

In collaborazione con



Ministero dell' Istruzione
Ufficio Scolastico Regionale per la Toscana

Con il sostegno della



"Il cervello emotivo"

Camaiore, 22 Ottobre 2022

A cura di: **Joseph LeDoux**

 FORUM
INTERNAZIONALE
della FORMAZIONE

Quinta Edizione

**LE NUOVE
FRAGILITÀ**

22 - 23 ottobre 2022
CAMAIORE (LU)
Teatro dell'Olivo



Istituto
degli
Innocenti



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Global Crisis in Mental Health

World Health Organization:

“An estimated 12 billion workdays are lost annually due to depression and anxiety costing the global economy nearly US\$ 1 trillion.”

But no matter how much we spend, if we don't understand what we are trying to treat, we will not solve the mental health crisis

The Problem. The *Mental* part of *Mental* Disorders has been marginalized

What Happened to the 'Mental' in Mental Disorders?



THE MODERN SAGA OF 'MENTAL' DISORDERS IS TYPIFIED BY EVENTS IN 1917 AND 2018

“There is no question that the problem of anxiety is a riddle whose solution would be bound to throw a flood of light on our whole **mental existence**.”

Sigmund Freud (1917)

Returning to an emphasis on subjective **mental experience** “would push us back well over a century to what was truly the dark ages of psychiatry.”

Michael Fanselow and Zachary Pennington (2018)

A Very Short and Incomplete Version of the Story (Taschereau-Dumouchel, Lau, Michel, Hoffman, LeDoux, 2022)

Behaviorists banned mental states from psychology in the early 20th Century

The mental approach of psychoanalysis was uninfluenced by behaviorism and thrived in Europe

Before and during WWII Jewish psychoanalysts fled to London and the Americas

A medical model of mental illness (i.e. using medications to treat latent disease states) was adopted to help psychiatry to become more scientific (less Freudian, less subjective). Instead of distancing the field from Freud, subjective experience was marginalized altogether

Some successes resulted from clinical studies of medications, but often from incidental findings. To improve the efficiency of drug discovery, pharmaceutical companies hired behaviorists to test new medicinal treatments in animals. The assumption was that mental states are quaint fictions, and that changing behavior will make any lingering mental problems disappear.

But few novel efficacious agents were discovered. After 50 years of disappointing results, Big Pharma reduced funding to search for new psychiatric treatments

But researchers in universities, equipped with better and better research tools, have persisted in studies using animal behavior to try to discover treatments for mental suffering, assuming the magic bullet is just waiting to be found. It still does not exist and mental suffering continues

Bottom line: People often seek therapy because they feel bad subjectively. If the therapy doesn't help with their subjective symptoms, they will continue to suffer mentally. Drugs based on animal behavior are appropriate for changing behavioral and physiological symptoms, but not for treating troubling mental states

This does not mean Freud was completely right and behaviorists completely wrong. Subjectivity and objective responses both have a role.

THE SCIENCE OF FEAR ILLUSTRATES THE PROBLEM



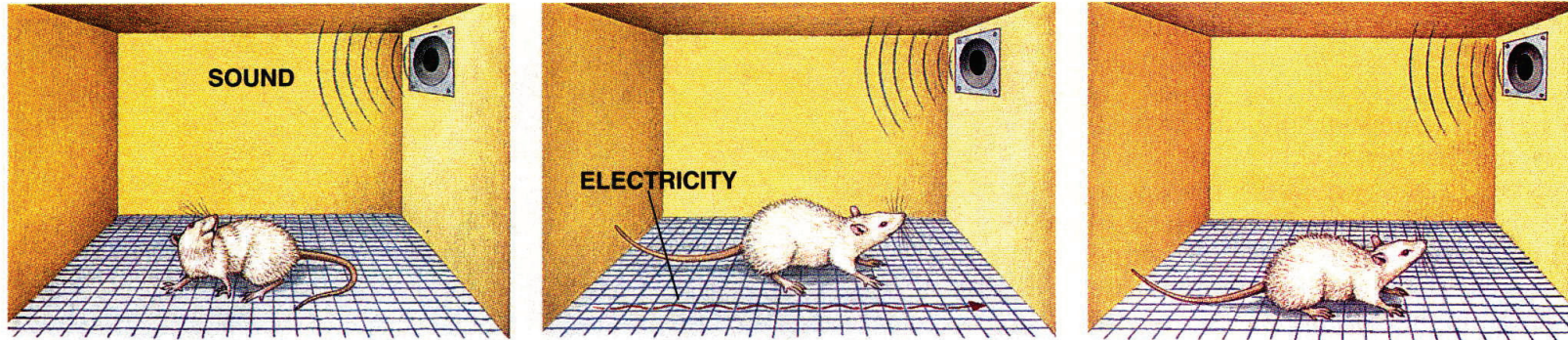
**Why is She Screaming?
“She’s afraid”**



