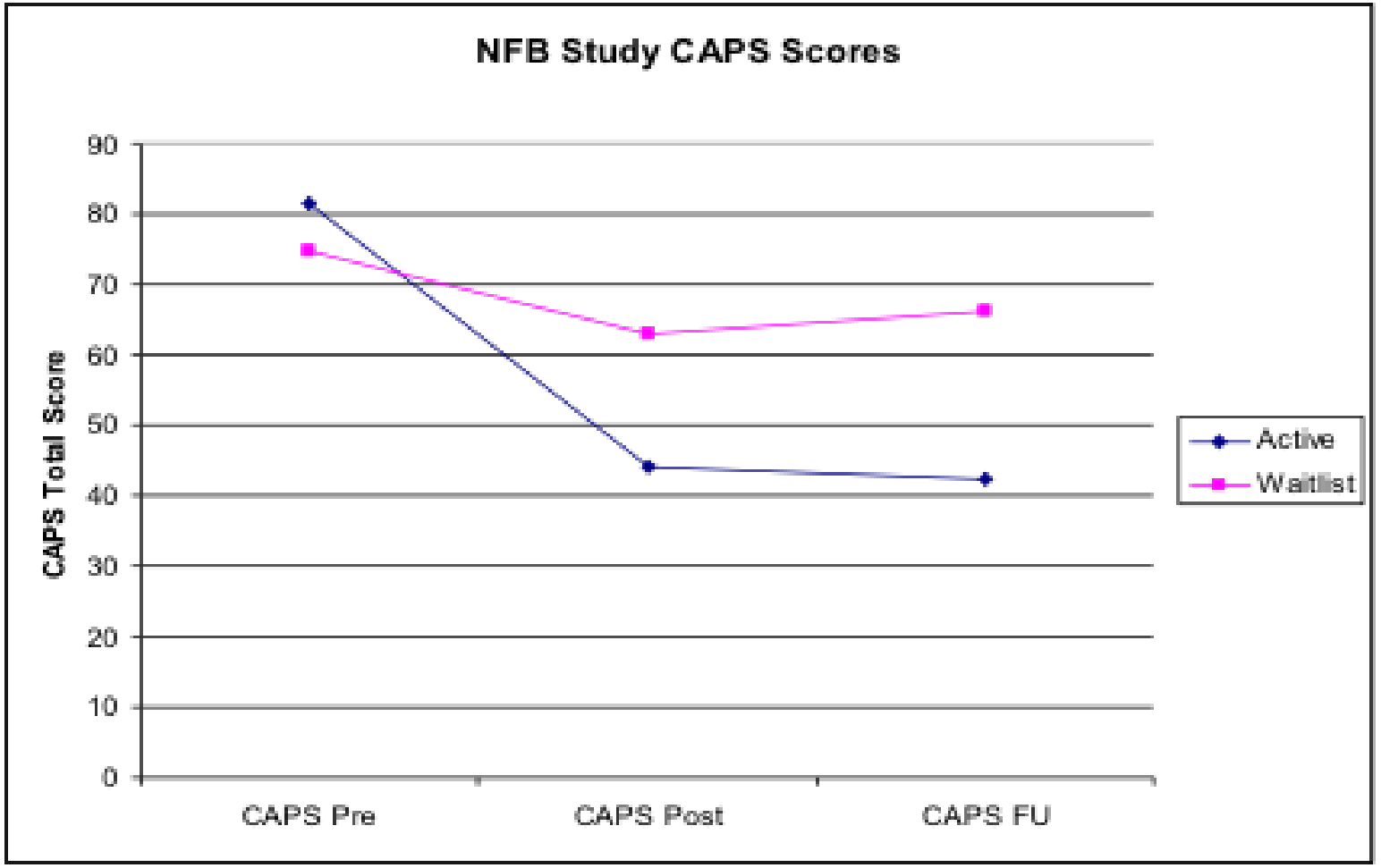
Published: December 16, 2016

Data Availability Statement: All relevant data are within the paper.

Funding: Funders did not contribute to the design or execution of the study

Competing Interests: No competing interests



Group Means: CAPS

	CAPS Pre	CAPS Post	CAPS FU
Active (N = 16)	82	44	42
Waitlist (N = 16)	75	63	66

		N	Correlation	Sig.
Pair 1	iasc affect dysregulation total scale at baseline & iasc affect dysregulation total scale at T24	16	.596	.015
Pair 2	iasc identity impairement total scale at baseline & iasc identity impairement total scale at T24	16	.784	.000
Pair 3	iasc idealization-disillusionment scale at baseline & iasc idealization-disillusionment scale at T24	16	-.015	.956
Pair 4	iasc abandonment concerns scale at baseline & iasc abandonment concerns scale at T24	16	.505	.046
Pair 5	iasc susceptibility to influence scale at baseline & iasc susceptibility to influence scale at T24	16	.836	.000
Pair 6	iasc interpersonal conflicts scale at baseline & iasc interpersonal conflicts scale at T24	16	.638	.008
Pair 7	iasc tension reduction activities scale at baseline & iasc tension reduction activities scale at T24	16	.733	.001

Profound effect on executive functioning

1) Planning and decision making
2) Error correction and trouble shooting
3) Mental flexibility
4) Figuring out novel & unfamiliar situations
5) Dealing with danger
6) Resisting temptation and being able to resist habitual impulses
7) Self-regulation

EEG neurofeedback

NF can help to regulate major brain networks such as the SN and the DMN.

For example, fMRI, single session NF vs SHAM aimed at voluntarily reducing the alpha rhythm amplitude to gain insight into potential mechanisms underlying this form of neurofeedback.

Activity in the alpha band (8–12 Hz) can be successfully modulated through (NFB) (Ros, Munneke, Ruge, Gruzelier, & Rothwell, 2010),

Alpha rhythm NFB may be beneficial in treating anxiety and attention problems (Hardt & Kamiya, 1978; Rasey, Lubar, McIntyre, Zoffuto, & Abbott, 1995)

Alpha neurofeedback training led to plastic modulation of both SN and DMN functional connectivity, effects which were not observed in the SHAM condition (Ros et al., 2013).

