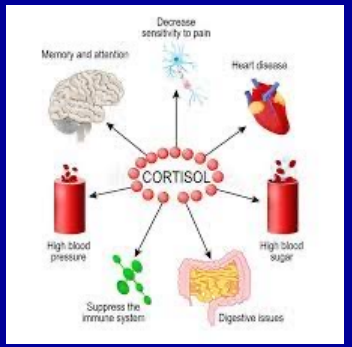
PNEI i eksposom

Vida Demarin
Croatian Academy of Sciences and Arts

PNEI

- presents the new concept of the impact of stress on health by emphasizing the closeness between the psyche, brain, and body systems,thus
- being the basis of a new discipline Psychoneuroendocrinoimmunology (PNEI).

- Demarin V, Toljan S et al 2020.

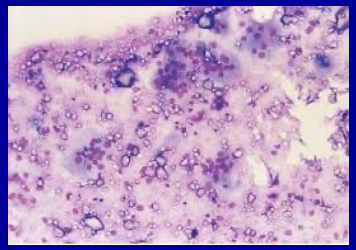
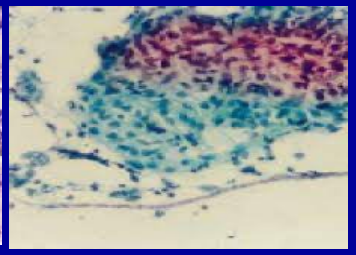
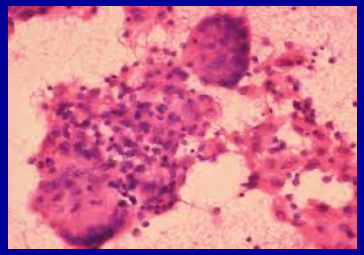
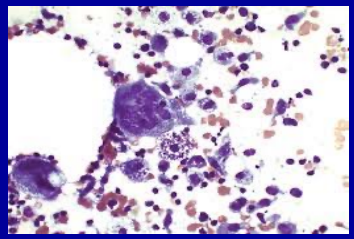
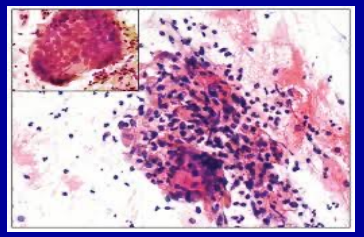


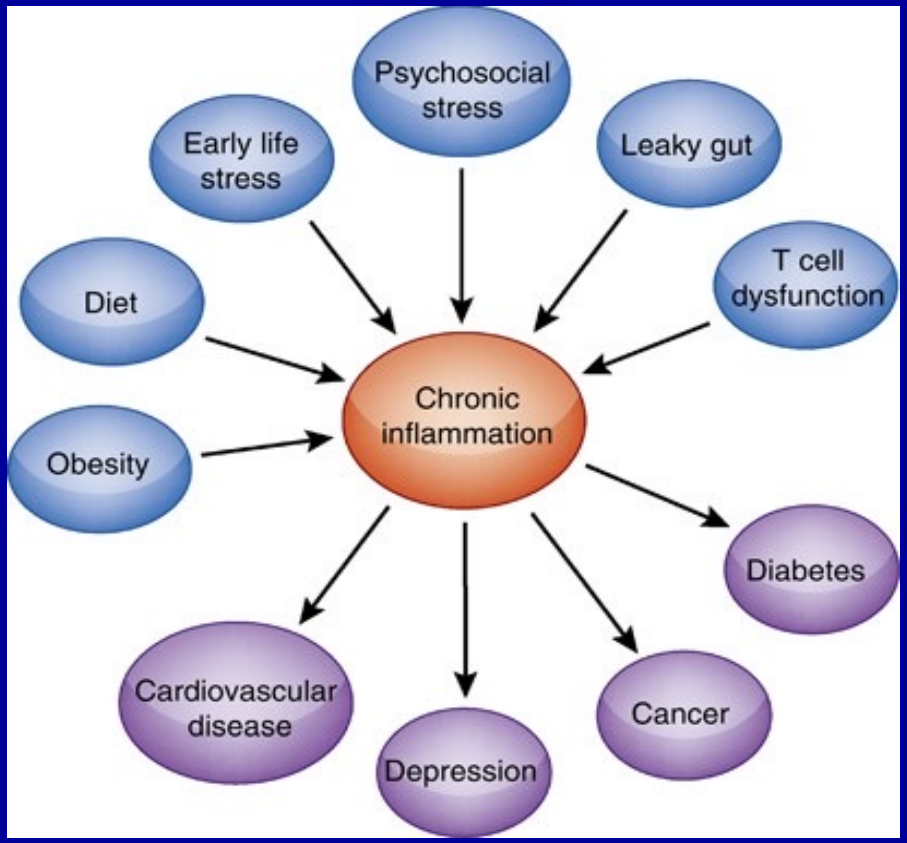
PNEI, which was first described in 1936, is the study of the interactions between the psyche, neural and endocrine functions and immune responses.

- The aim of PNEI is to apply medical knowledge to the treatment of different allergic, immune, autoimmune, rheumatic, endocrine, cardiovascular, neurologic and dental pathologies, among other disorders.

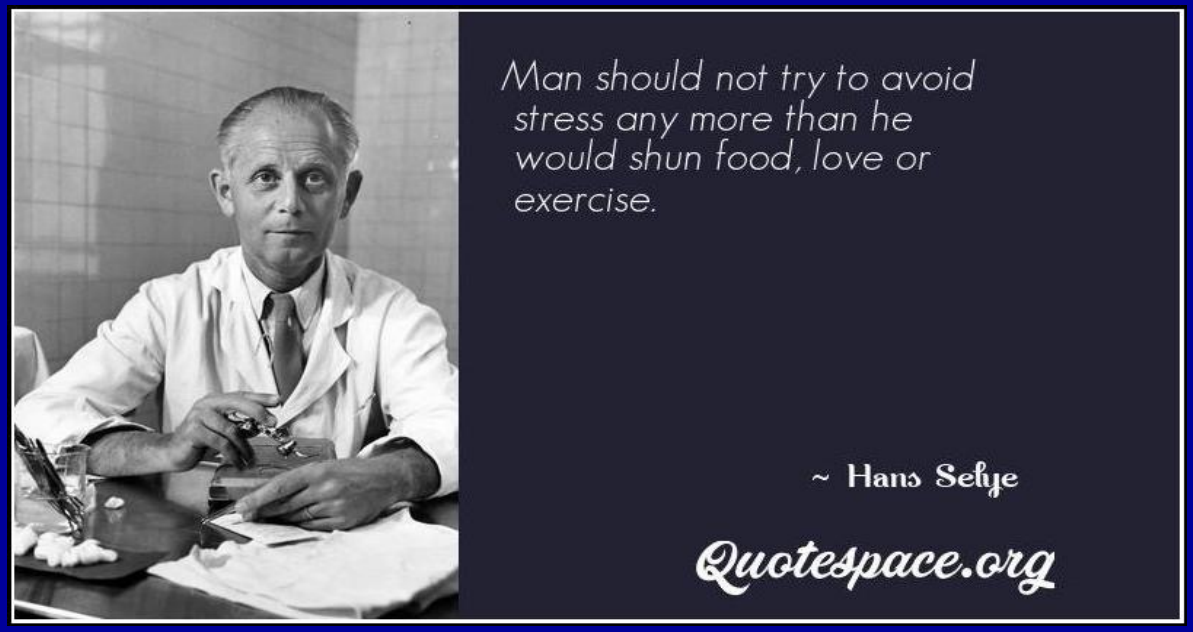
- Epigenetic factors and major stresses from different types of stimuli acting through distinct pathways and neurotransmitters are highly involved in altering the PNEI axis, resulting in the emergence of disease.

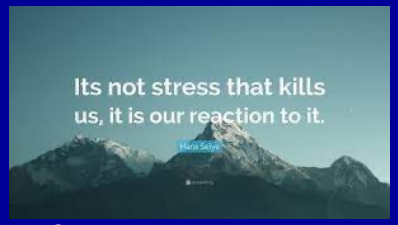
- Bottacioli F, Bottacioli A, 2018.

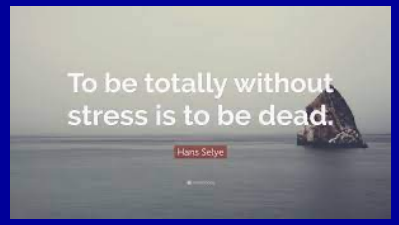







Psychosocial stress
Early life stress
Leaky gut
Diet
T cell dysfunction
Chronic inflammation
Obesity
Diabetes
Cardiovascular disease
Depression
Cancer