But is her 'fear' the cause of her scream



**I HAVE SPENT MUCH OF MY CAREER STUDYING
PAVLOVIAN FEAR CONDITIONING AS A MODEL OF EMOTIONAL BEHAVIOR**



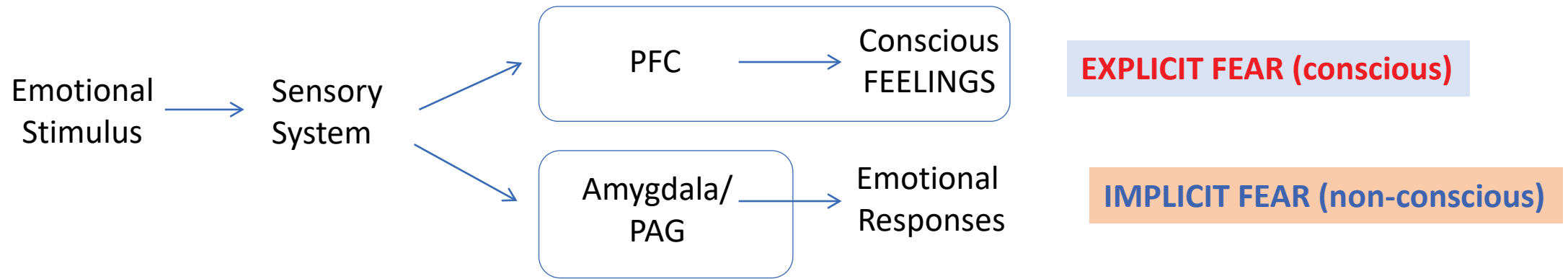
Tone

Tone + Shock

Freezing

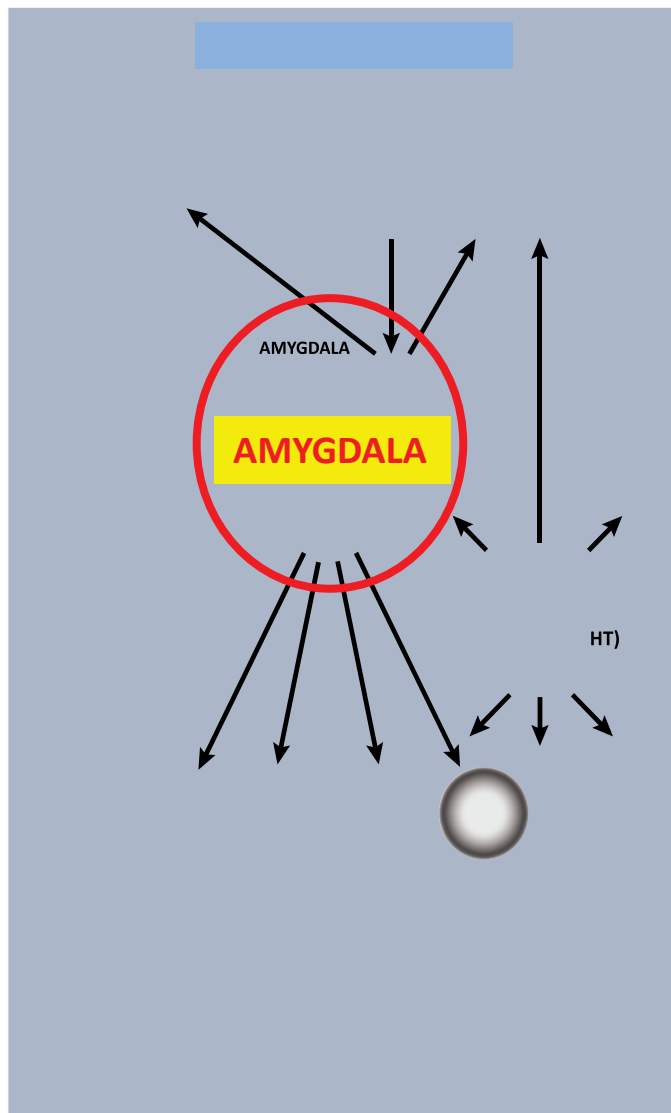
**A simple stimulus and a reliable, stereotyped response seemed
Ideal for tracing circuits from sensory to motor neurons**