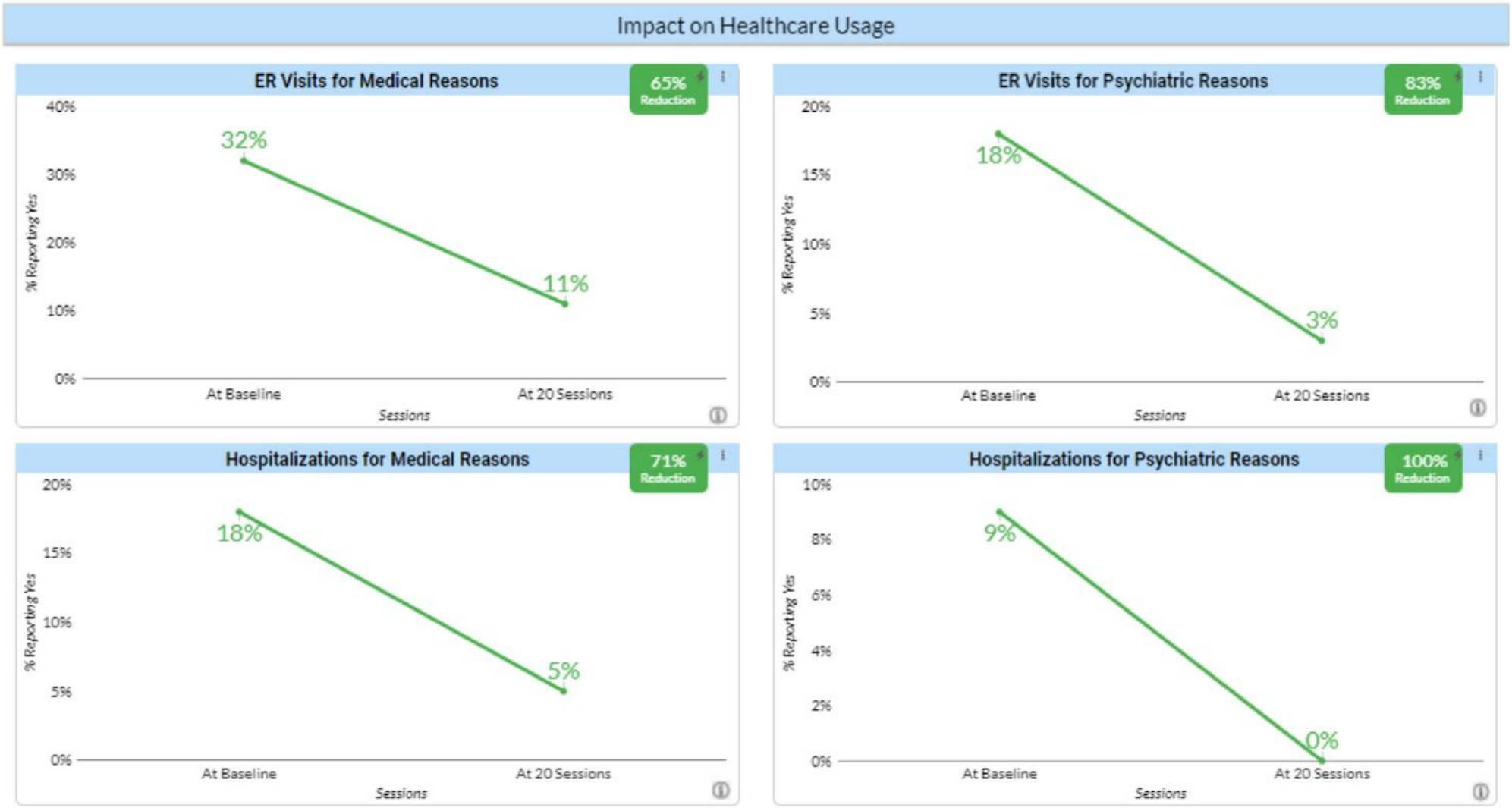


FIGURE 4 | Impact of neurofeedback on healthcare usage. Percentages of clients reporting emergency room visits or hospitalizations for either medical or psychiatric reasons before and after 20 neurofeedback sessions.

FIGURE 2 | Impact of neurofeedback on behavior. Clients reported the occurrence of behaviors such as self-harm/suicide ideation, arrest and/or incarceration, discipline action at school, drug and alcohol relapses, nicotine use, and marijuana use before and after receiving neurofeedback therapy.

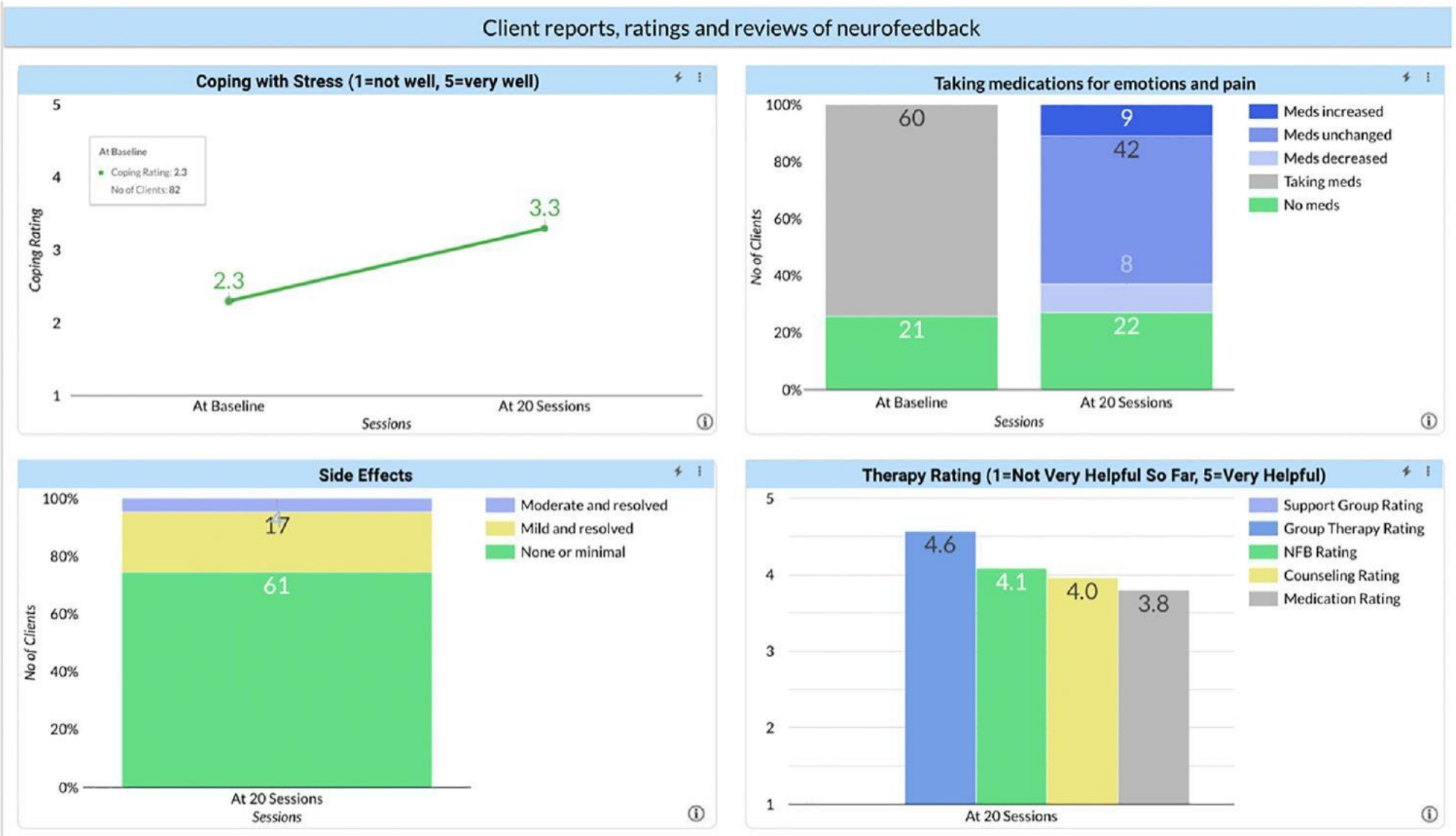


FIGURE 5 | Client reports, ratings, and reviews of neurofeedback. Reported outcomes from clients at baseline and after 20 neurofeedback sessions for: coping with stress, taking medications for emotions and pain, side effects, and the helpfulness of therapy.

Pychedelics to help with trauma processing?

Acute Subjective Qualities Differ Across Psychedelics

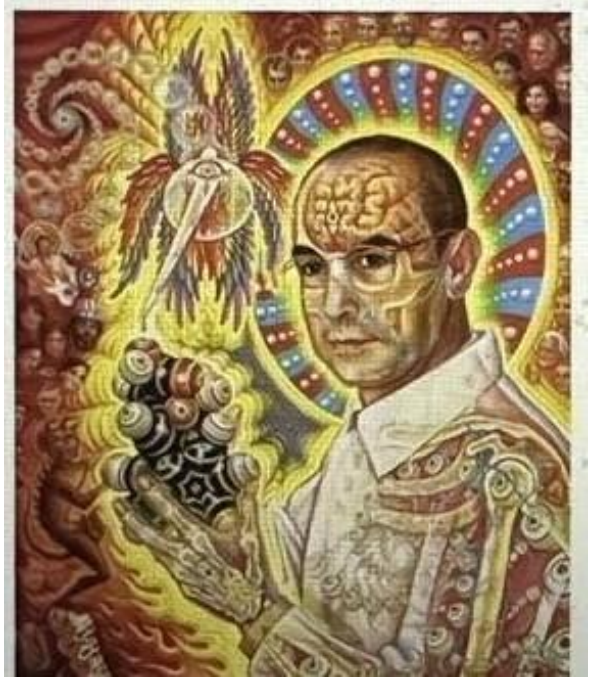
KETAMINE
PCP

D'issociative

Empathogen

MDMA

Hallucinogen



LSD
DMT
PSILOCYBIN
MESCALINE

Oneirogen

IBOGA

Psilocybin 2 mg IV Robin Carhart Harris

"that was undoubtedly the most intense psychedelic experience of my life";

"[it] was like hitting a brick wall, and then you're somewhere else"; "you just take off";

"I could have been there a minute or a million years";

"[It was] quite difficult to know where I ended and melted into everything around me";

"Everything fragmented; things were all in bits & it was very hard to hold it all together in a coherent stream";

"[That was] real ego death stuff, [a] total dissolving of my sense of self"

MDMA assisted psychotherapy

What have we learned about mechanisms of recovery?