Vienna 1907- Montreal 1982







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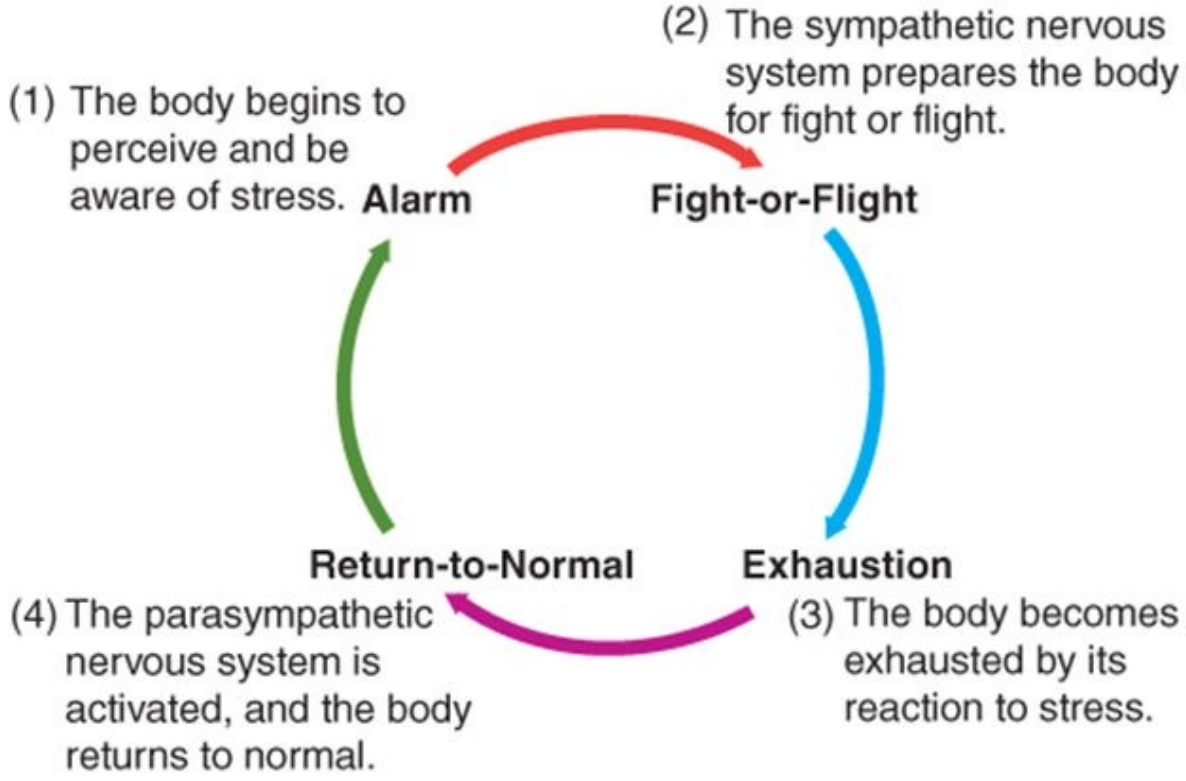
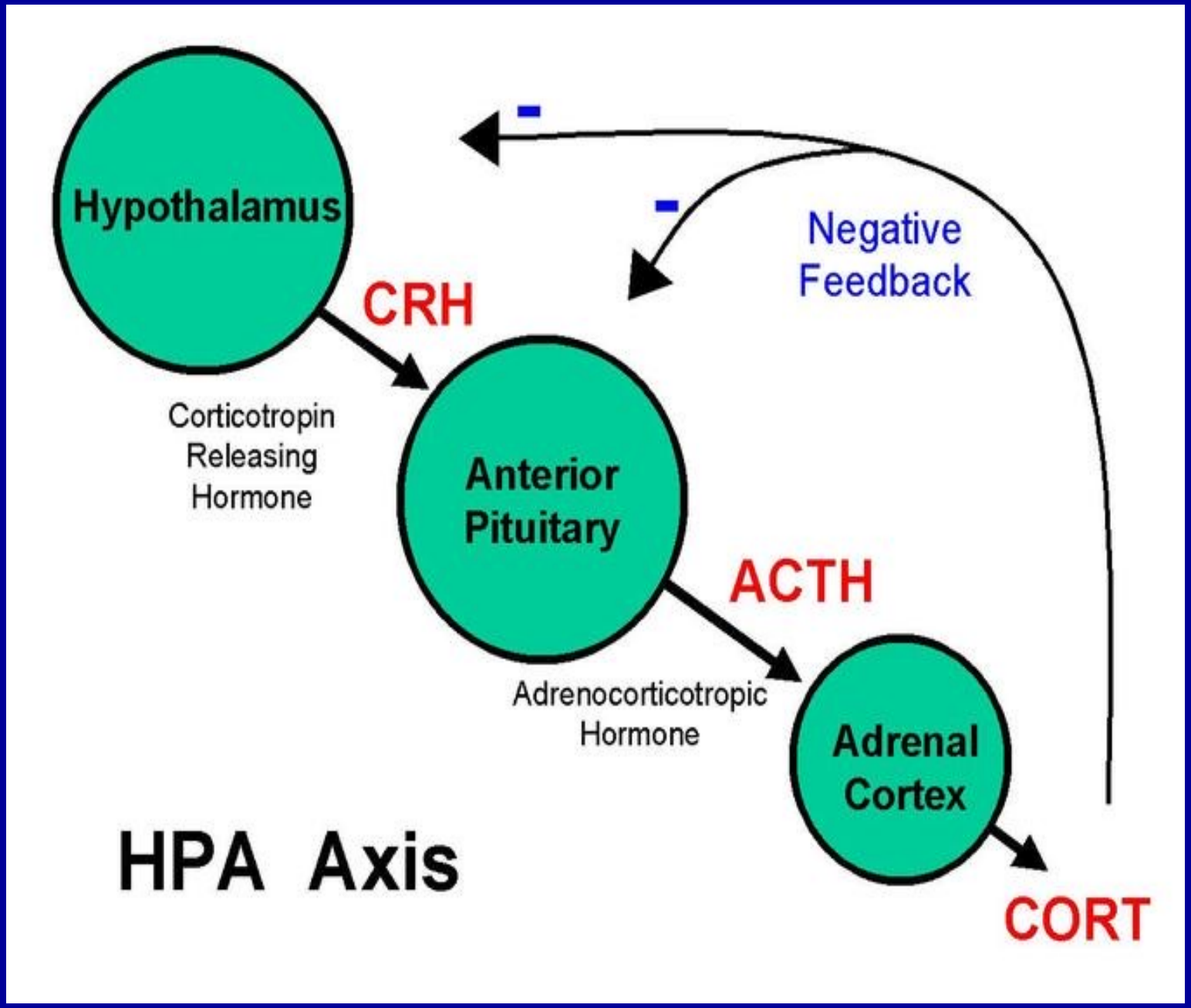
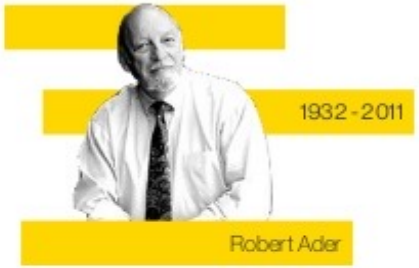
Adaptation to Stress



^^ Hans Selye's General Adaptation Syndrome (GAS) theory proposes that four stages are involved in adapting to stress.


Hypothalamus
CRH
Corticotropin
Releasing
Hormone
Anterior
Pituitary
ACTH
Adrenocorticotropic
Hormone
Adrenal
Cortex
CORT
Negative
Feedback
HPA Axis

Robert Ader 1932 - 2011 **PNI**

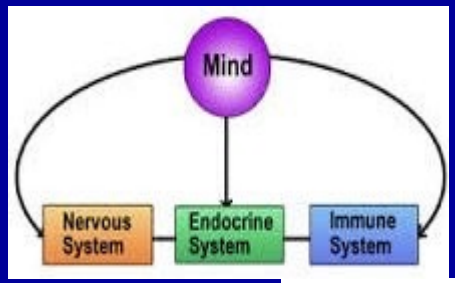


director of the division of behavioral and psychosocial medicine at New York's University of Rochester

History

▶▶▶ term of PNI - 1975

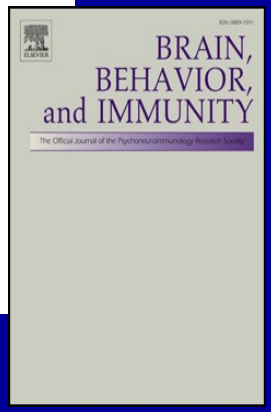
There is a **link** between what we think (our state of mind) and our health and our ability to heal ourselves.
It is possible that a state of mind or emotional state to **affect the immune response** that the system is responsible to keep the human body healthy.



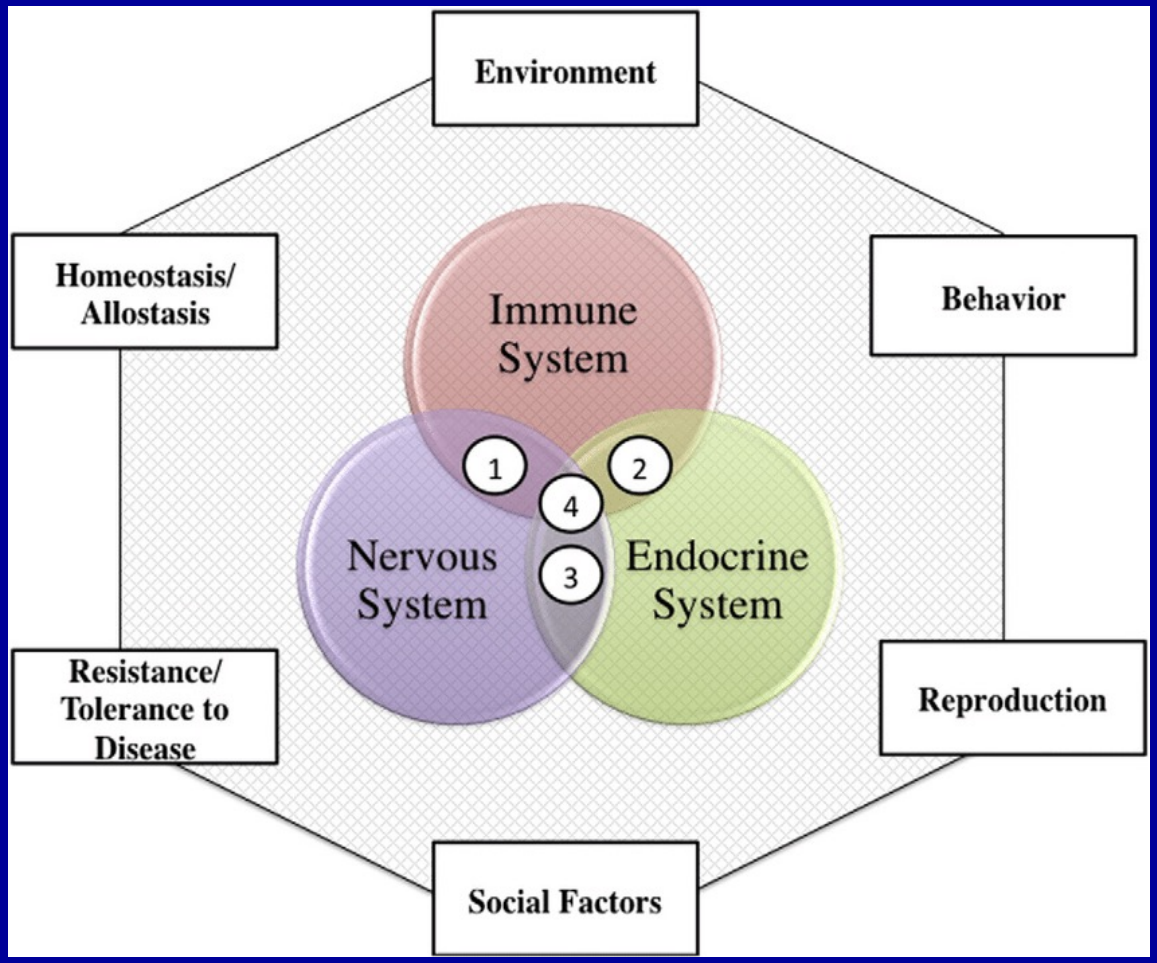
Introduction

- **Psychoneuroimmunology** (**PNI**), also called **psychoendoneuroimmunology** (**PENI**), deals with the study of the interaction between psychological processes and the nervous and immune systems of the human body.