FEAR = Cognitive/HO Interpretation



Freezing = Innate Emotional Behavior

**THROUGH STUDIES OF BEHAVIORAL
AND PHYSIOLOGICAL RESPONSES
ELICITED BY THREATS**



**Implicit vs Explicit distinction did not
catch on in emotion research the way
it did in memory**

fear was "FEAR"



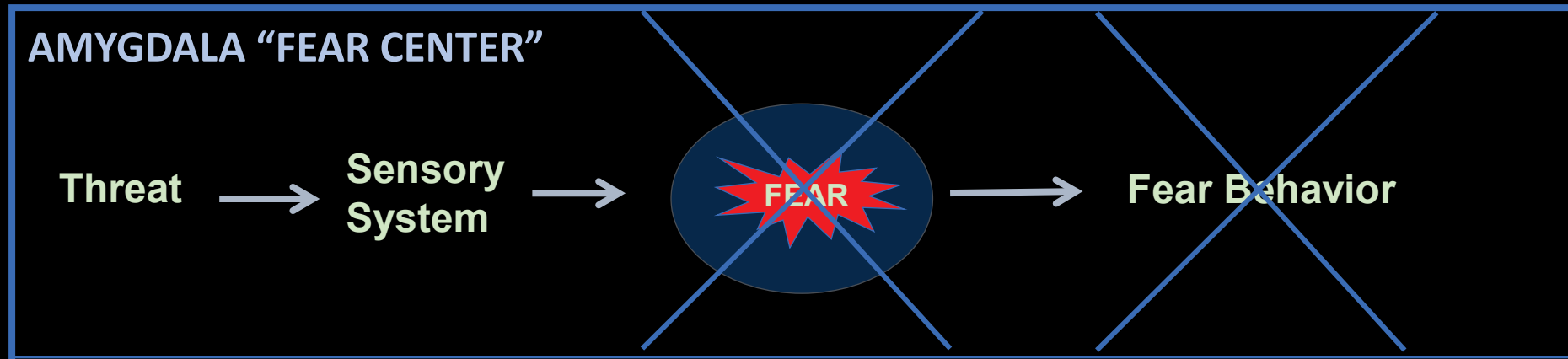
**The Amygdala Became a
FEAR CENTER**

What's Wrong With the Amygdala Fear Center Idea?

1. Behavioral and physiological responses do not always correlate strongly with subjectively experienced fear; they should if they are all products of fear in the amygdala.
2. Non-consciously processed threats elicit both amygdala activity and behavioral and physiological responses in the absence of subjective awareness of the stimulus and without any feeling of fear (masking; blindsight)
3. Damage to the amygdala interferes with the ability of threats to elicit behavioral and physiological responses but does not *necessarily* eliminate feelings of fear.

Rethinking the Emotional Brain

Joseph LeDoux^{1,2,*}



WHY DOES IT MATTER WHAT WE CALL THINGS

Francis Bacon (1620) Scientists should be vigilant and guard against tacitly granting reality to things simply because we have words for them.

George Mandler and William Kessen (1964) The common language is full of quasi-psychological assertions, and the language in which these are framed is inadequate

Jack Block (1995) Psychologists have tended to be sloppy with words. Summary labels and short hand ideas come to control the way we think

Melvin Marx (1951) There is a semantic danger that results when a common language term is used as a scientific name for an intervening variable or hypothetical construct... the variable or construct becomes infected with the subjective properties of the common meaning

Psychology and Neuroscience Have Unique Conceptual/Linguistic Challenges

Biologists call a family of genes 'hedgehog' because of the spiky features of the gene. No one in biology believes the gene has anything to do with the animal called hedgehog.