www.traumaresearchfoundation.org

Or: the symphony without conductor

Marine Veteran

2 tours in Iraq as Humvee turret gunner

Middle of first MDMA session

75mg + 37.5mg

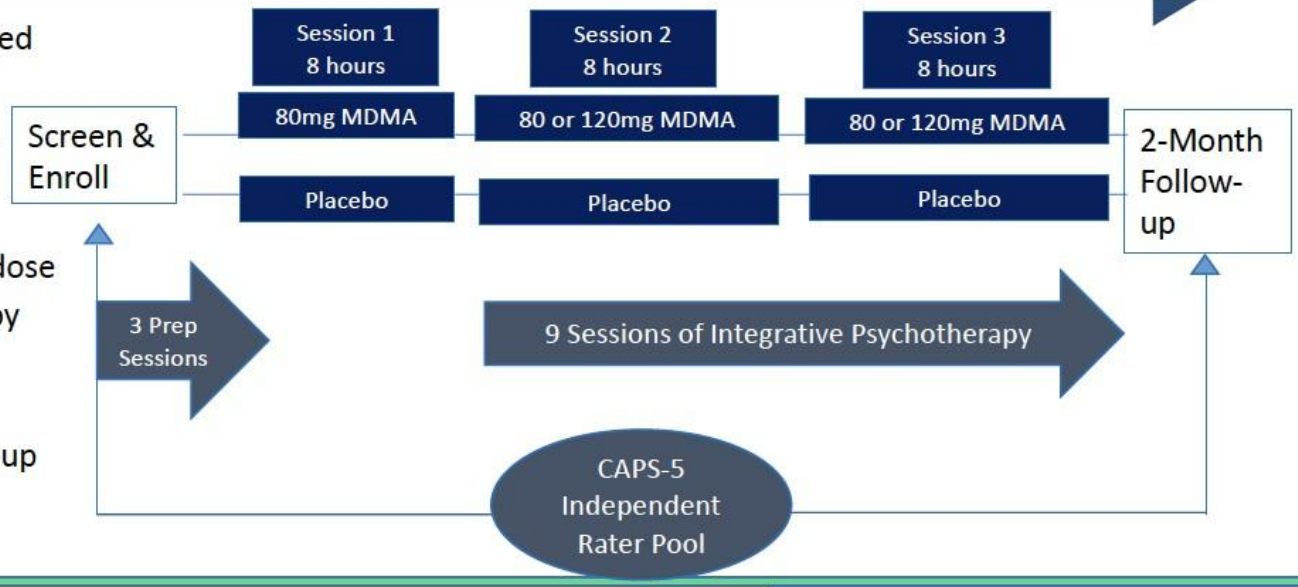
Efficacy and Safety Results From the First Pivotal Phase 3 Randomized Controlled Trial of MDMA-Assisted Therapy for Treatment of Severe Chronic PTSD

Bessel van der Kolk, M.D.
Boston University School of Medicine
Phase 3 Trial Clinical Investigator

Sponsor: Multidisciplinary Association for Psychedelic Studies
Sponsor Delegate & Trial Organizer: MAPS Public Benefit Corporation
NCT03537014

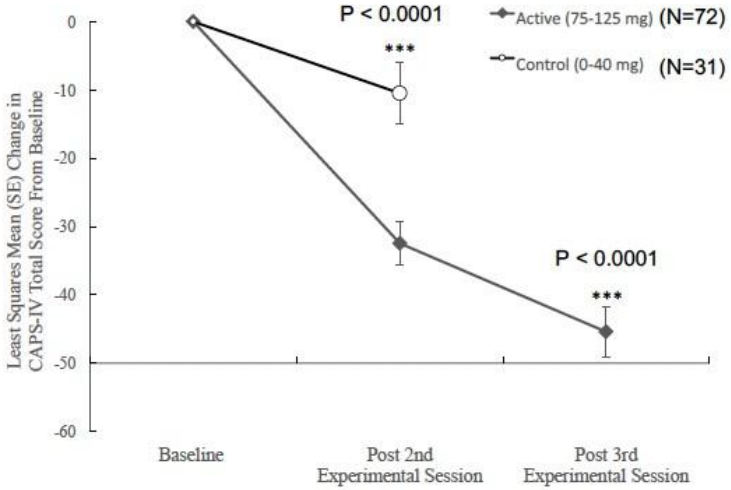
MDMA-Assisted Therapy Trial Design

- Pivotal Phase 3 study N=90 completed
- 14 site-study with 80+ therapists
- 80 mg or 120mg Initial dose MDMA vs. Placebo
- 40 mg or 60 mg Supplemental dose administered 1.5-2 hours post first dose
- Both groups receive identical therapy
- Blinded Independent Rater Pool for Outcome Assessments
- Open label crossover for control group
- 12-month Long-term Follow-up



Efficacy of MDMA-Assisted Therapy for PTSD

- **Subjective Effects**
  - Enhanced mood & well-being
  - Increased responsiveness to to emotional and sensory stimuli
  - Sense of closeness to other people, oneness, empathy
  - Heightened openness, "emotional communion"
  - Empathogen/entactogen
- **Therapeutic Effects**
  - Robust significant reduction in PTSD symptom severity
  - Compared to other relatively effective treatments, "the effect sizes are so large there is no way they are produced by chance" per randomization inference analysis



(Pooled Phase 2 results: Mithoefer et al. 2019)

Phase 3 efficacy results (n=90) confirmed Phase 2 results and was statistically significant.

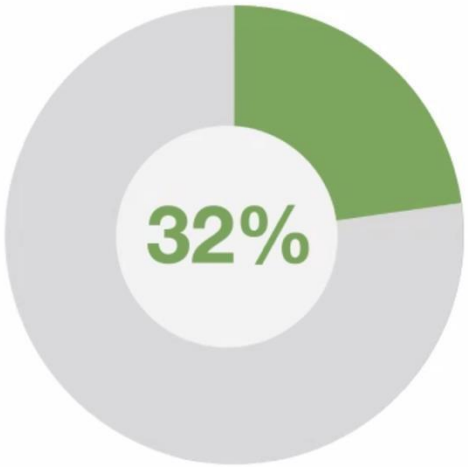
Van der Kolk et al, 2021

Demographics

	MDMA-assisted therapy (N=46)	Placebo with therapy (N=44)	Total (N=90)
Age, mean (SD)	43 (13)	38 (10)	41 (12)
Female, biological, n(%)	59%	73%	66%
Race			
American Indian/Alaska Native	6%	0%	3%
Asian	4%	11%	8%
Black/African American	0%	4%	2%
Native Hawaiian/Pacific Islander	0%	0%	0%
White	85%	68%	77%
Multiple	4%	14%	9%
Ethnicity			
Hispanic/Latinx, n(%)	11%	7%	9%
Trauma History n (%)			
Developmental	87%	82%	84%
Veteran	22%	14%	18%
Combat exposure	13%	11%	12%
Multiple	89%	86%	88%

Phase 3 Results - ⅔ of the MDMA + Therapy study participants no longer qualified for a PTSD diagnosis after three MDMA sessions