- Until 1970, it was thought among the modern Western medical community that immune system function without any influence from any other parts or functions of body
- .
- **Dr. Robert Ader in 1975** coined the term **Pyschoneuroimmunology** to show that there exists a link between the way people think and about their health.

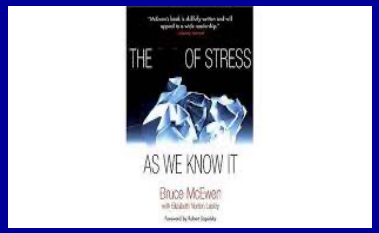


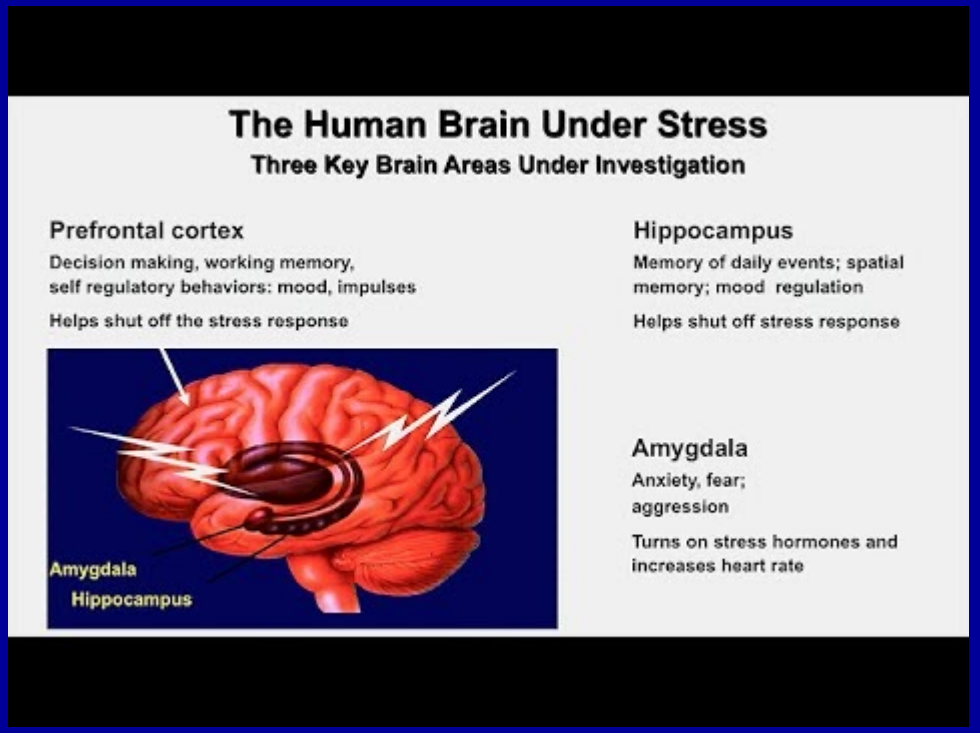
Such cross-talk among systems is dependent upon feedback loops working to maintain homeostatic equilibrium.



Bruce Mc Ewen 1938-2020

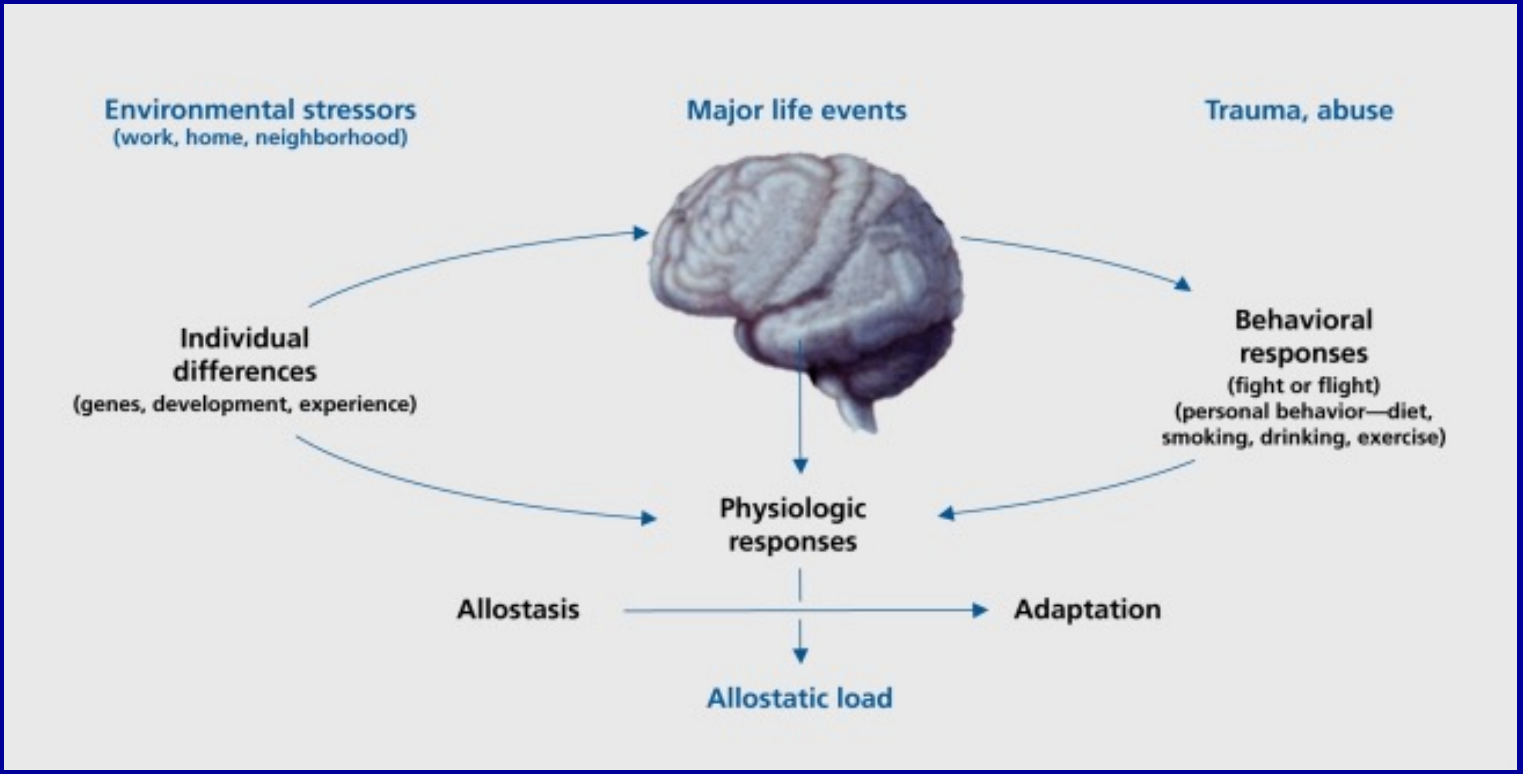
- cortisol – hypocampal structure changes- allostasis –allostatic load



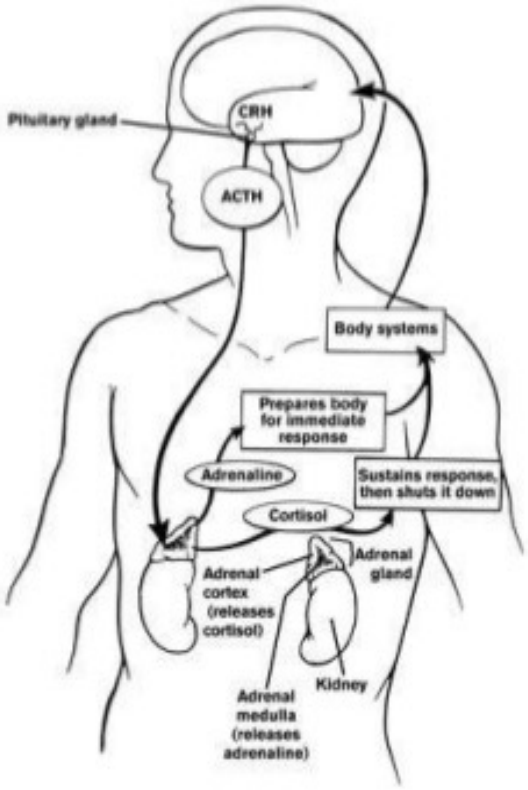


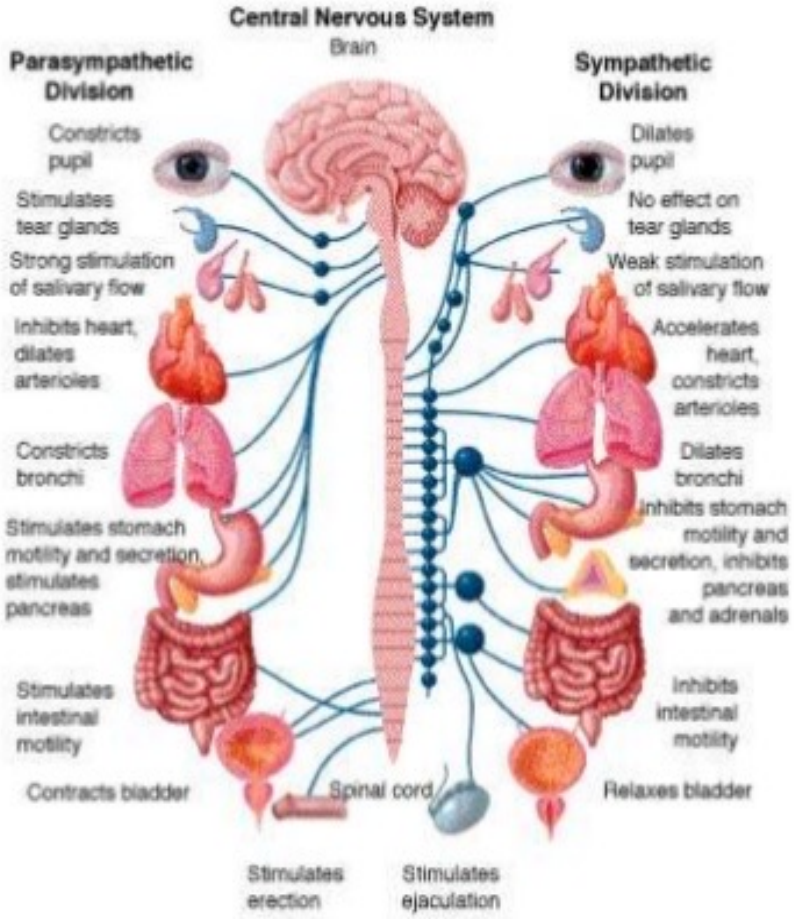
Allostasis and the Epigenetics of Brain and Body Health Over the Life Course
The Brain on Stress, JAMA Bruce McEwen,2017.