But when psychologists use a word like fear the assumption is that the subject matter is our everyday experiences of fear when in danger.

PRACTICAL EXAMPLE OF WHY WORDS MATTER

Anxiolytic Drug Development

Tests of defensive behavior in animals are assumed to measure a **brain state of fear or anxiety**

Drugs that alter defensive behavior are assumed to change the **brain state** by targeting a fear/anxiety brain circuit

Because humans have inherited this circuit from mammalian ancestors, giving the the drug to humans should change this brain state and make people feel less fearful or anxious

In 2010 Andrew Witty, CEO of GSK, concluded the effort has failed and new investments would not be made because of the low probability of success.

Andrew Holmes, a leading researcher, reached a similar conclusion: “these efforts have been disappointing, as promising results with novel agents in rodent studies have very rarely translated into effectiveness in humans”.

Eric Nestler and Steven Hyman, leading psychiatrists, echoed this sentiment, noting that the molecular targets of current major classes of psychotherapeutics were all reverse engineered in animal studies from drugs discovered incidentally prior to 1960 by clinical observation. Hence, nothing new has been discovered because the same thing has been searched for over and over.

Yet, the effort continues because of a commitment to poorly conceived constructs, both psychologically and psychiatrically.

Psychologically: mental states of fear can be measured by innate or conditioned behaviors in animals and people

Psychiatrically: pathological fear is product of a malfunctioning genetically wired fear circuit, and that delivery of the right chemical to this fear circuit will fix the problem, as measured by innate (freezing, fleeing) or conditioned (avoidance) behavioral responses

TWO MEDICATION SCENARIOS IN SOCIAL ANXIETY

Fear/anxiety scenario

- the medication will turn off your fear center.
- you will be able to go to the party and not feel afraid or anxious.