Control + Therapy Group



Phase 2 result: 23%

MDMA + Therapy Group

2-Month Follow Up

Phase 2 result: 56%

12-Month Follow Up

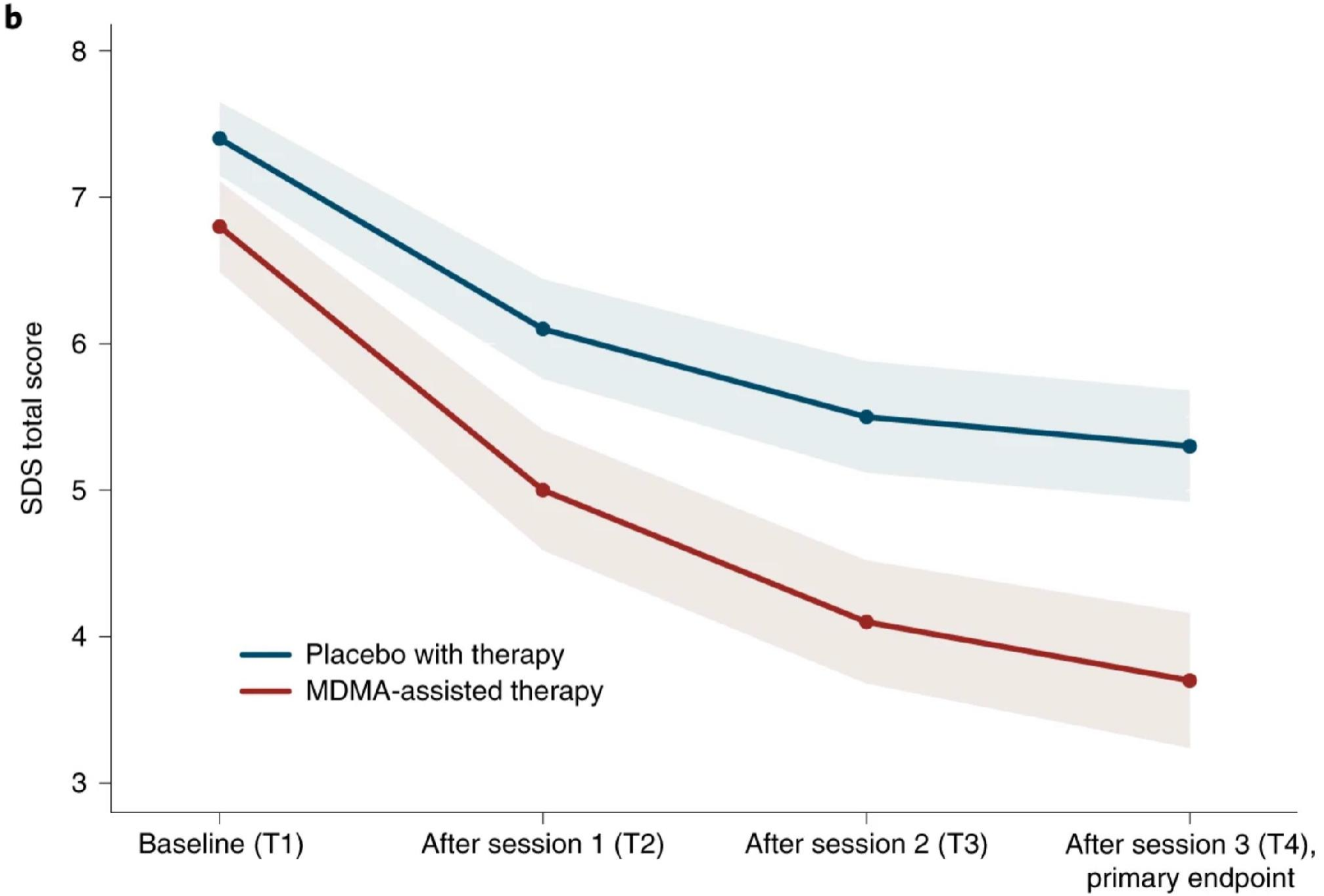
(Available next year)

Phase 2 result: 68%

Meet PTSD diagnosis requirements

No longer meet requirements for a PTSD diagnosis

Sources: MAPP1 Results
Notes: "Control + Therapy Group" value was 23% and "MDMA + Therapy Group" at the 2-Month Follow Up was 56%


b
8
7
6
5
4
3
SDS total score
Placebo with therapy
MDMA-assisted therapy
Baseline (T1)
After session 1 (T2)
After session 2 (T3)
After session 3 (T4), primary endpoint

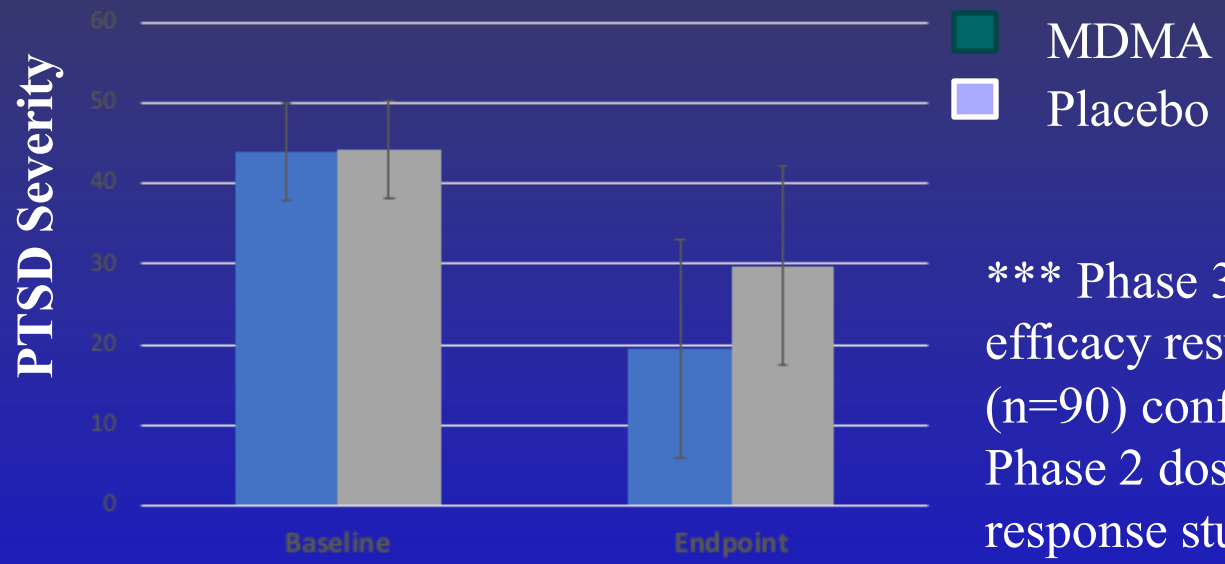
Efficacy of MDMA-Assisted Therapy for PTSD

Subjective Effects

- Enhanced mood & well-being
- Increased responsiveness to to emotional and sensory stimuli
- Sense of closeness to other people, oneness, empathy
- Heightened openness, "emotional communion"
- Empathogen/entactogen

Therapeutic Effects

- Large effect size (0.9)
- Robust significant reduction in PTSD symptom severity in Phase 2&3 studies
- No effect of Adverse Childhood Experiences (ACE) on outcomes
- Dissociative subtype of PTSD (N=13) responded ≧ non-dissociative PTSD (N=77) per CAPS-5



*** Phase 3 efficacy results (n=90) confirme Phase 2 dose response study results and was clinically & statistically significant.

Treatment Emergent Adverse Reactions

Adverse Drug Reaction (>7%)	MDMA (N=46)	Placebo (N=44)	Adverse Drug Reaction (>7%)	MDMA (N=46)	Placebo (N=44)
Muscle tightness	63%	11%	BP increased	11%	-
Decreased appetite	52%	11%	Feeling jittery	11%	-
Nausea	30%	11%	Chest pain (non-cardiac)	11%	2%
Hyperhidrosis	20%	2%	Dry Mouth	11%	4%
Feeling cold	20%	7%	Vision Blurred	9%	2%
Restlessness	15%	-	Pollakiuria	9%	2%
Mydriasis	15%	-	Intrusive Thoughts	9%	-
Dizziness (postural)	13%	4%	Vomiting	9%	-
Bruxism	13%	2%	Stress	9%	-
Nystagmus	13%	-	Musculoskeletal Pain	9%	-

Adverse reactions resolve within few days post-dosing. MDMA is sympathomimetic.

Unexpected Serious Adverse Reactions are rare in controlled studies of MDMA

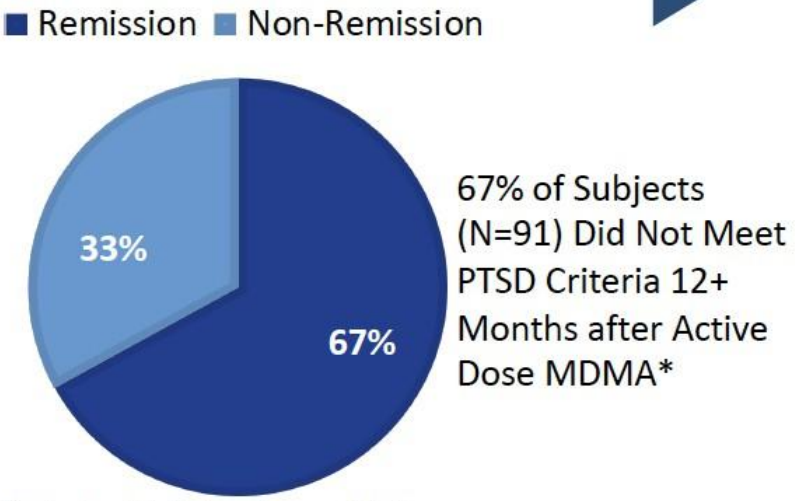
- 1 of 341 (<1%): expected SAR of exacerbation of pre-existing ventricular extrasystoles