- Allostasis means achieving stability through change – to maintain the homeostasis, recognizing that “set points” and other bounderies of control may change with environmental condition



Psycho-physiology - Stress





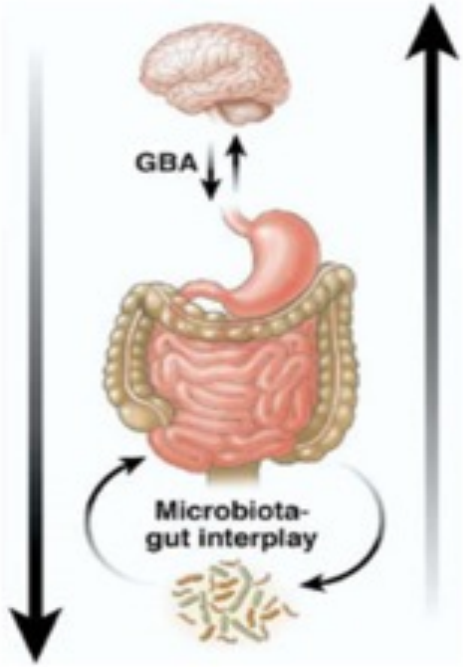
The Bidirectional Gut-Brain Axis

The ability of the brain to influence the intestinal microbiota

Perturbation of your normal habitat via stress-induced changes in gastrointestinal:

- Physiology
- Epithelial function
- Mucin production
- EE cell function
- Motility

Release of Neurotransmitters



The ability of the microbiota to influence brain, behavior, and mood

Activation of neural pathways to the brain

Activation of musosal immune responses

Production of metabolites that directly affect the CNS

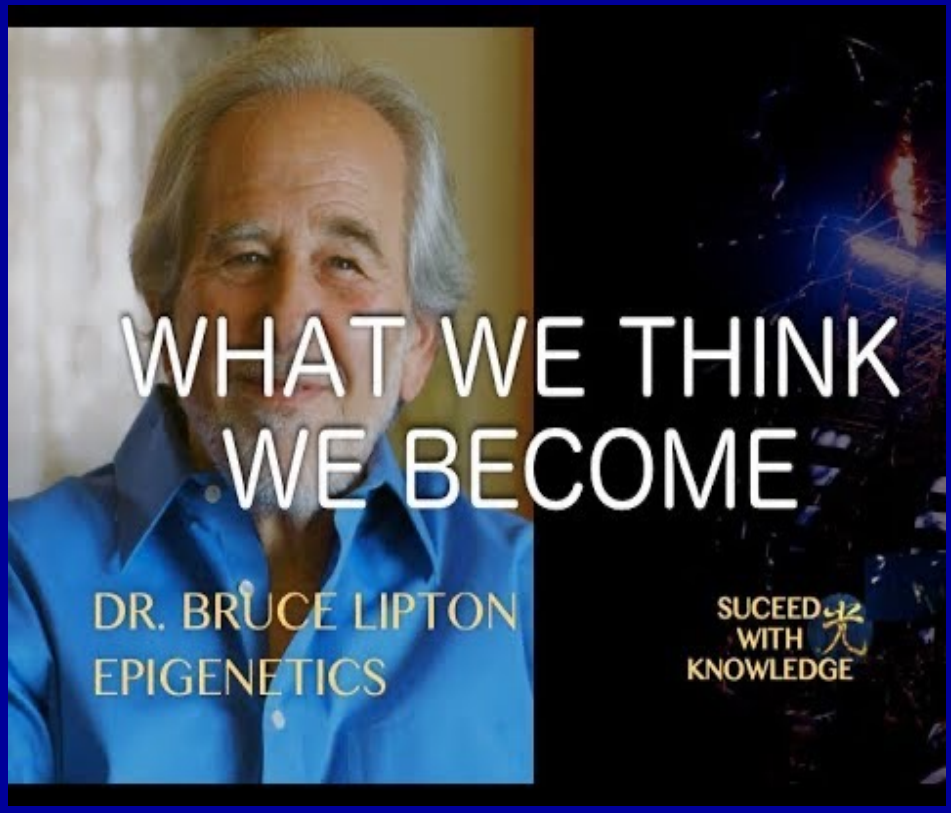
Grenham S, Clarke G, Cryan JF, Dinan TG. Brain-gut-microbe communication in health and disease. Front Physiol. 2011;2:94. Epub 2011 Dec 7. PubMed PMID: 22162969; PubMed Central PMCID: PMC3232439

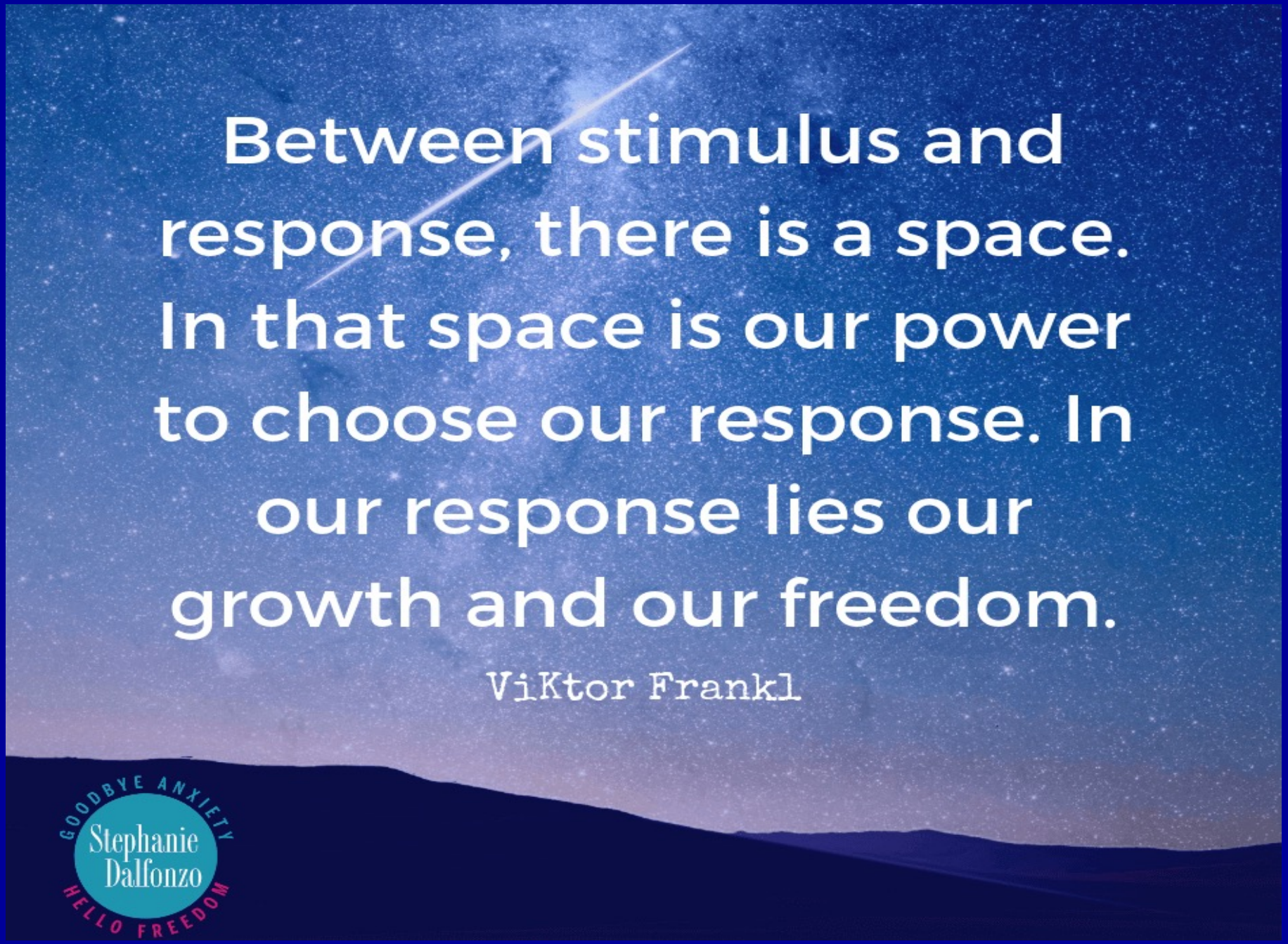
Francesco Bottacioli

Bruce Lipton, PhD: The Jump From Cell Culture to Consciousness

C.Gustafson,Integr.med.2017

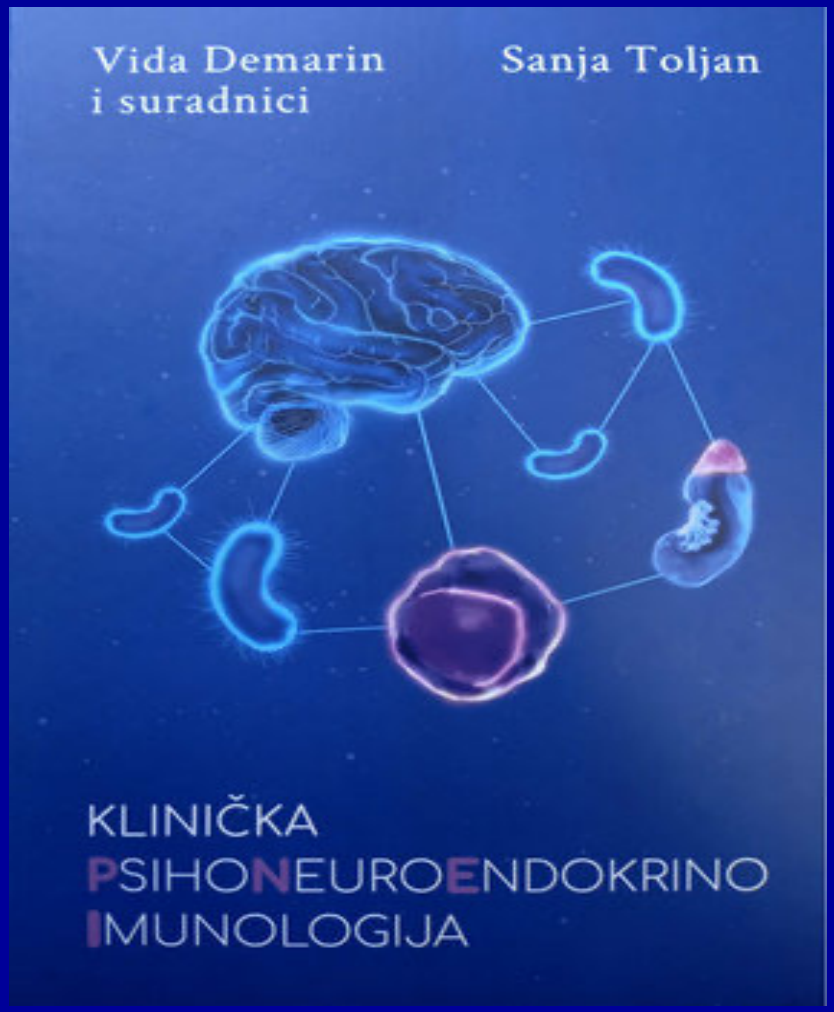
- Epigenetics - How your mind can reprogram your genes




Between stimulus and response, there is a space. In that space is our power to choose our response. In our response lies our growth and our freedom.
ViKtor Frankl
GOODBYE ANXIETY
Stephanie Dalfonzo
HELLO FREEDOM

- Diseases are the result of an alteration at the bio-psycho-social level that can indicate lifestyle changes (circadian rhythm) that should be made in addition to appropriate medical management and treatment.