**This is what everyone hopes will happen:
It's an anti-anxiety drug and will reduce fear and anxiety**

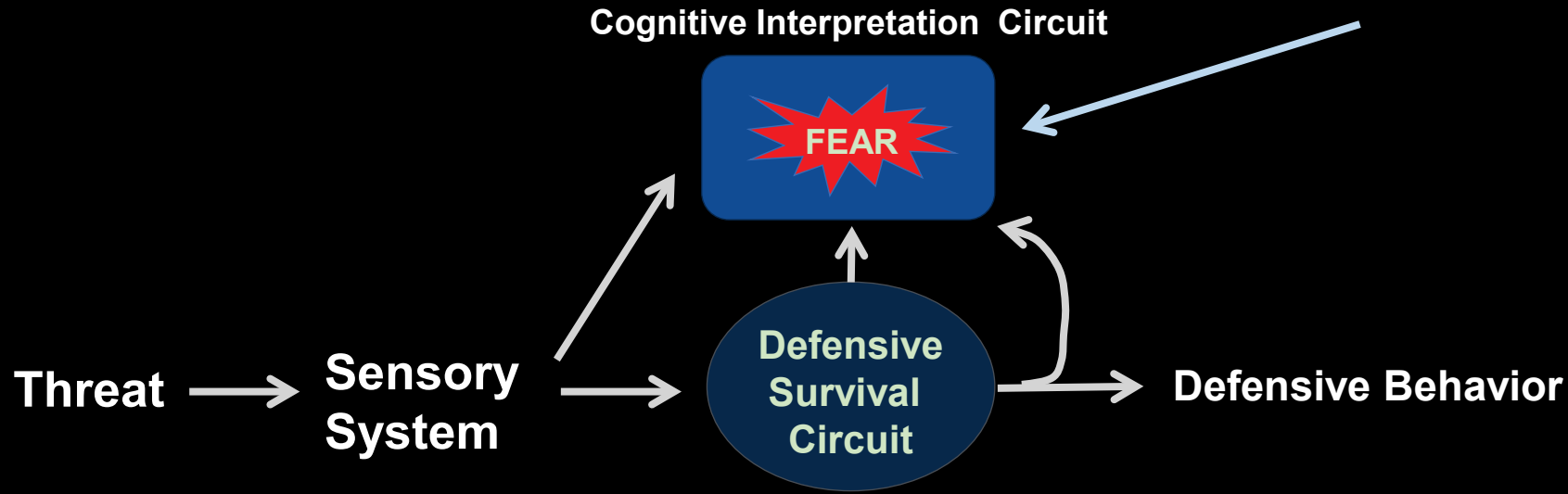
Physiological symptom scenario

- the medication affects systems that control behavioral and physiological responses in challenging situations.
- you will find it easier to go to the party (be less avoidant) and will feel less jittery (less aroused).
- while you will probably still feel anxious, you will be better able to cope with the threatening situation and can use it as a way to become physically more comfortable being there.
- this is not a cure but it might help you cope with your symptoms.

**This is what the animal research predicts:
The drug reduces behavioral inhibition (timidity) and/or hyper-arousal**

Here they are inappropriate

But if people experience fear here, it's not surprising that the drugs are not more effective for mental problems



Behaviorist accounts work just fine here

Drugs developed in animal studies are designed to work here to change behavior

We need a conception of fear and anxiety that recognizes the importance of innate conditions circuits which have been Inherited from animals

But one that does not confuse those circuits with circuits that underlie conscious feelings of fear or anxiety

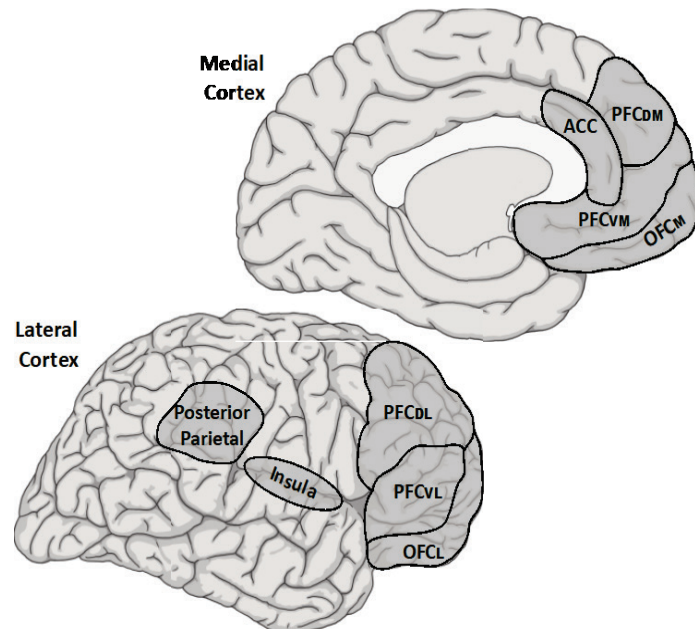
EMOTIONAL CONSCIOUSNESS



HYPOTHESIS

The brain mechanisms underlying emotional states of consciousness are not different from those underlying other states of awareness

Cortical Higher-Order Networks (fronto-parietal circuits)



What's different about

- *emotional vs. non-emotional experiences
- *different kinds of emotional experiences