Risk Assessment:

- No high level risks
- Medium level: Cardiovascular, Psychological Distress

Durability in Response & Remission of PTSD

- **In pooled Phase 2 trials:**
- ~18 years of PTSD before MDMA studies
- 82% Response at Treatment Exit
- 56% Loss of Diagnosis at Treatment Exit
- No significant change in PTSD severity from Treatment Exit, 12+ months later
- Clinically significant gains in symptom relief were sustained (N=91)
- 11 of 91 (12%) relapsed, 9 due to additional stressors



67% of Subjects (N=91) Did Not Meet PTSD Criteria 12+ Months after Active Dose MDMA*

* Includes blinded and open-label crossover
(Pooled Phase 2 results: Jerome et al. 2020)

PLOS ONE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Effects of MDMA-assisted therapy for PTSD on self-experience

Bessel A. van der Kolk, Julie B. Wang, Rachel Yehuda, Leah Bedrosian, Allison R. Coker, Charlotte Harrison, Michael Mithoefer, Berra Yazar-Klosinki, Amy Emerson, Rick Doblin

Published: January 10, 2024 • https://doi.org/10.1371/journal.pone.0295926

Abstract

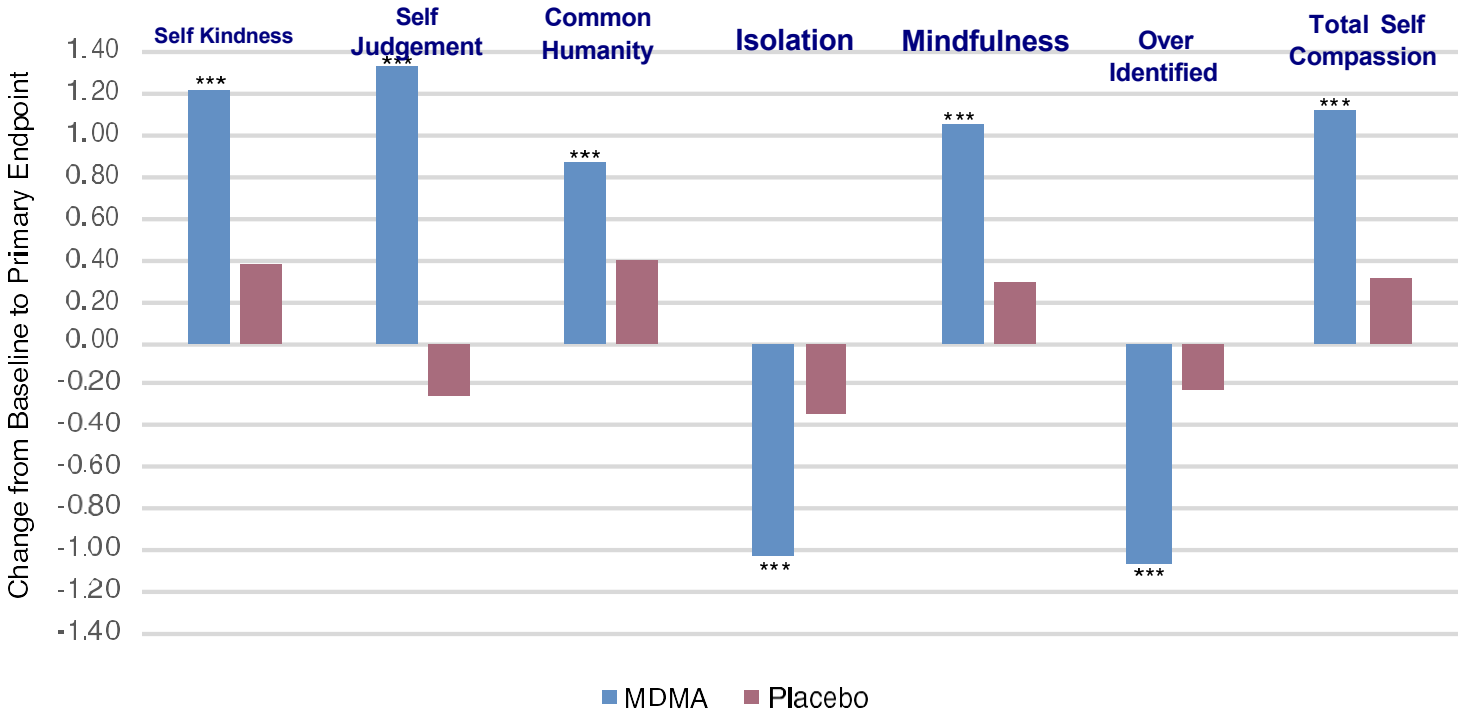
Introduction

There is a resurgence of interest in the therapeutic potential of psychedelic substances such as 3,4-methylenedioxymethamphetamine (MDMA). Primary findings from our randomized, double-blind, placebo-controlled, multi-site Phase 3 clinical trial of participants with severe PTSD (NCT03537014) showed that MDMA-assisted therapy induced significant attenuation in the Clinician-Administered PTSD Scale for DSM-5 compared to Therapy with placebo. Deficits in emotional coping skills and altered self-capacities constitute major obstacles to successful completion of available treatments. The current analysis evaluated the differential effects of MDMA-assisted therapy and Therapy with placebo on 3 transdiagnostic outcome measures and explored the contribution of changes in self-experience to improvement in PTSD scores.

Methods

Participants were randomized to receive manualized therapy with either MDMA or placebo during 3 experimental sessions in combination with 3 preparation and 9 integration therapy visits. Symptoms were measured at baseline and 2 months after the last experimental session using the 20-item Toronto Alexithymia Scale (TAS-20), the 26-item Self Compassion Scale (SCS), and the 63-item Inventory of Altered Self-Capacities (IASC).

Self Compassion Scale (SCS)