- Emotions and stress significantly affect health and one's susceptibility to a pathology, as well as one's ability to recover from an illness.

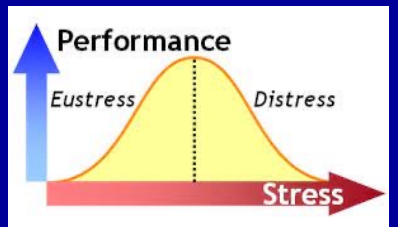

Vida Demarin
i suradnici
Sanja Toljan
KLINIČKA
PSIHONEUROENDOKRINO
IMUNOLOGIJA

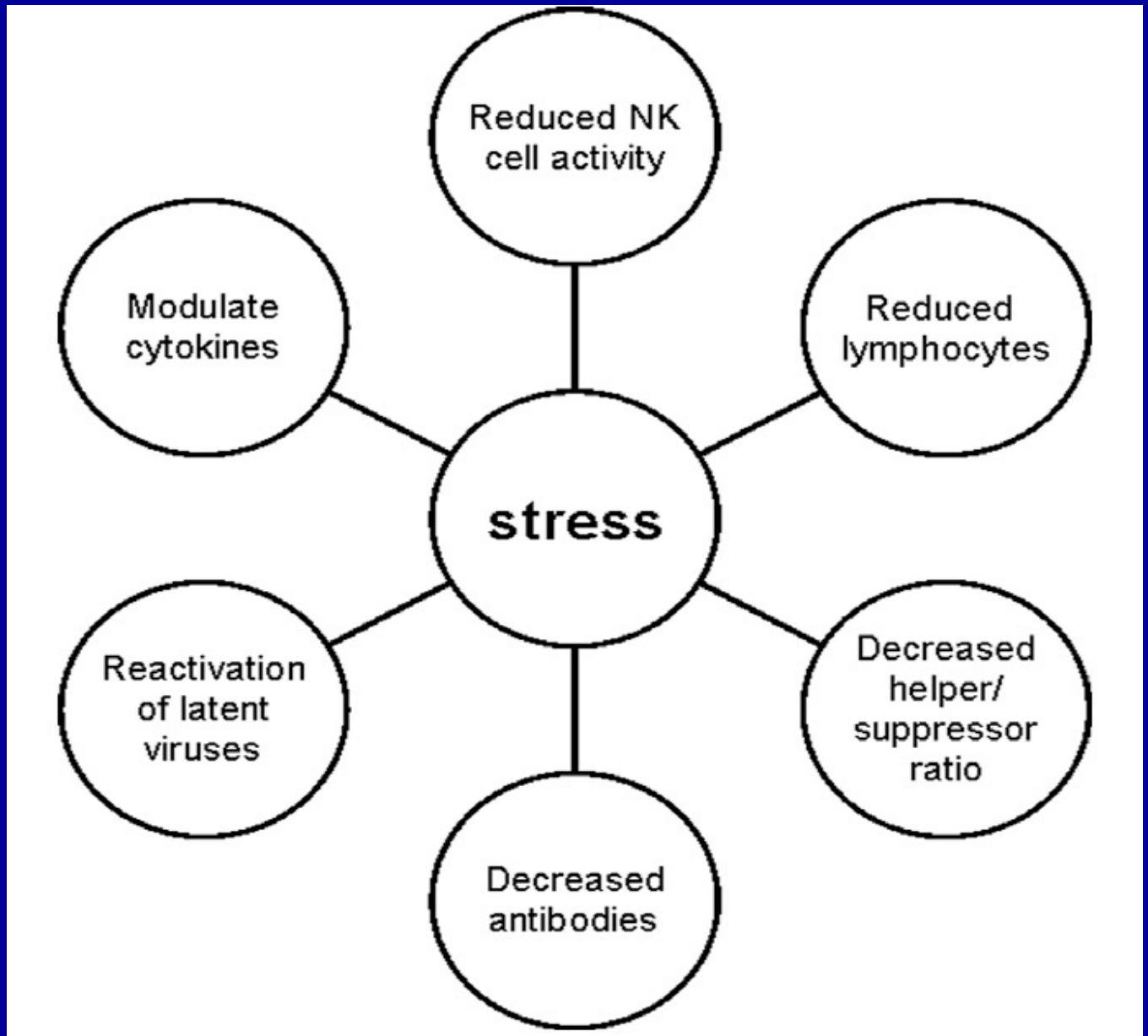

Body
Mind
headaches
frequent infections
taut muscles
muscular twitches
fatigue
skin irritations
breathlessness
worrying
muddled thinking
impaired judgement
nightmares
indecisions
negativity
hasty decisions
Stress
loss of confidence
more fussy
irritability
depression
apathy
alienation
apprehension
accident prone
loss of appetite
loss of sex drive
drinking more
insomnia
restlessness
smoking more
Emotions
Behavior

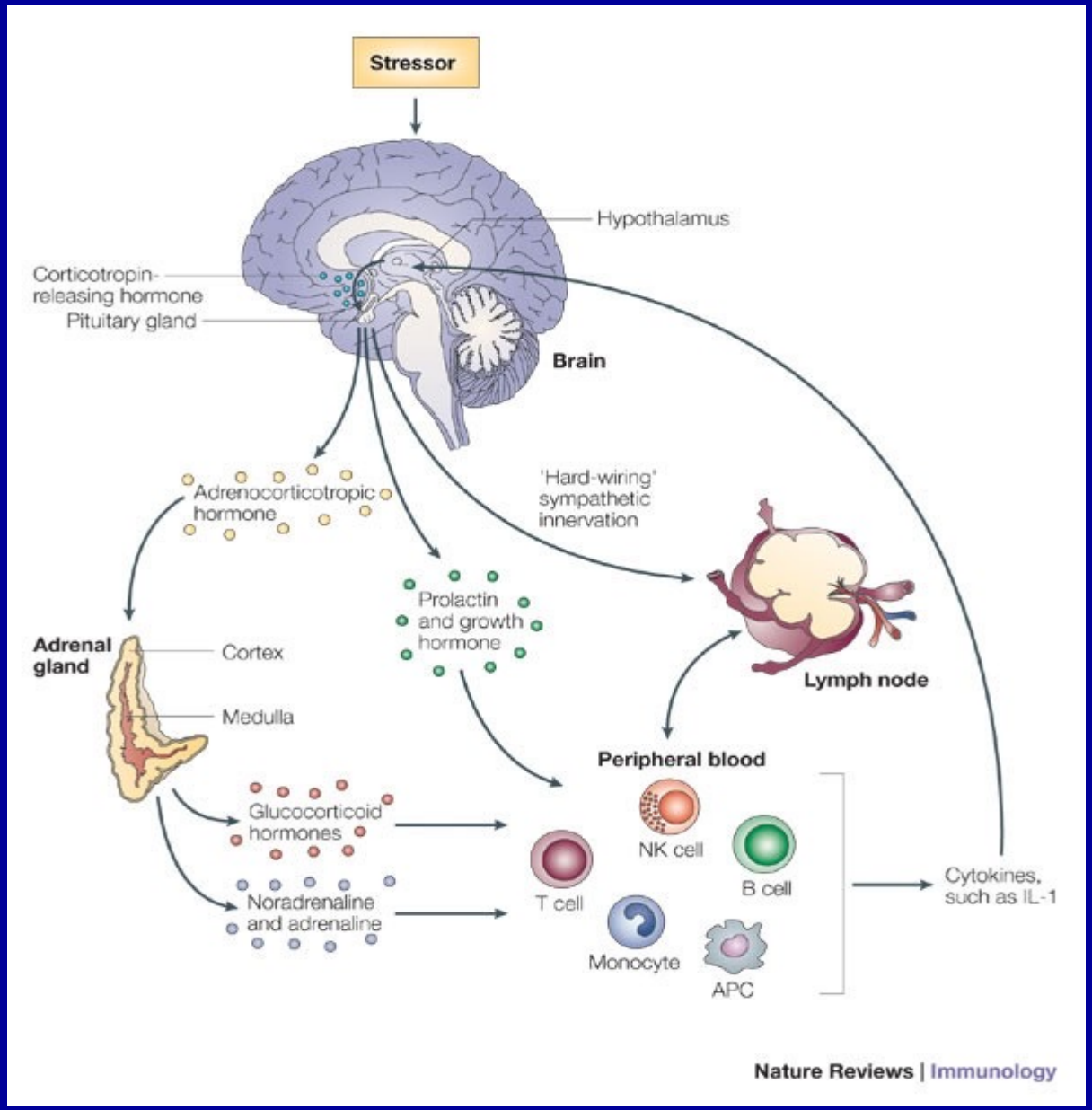
How does chronic stress affects our health?

- The bodily changes that happen during moments of stress can be very helpful when they happen for a short time.

- But when the response is drawn out for a long period of time, producing too many stress hormones can affect our health. The long-term effect of chronic stress (called *allostatic load*) causes wear and tear on the body.




Reduced NK cell activity
Modulate cytokines
Reduced lymphocytes
stress
Reactivation of latent viruses
Decreased helper/ suppressor ratio
Decreased antibodies


Stressor
Hypothalamus
Corticotropin-releasing hormone
Pituitary gland
Brain
Adrenocorticotropic hormone
'Hard-wiring' sympathetic innervation
Prolactin and growth hormone
Adrenal gland
Cortex
Medulla
Lymph node
Peripheral blood
Glucocorticoid hormones
Noradrenaline and adrenaline
NK cell
B cell
T cell
Monocyte
APC
Cytokines, such as IL-1
Nature Reviews | Immunology

Psychological Stress and the Human Immune System:A Meta - Analytic Study of 30 Year of Inquiry,

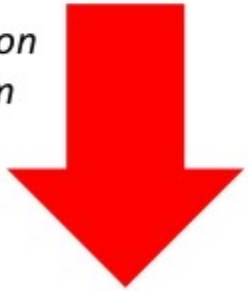
Segestrom SC, Miller GE, Psychol Bull 2004.