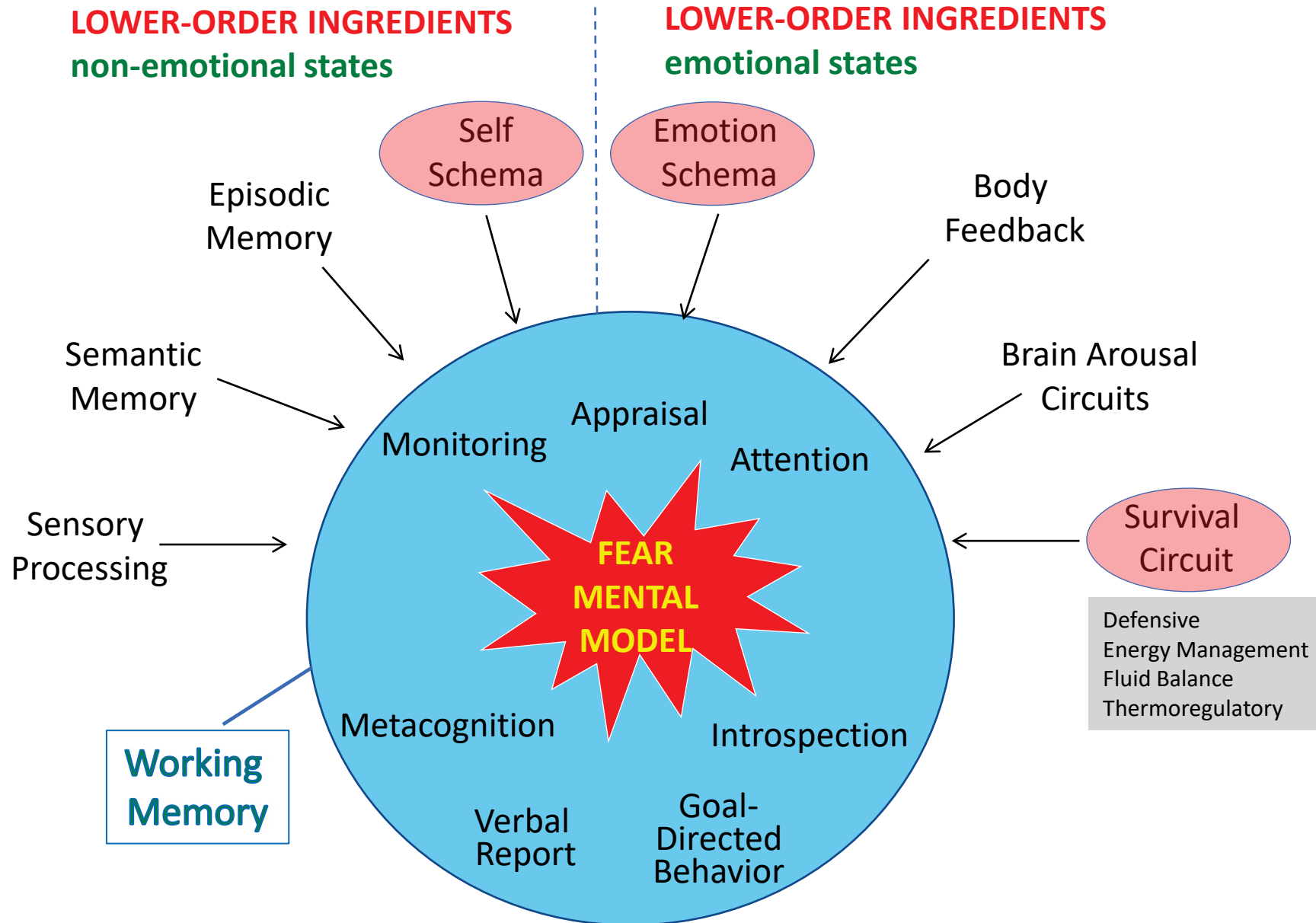
Inputs Processed by a Cortical Higher-Order Cognitive Network

Rather than having different subcortical circuits for different emotions (basic emotions theory)

Higher-order cortical cognitive representations/ redescriptions/indexes can account for emotional and non-emotional experiences in one system

The information processed by the higher-order circuit is different in emotional than in non-emotional situations, and in different kinds of emotional situations

Inputs to Higher Order Network that Contribute to the Conscious Experience of Fear



WHAT IS AN EMOTION?

a mental model-based, narrative-driven, culturally shaped, subjective experience in a biologically or psychologically significant situation

Danger
(not Fear)
is universal.

All humans must deal with danger, and all cultures have words for danger and words for experiences that occur when in danger. But emotional experience varies across cultures.

Because we can translate words like fear across some cultures, we assume people in these cultures have the same basic experience named by the word.

Cultural differences in experience are based on differences in the schema involved. That is, schema are personal so that different people within a culture have different schema and hence different experiences, and people in different cultures also have different schema and experiences

Other animals, lacking our specific kind of cognition and brain can't have our kind of schema and our kind of fear. But they may have their own emotions made possible by their own brains

She Screaming and She's Afraid

But these are not the same



WHAT HAPPENED BETWEEN 1917 and 2018?