*** $p < 0.01$

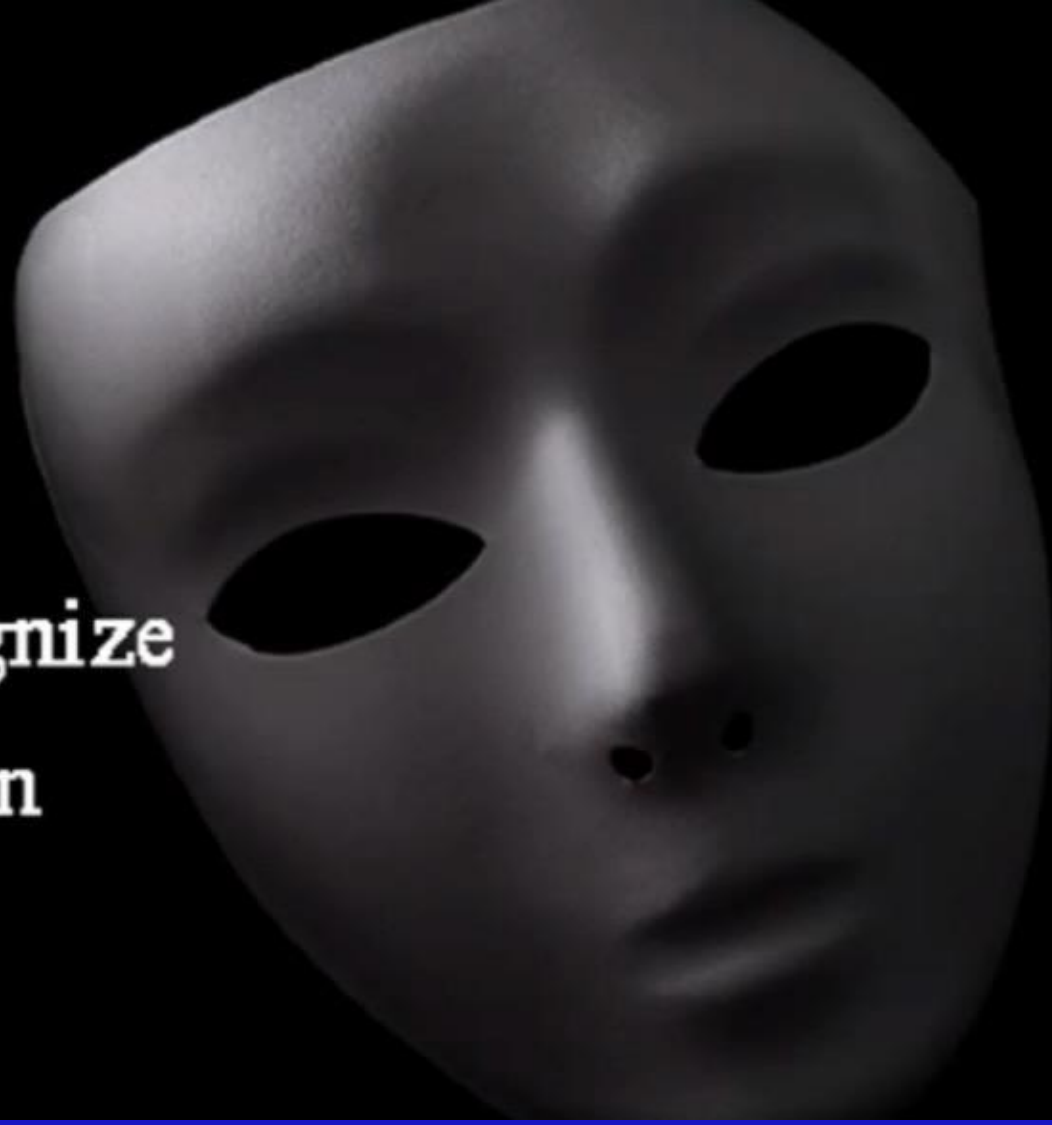
MAPS Public Benefit Corporation

alexithymia

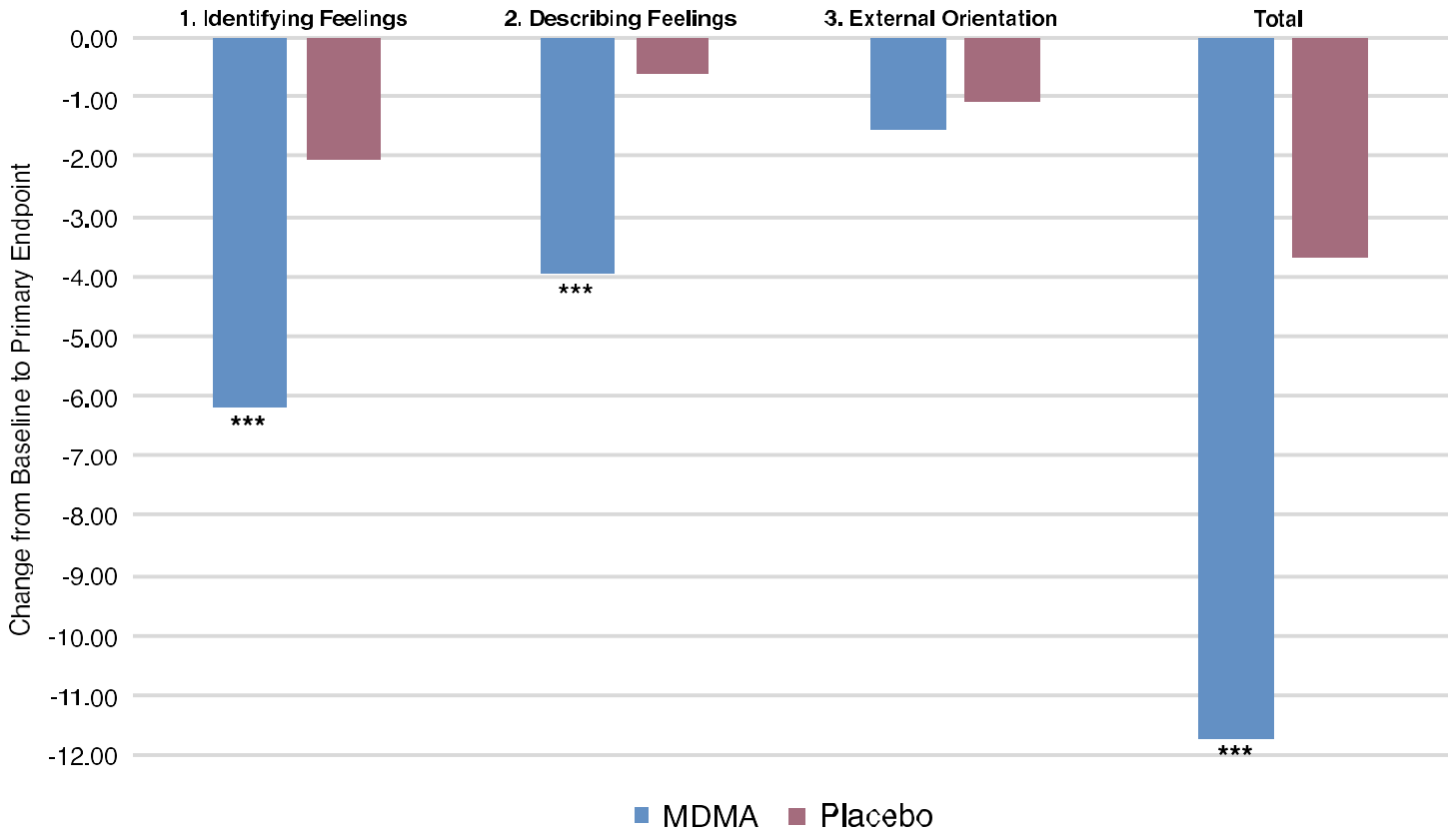
/əˌlɛksɪˈθʌɪmɪə/

noun

the inability to recognize or describe one's own emotions.

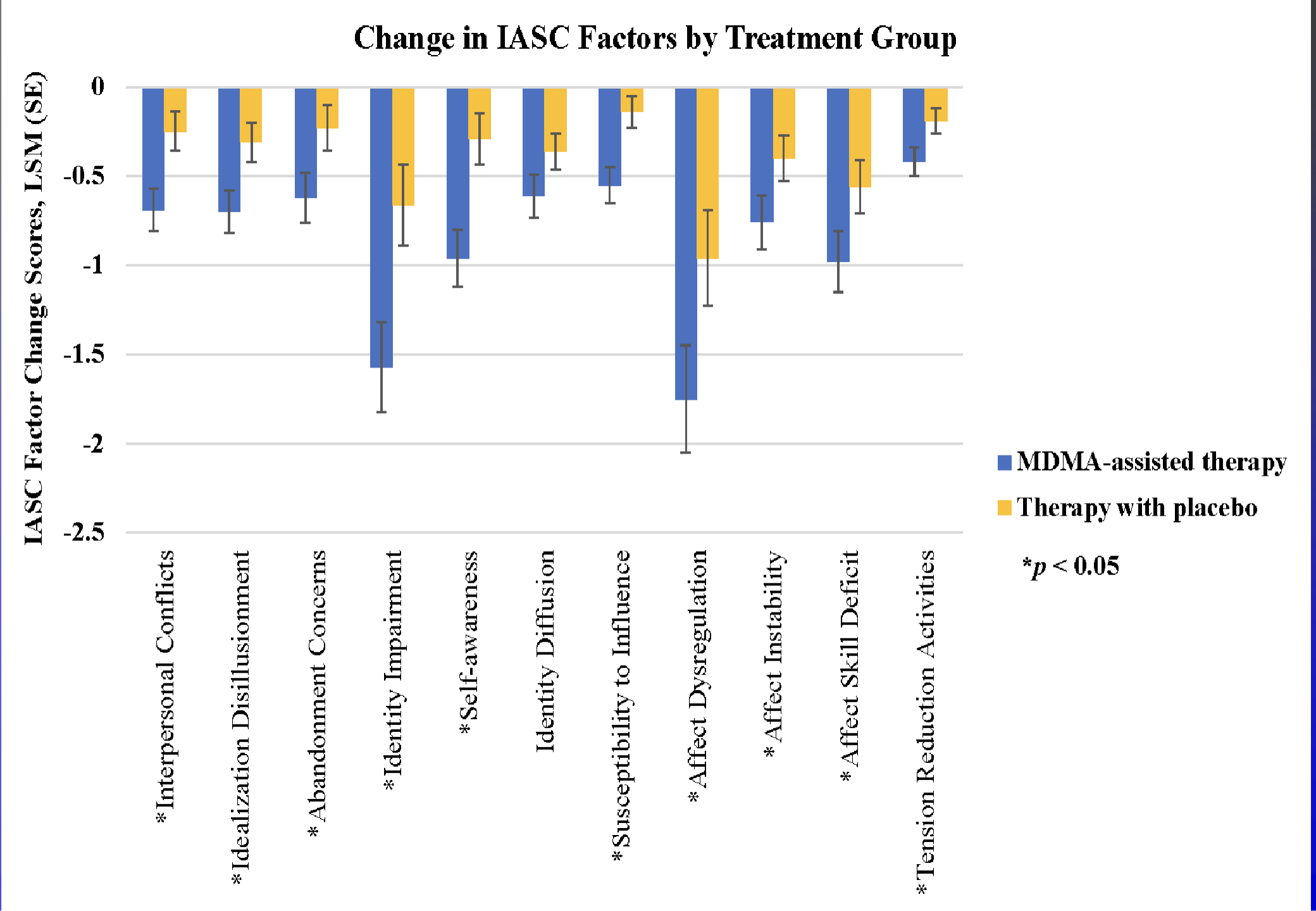


Toronto Alexithymia Scale (TAS-20)