Impact of stress on the immune system

Stress may have a general impact on the immune system, e.g. **Immunosupression** Alternatively it may affect natural or specific immunity or even alter the balance between cellular and humoral immunity

Acute stressors can lead to an upregulation (increased strength) of natural immunity

Chronic stressors can lead to downregulation of the immune system



Sergerstrom & Miller (2004) conducted meta-analysis and concluded that stress can strengthen natural immunity

Current Directions in Stress and in Human Immune Function

Morey JN et al, Curr Opin in Psychol 2015.

- Psychological stress can dysregulate the human immune system
- Stress can impact immunity differentially across individuals and contexts
- Recent work in this area has made strides towards elucidating these differences
- Future work holds promise for reducing stress's effects on physical health

Cytokine secretion responsiveness of lymphomonocytes following cortisol cell exposure: Sex differences

Da Pozzo E et al, PLOS ONE 2018.

- Anti-inflammatory cytokines, IL-4 and IL-10, did not change in male cells and increased in female cells. Interestingly, kynurenine levels were higher in female cells than in male cells following cortisol stimulus.

- Obviously,cortisol differently affects male and female lymphomonocytes, shifting the cytokine release in favour of a pro-inflammatory pattern in male cells and an anti-inflammatory secretion profile in female cells, opening the way to study the influences of other stressful factors involved in the neurohumoral changes occurring in the response to stress conditions.

A Possible Change Process of Inflammatory Cytokines in the Prolonged Chronic Stress and Its Ultimate Implications for Health

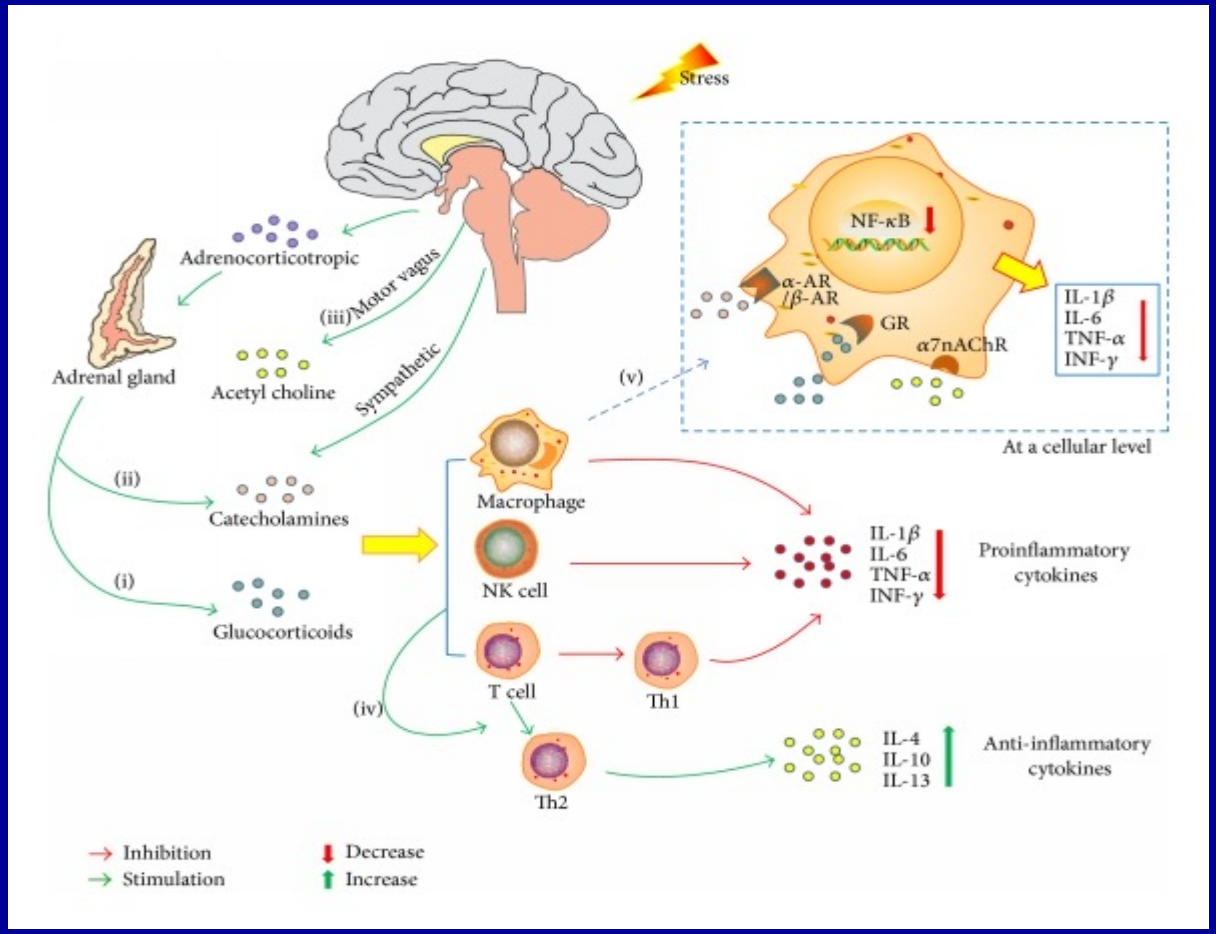
Rui Tian et al, Scientific World Journal 2014

- Additionally, the inflammatory cytokines mediate a negative feedback regulation on themselves.

- Collectively, these regulations may increase the proinflammatory cytokines while decreasing the anti-inflammatory cytokines. This may further activate NF-*κ*B and increase the proinflammation cytokines, which in turn reduce the inflammatory responses, contributing to various diseases.

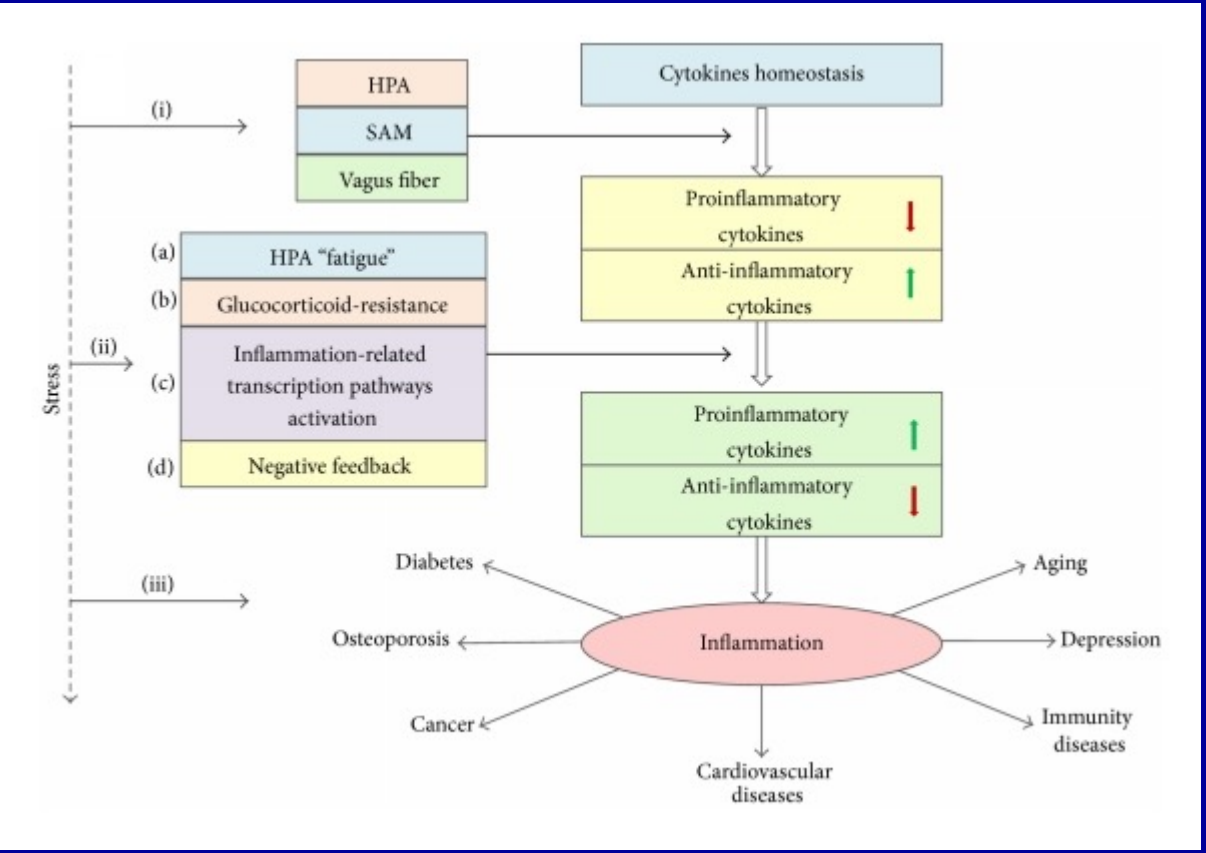
A Possible Change Process of Inflammatory Cytokines in the Prolonged Chronic Stress and Its Ultimate Implications for Health, Rui Tian et al