**In the effort to put Freud in the rearview mirror,
Psychology, psychiatry, and brain science,
threw the mental baby out with the bathwater.**

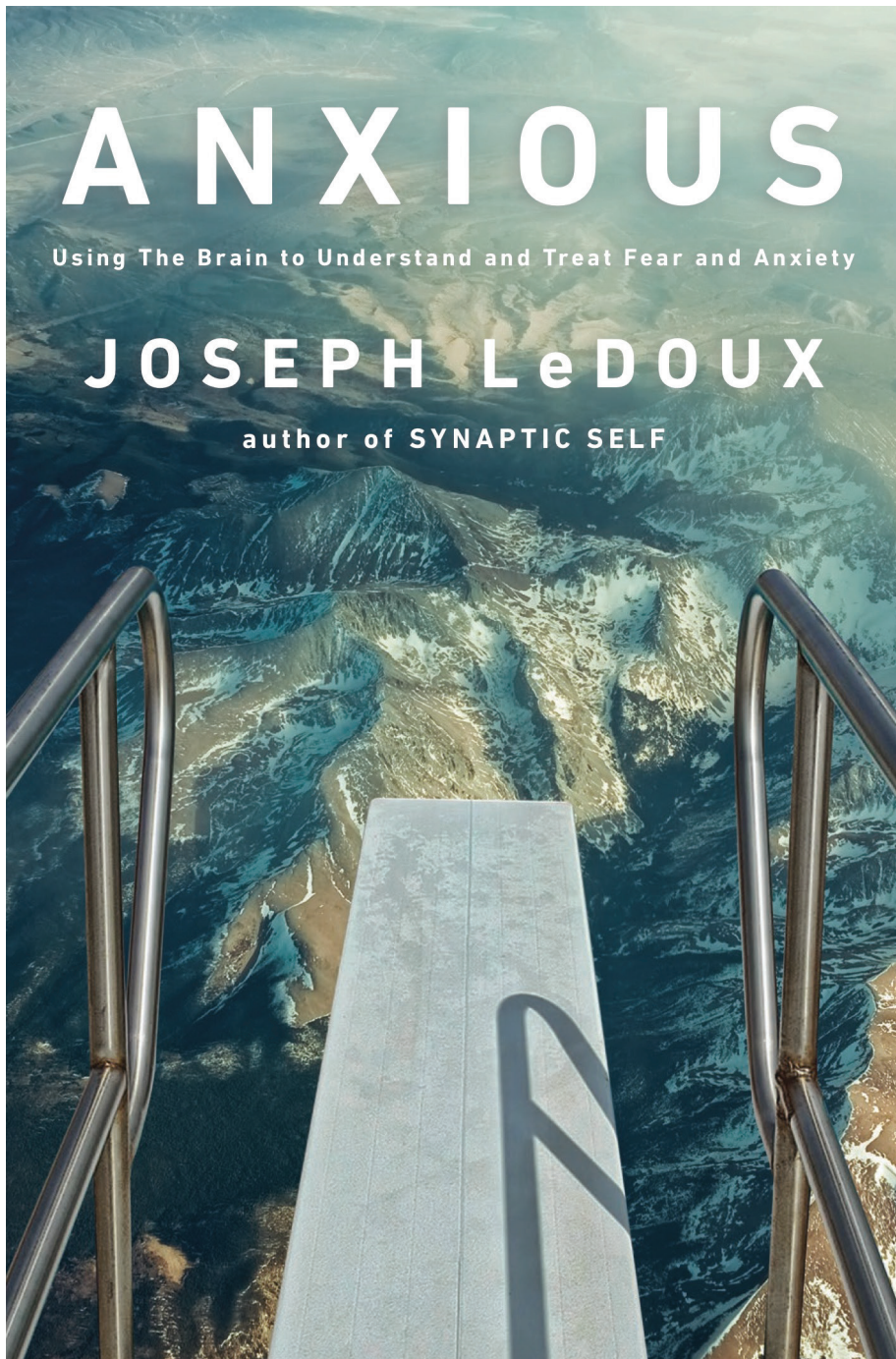
**Until we accept that emotions are first and
foremost mental states, efforts to treat
mental disorders will languish, and
patients, therapists, pharmaceutical
companies, and researchers will
all continue to be disappointed**