*** $p < 0.01$

MAPS Public Benefit Corporation


Change in IASC Factors by Treatment Group
IASC Factor Change Scores, LSM (SE)
0
-0.5
-1
-1.5
-2
-2.5
*Interpersonal Conflicts
*Idealization Disillusionment
*Abandonment Concerns
*Identity Impairment
*Self-awareness
Identity Diffusion
*Susceptibility to Influence
*Affect Dysregulation
*Affect Instability
*Affect Skill Deficit
*Tension Reduction Activities
MDMA-assisted therapy
Therapy with placebo
*p < 0.05

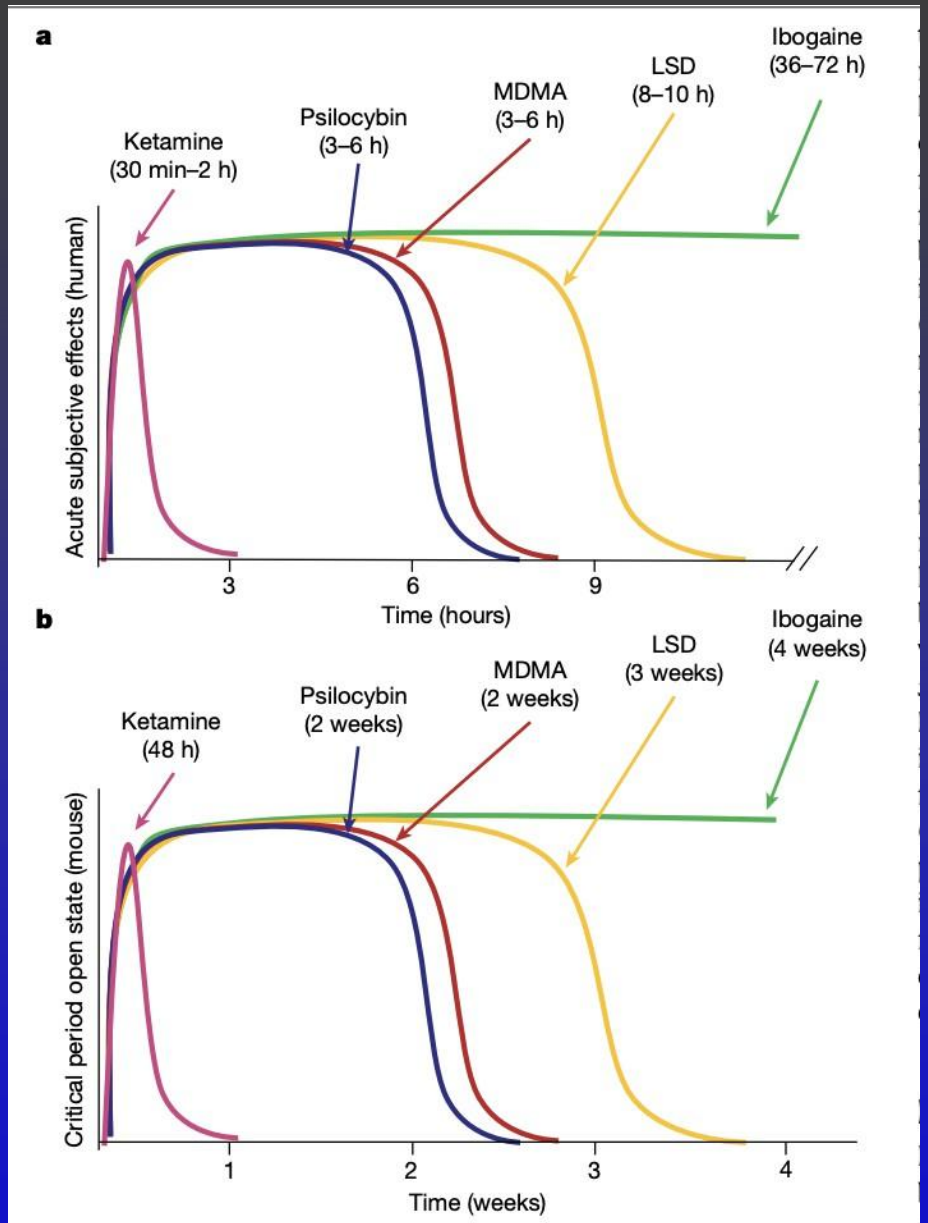


Fig. 3 | The durations of acute subjective effects in humans are proportional to the durations of the critical period open state in mice. a, Durations of the acute subjective effects of psychedelics in humans (data from refs. 15,16,20–22). **b**, Durations of the critical period open state induced by psychedelics in mice. Based on ref. 11 and Figs. 1 and 2 and Extended Data Fig. 5.

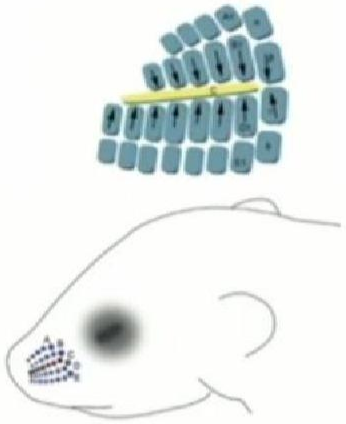
Opening of critical windows of development

Gul Dolen

‘Critical’ or ’Sensitive’ Periods

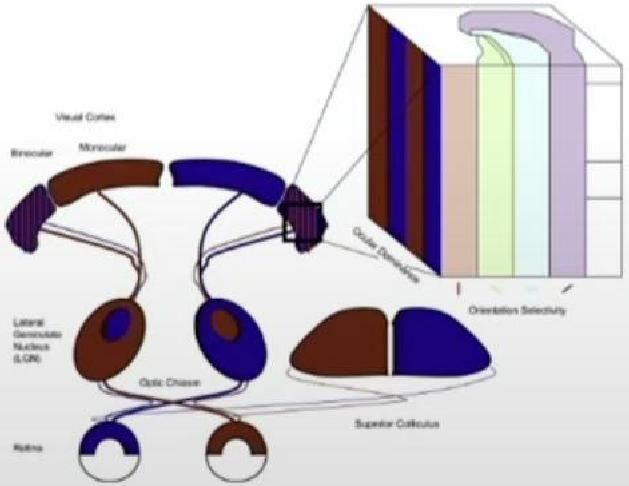
Lorenz, K. *Journal für Ornithologie,* 1935