Scientific World Journal 2014



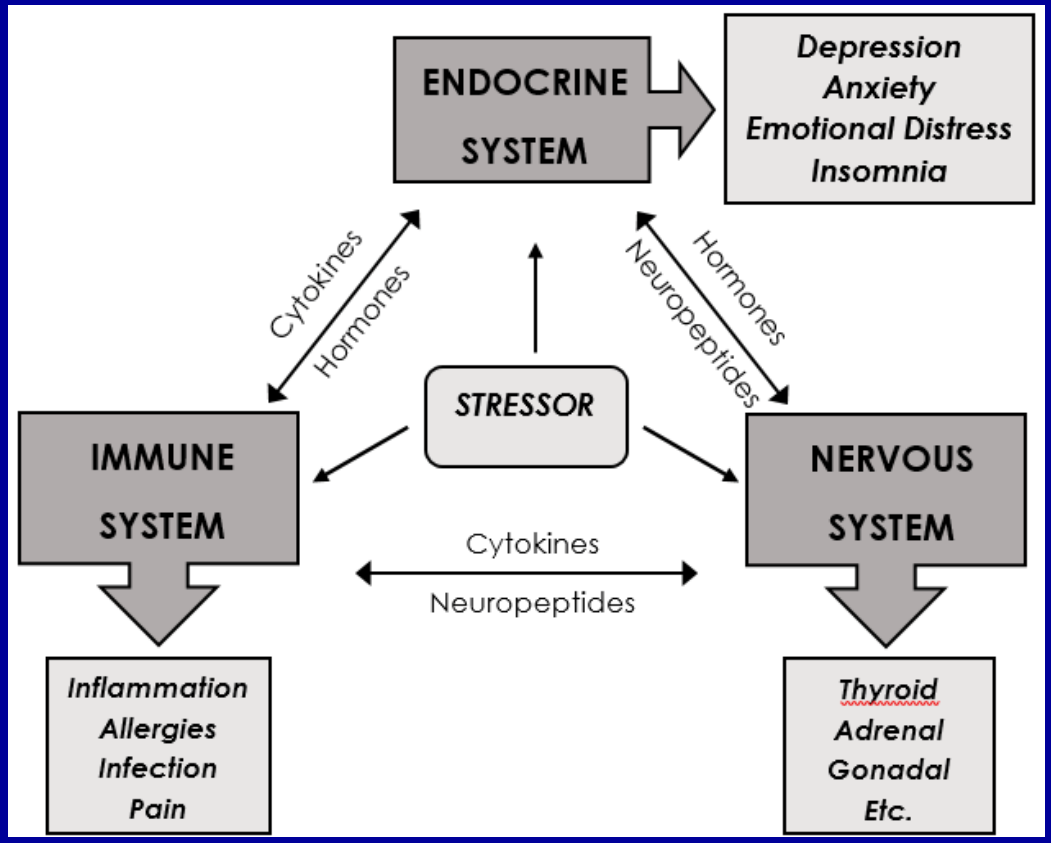
A Possible Change Process of Inflammatory Cytokines in the Prolonged Chronic Stress and Its Ultimate Implications for Health, Rui Tian et al

Scientific World Journal 2014



PNEI and Longevity

Healthy Aging Research 2018. Cavezzi A et al



The exposome:from concept to utility

Intern Journ of Epidemiology 2012. Chris Wild

HERIOT WATT UNIVERSITY

IOM

The Exposome…

The exposome is composed of every exposure to which an individual is subjected from conception to death.

Chris Wild

It comprises:

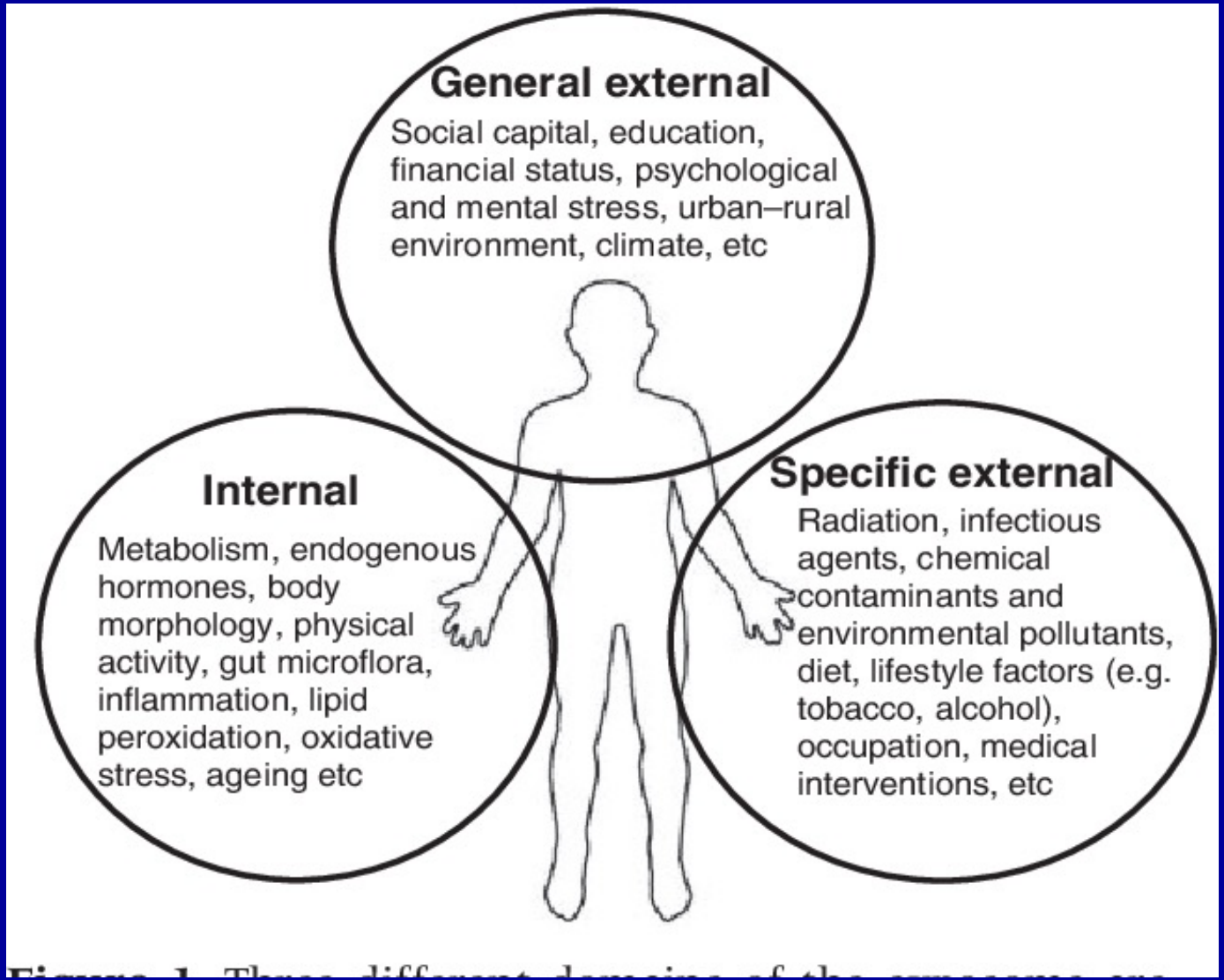
- processes internal to the body such as metabolism, gut microflora, inflammation…
- external exposures including infectious agents, chemical contaminants, diet…
- social, economic and psychological influences.

Wild, C. P. (2012). The exposome: from concept to utility. *International Journal of Epidemiology, 41(1), 24–32.*

Distinctly Innovative

The exposome: from concept to utility

International Journal of Epidemiology 2012, Wild Ch. P.

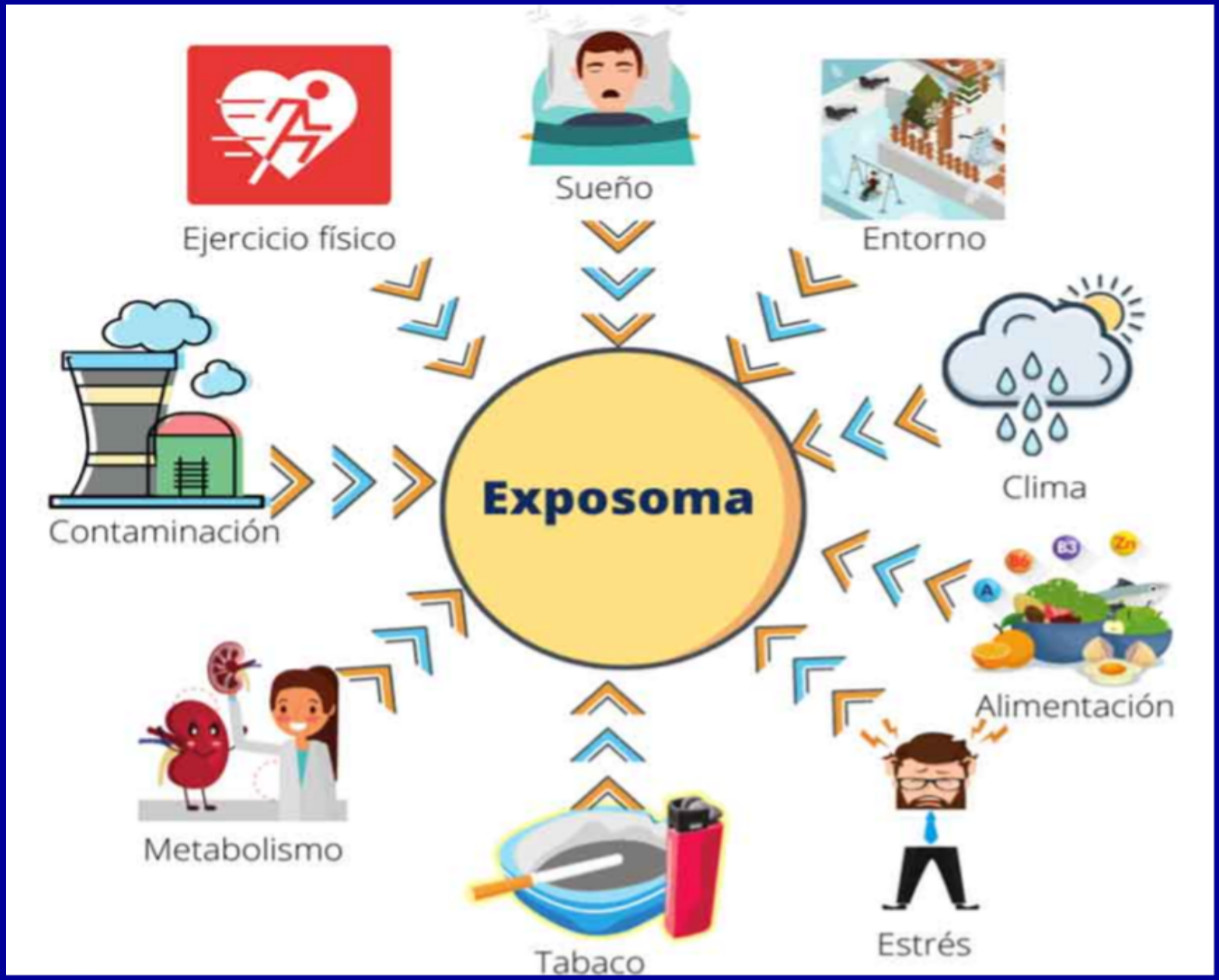


The Exposome and the Medicine of the Future

Neolife 2021. *Débora Nuevo*

- **The exposome is defined as the set of non-genetic factors to which we are exposed throughout our lives and which condition our state of health and disease.**