ANXIOUS

Using The Brain to Understand and Treat Fear and Anxiety

JOSEPH LeDOUX

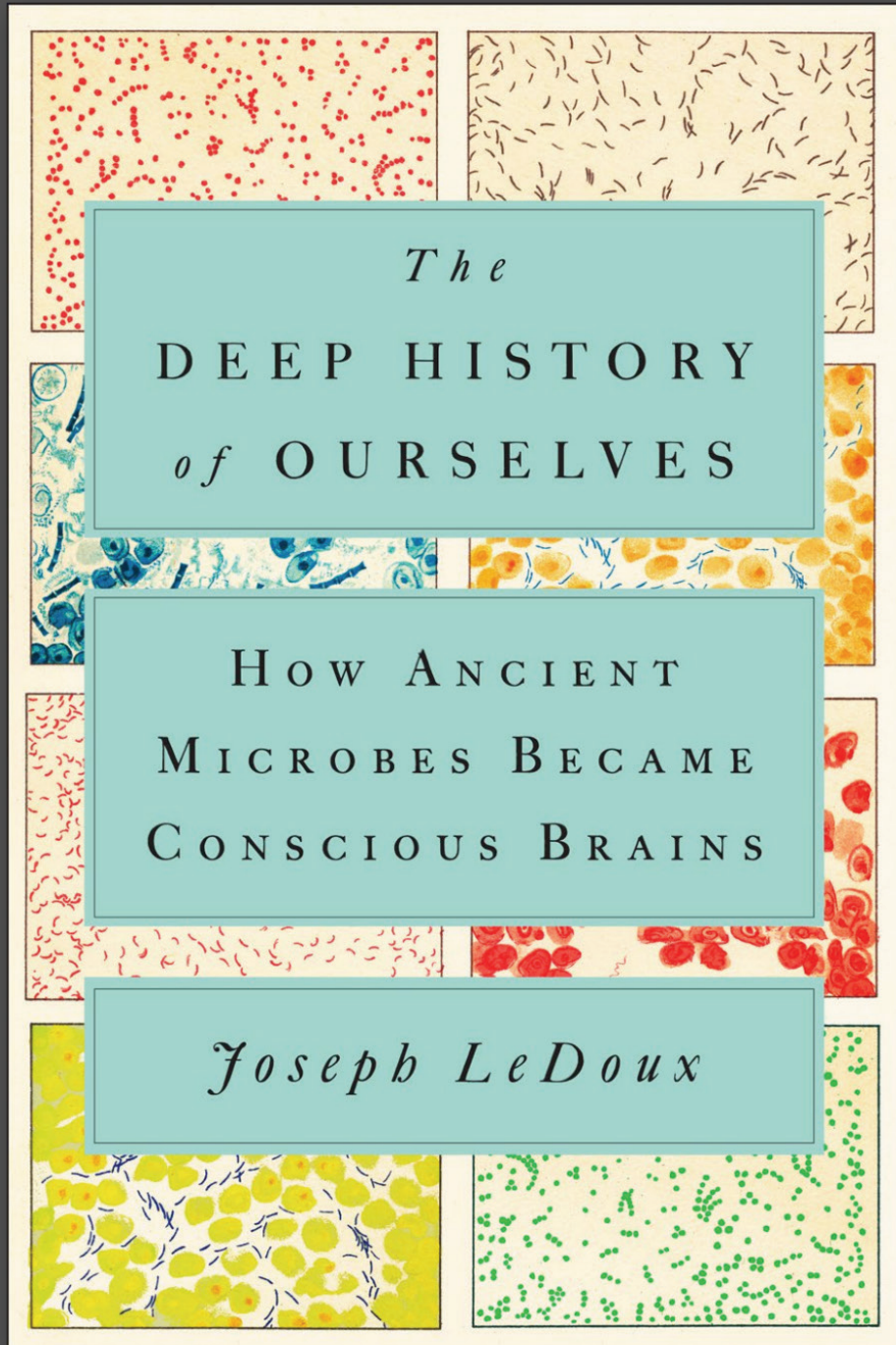
author of SYNAPTIC SELF



The
DEEP HISTORY
of OURSELVES

HOW ANCIENT
MICROBES BECAME
CONSCIOUS BRAINS

Joseph LeDoux





Thank You

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