Woolley, S. and Rubel, E. *J Neuroscience,* 2002



Erzurumlu and Gaspar; EJN, 2012

E. Lenneber; *Biological Foundations of Language*, 1967



Hooks and Chen; *Neuron*, 2007

Dromerick, et al., *PNAS*, 2021

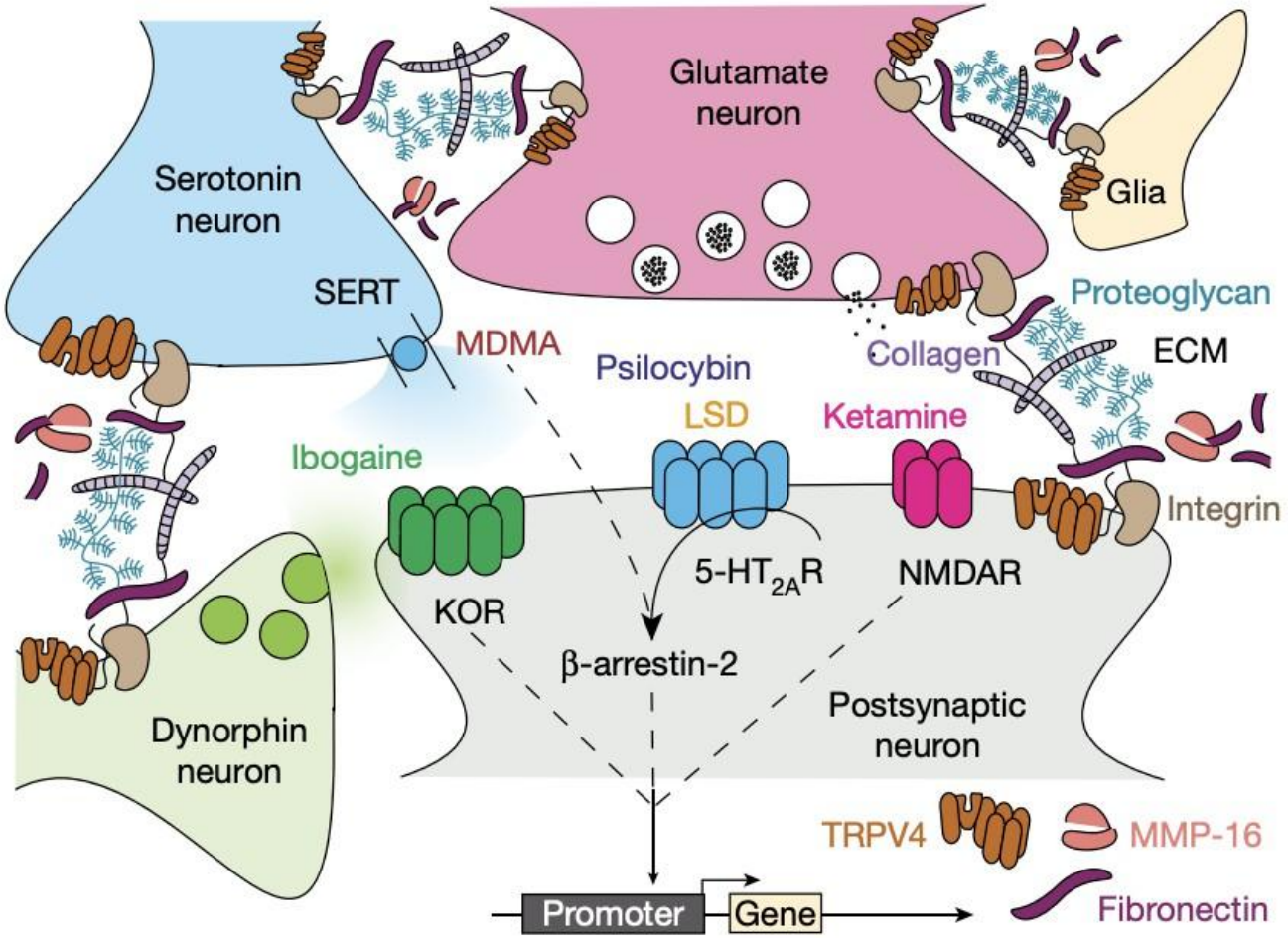


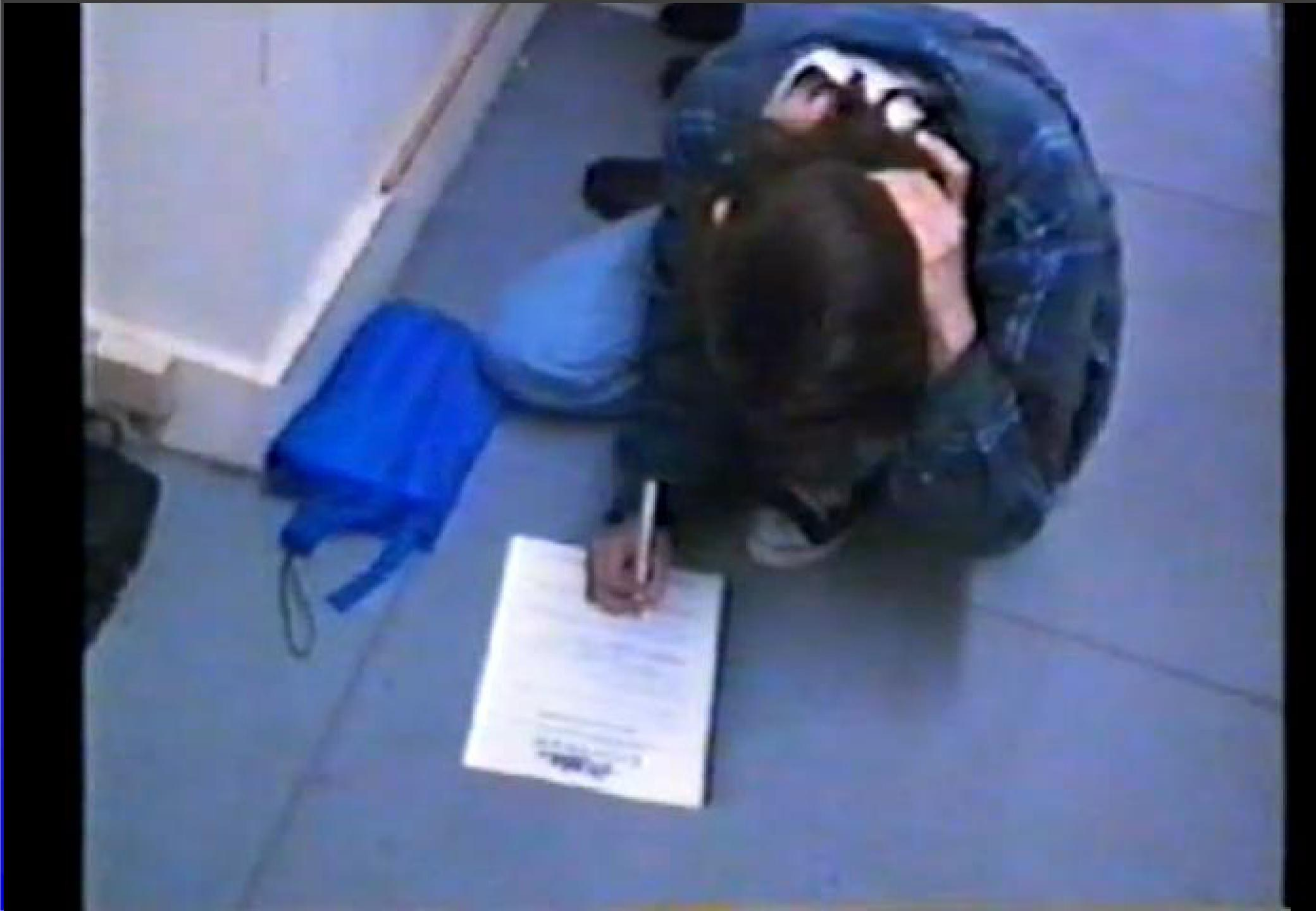
Fig. 6 | Working model of convergent cellular mechanisms of psychedelics. Psychedelics act on a diverse array of principal binding targets and downstream signalling mechanisms that are not limited to the serotonin 2A receptor (Extended Data Fig. 7) or β-arr2 (Extended Data Fig. 9). Instead, mechanistic convergence occurs at the level of DNA transcription (Fig. 5). Dynamically regulated transcripts include components of the extracellular matrix (ECM) such as fibronectin, as well as receptors (such as TRPV4) and proteases (such as MMP-16) implicated in regulating the ECM. Adapted from ref. 25.

"I don't know about you, but I say it's time we started experimenting with drugs."


YEAH, I'VE BEEN TAKIN' ALOTTA DOPE...IT REALLY OPENED THINGS UP FOR ME... GAVE ME A NEW PERSPECTIVE.

Overcoming trauma

1. (re-)establishing community
2. Effective action
3. Dealing with affect regulation
4. Accessing the emotional brain- knowing one's self
5. ***Providing reparative experiences (e.g. psychodrama)***
6. Dealing with parts
7. Processing traumatic memories
8. Re-wiring neural circuits (neurofeedback)




This is your space.
What would you like to work on?

The goal of treatment

.. to strengthen the self: to widen the field of perception and enlarge its organization so it can appropriate fresh portions of "it":

where "it" was, "I" shall come to be.

It is a work of culture - not unlike the draining of the Zuyderzee.

Freud, New Introductory lectures
Vol XXII, p.80, 1932