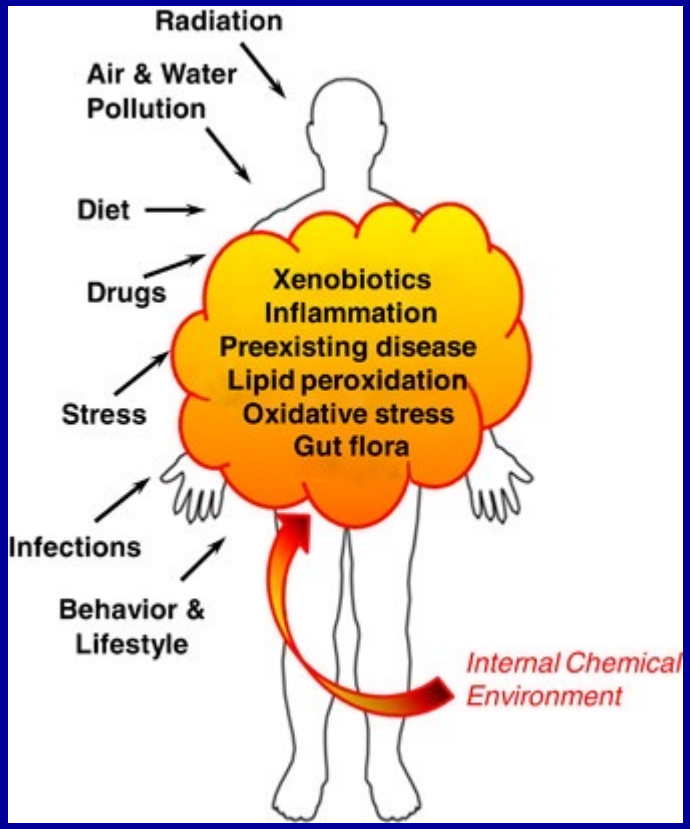
- The WHO estimates that approximately 25% of diseases are related to these non-genetic factors, which could be avoided. Therefore, it provides extremely valuable information in the design of preventive, diagnostic, and therapeutic strategies in the medicine of the future


Ejercicio físico
Sueño
Entorno
Contaminación
Exposoma
Clima
Metabolismo
Alimentación
Tabaco
Estrés

Implications of the exposome for exposure science

J Expo Sci Environ Epidemiol,2010.

Rappaport, S.



Using exposomics to assess cumulative risks and promote health

Environ Mol Mutagen 2015, Smith TM et al

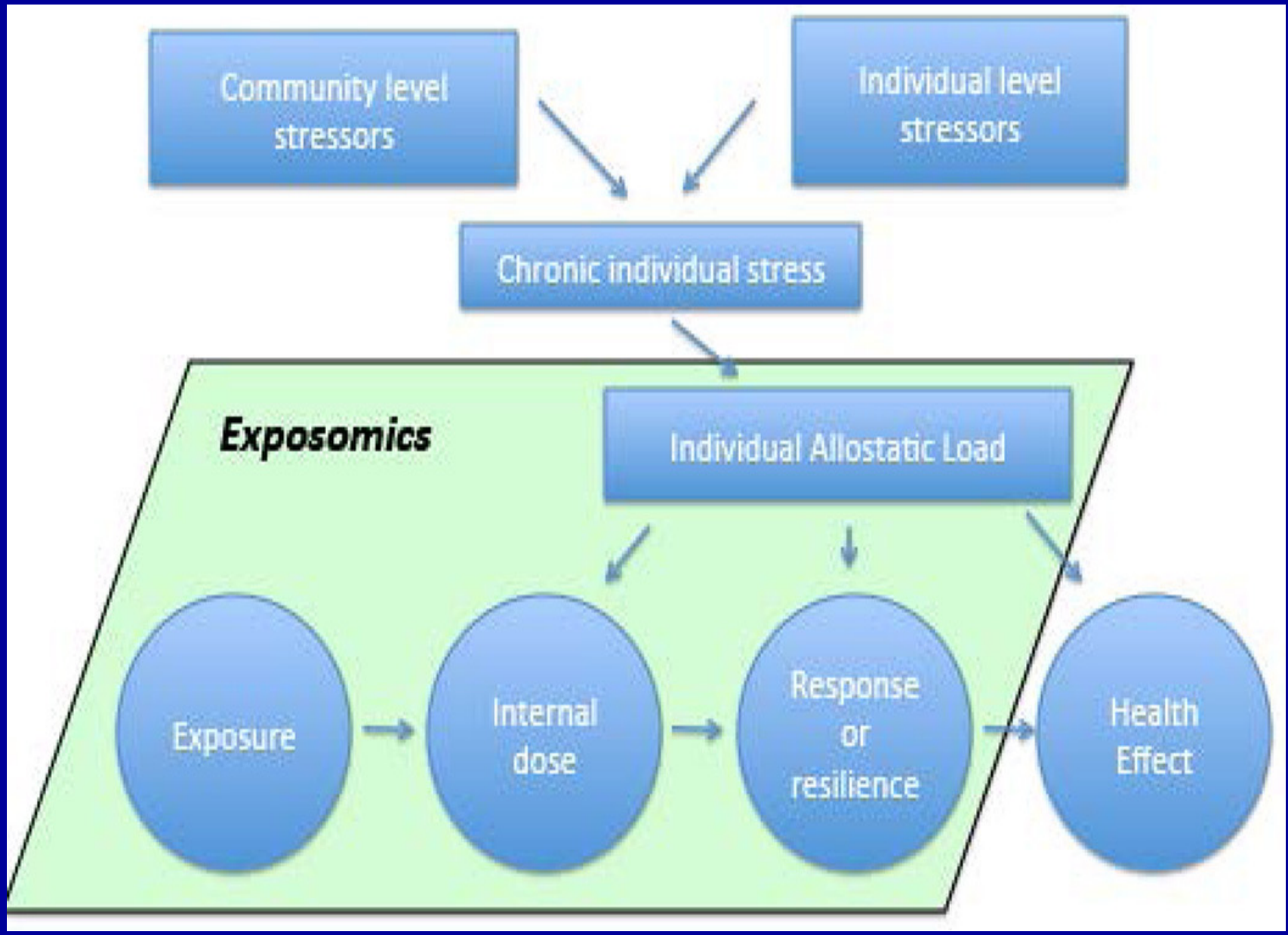
- Under the exposome paradigm all nongenetic factors contributing to disease are considered to be 'environmental' including chemicals, drugs, infectious agents, and psychosocial stress.

- We can consider these collectively as **environmental stressors**.

Using exposomics to assess cumulative risks and promote health

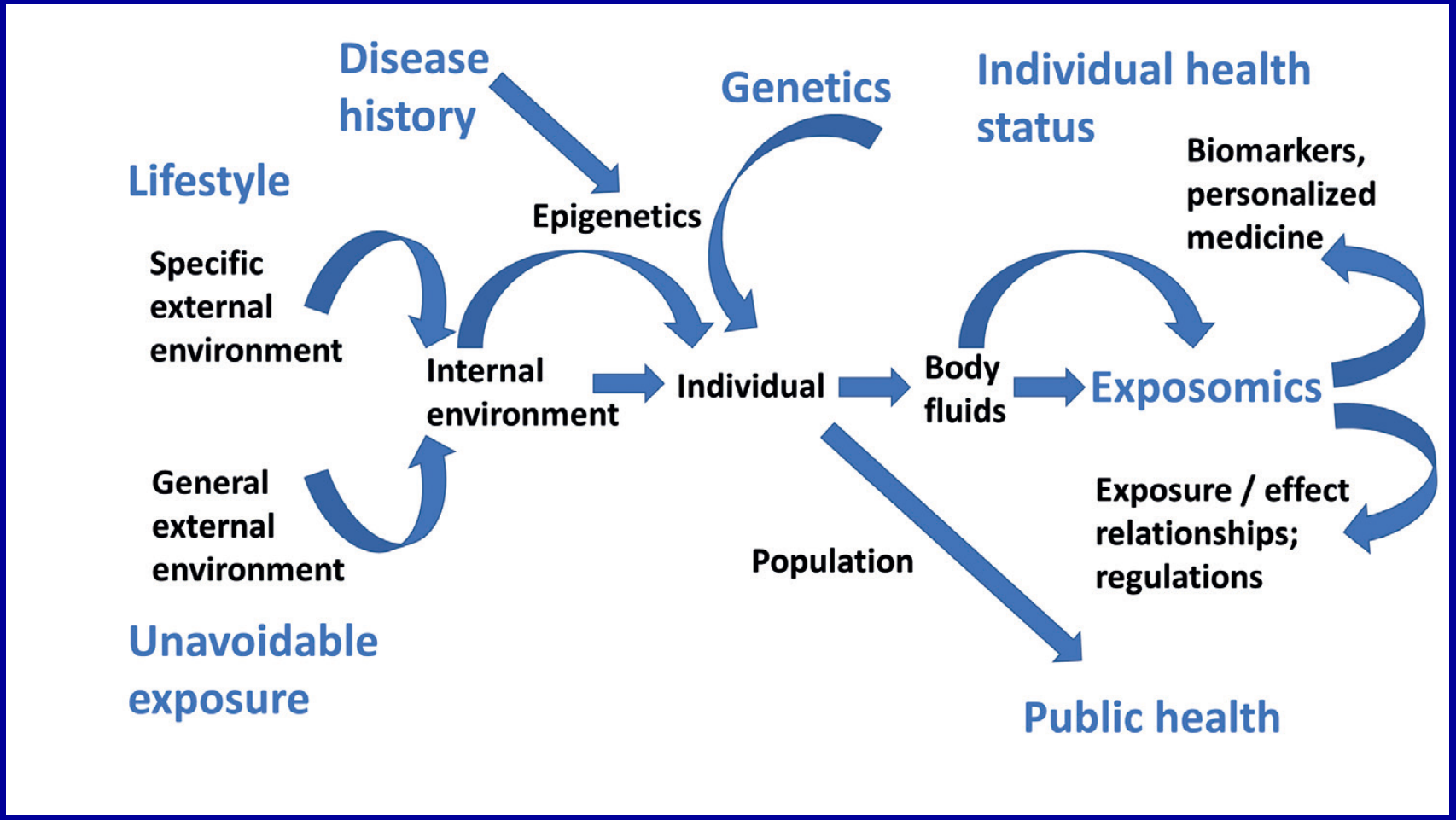
Environ Mol Mutagen 2015, Smith TM et al

- Exposomics is the comprehensive analysis of exposure to all environmental stressors and should yield a more thorough understanding of chronic disease development.
- We can operationalize exposomics by studying all the small molecules in the body and their influence on biological pathways that lead to impaired health.


Community level stressors
Individual level stressors
Chronic individual stress
Exposomics
Individual Allostatic Load
Exposure
Internal dose
Response or resilience
Health Effect

The Exposome – a New Approach for Risk Assessment

Altex,2020. Sille FCM et al



The Psychoexposome: A holistic perspective beyond health and disease

Psicothema 2018.,Colomina MT et al.

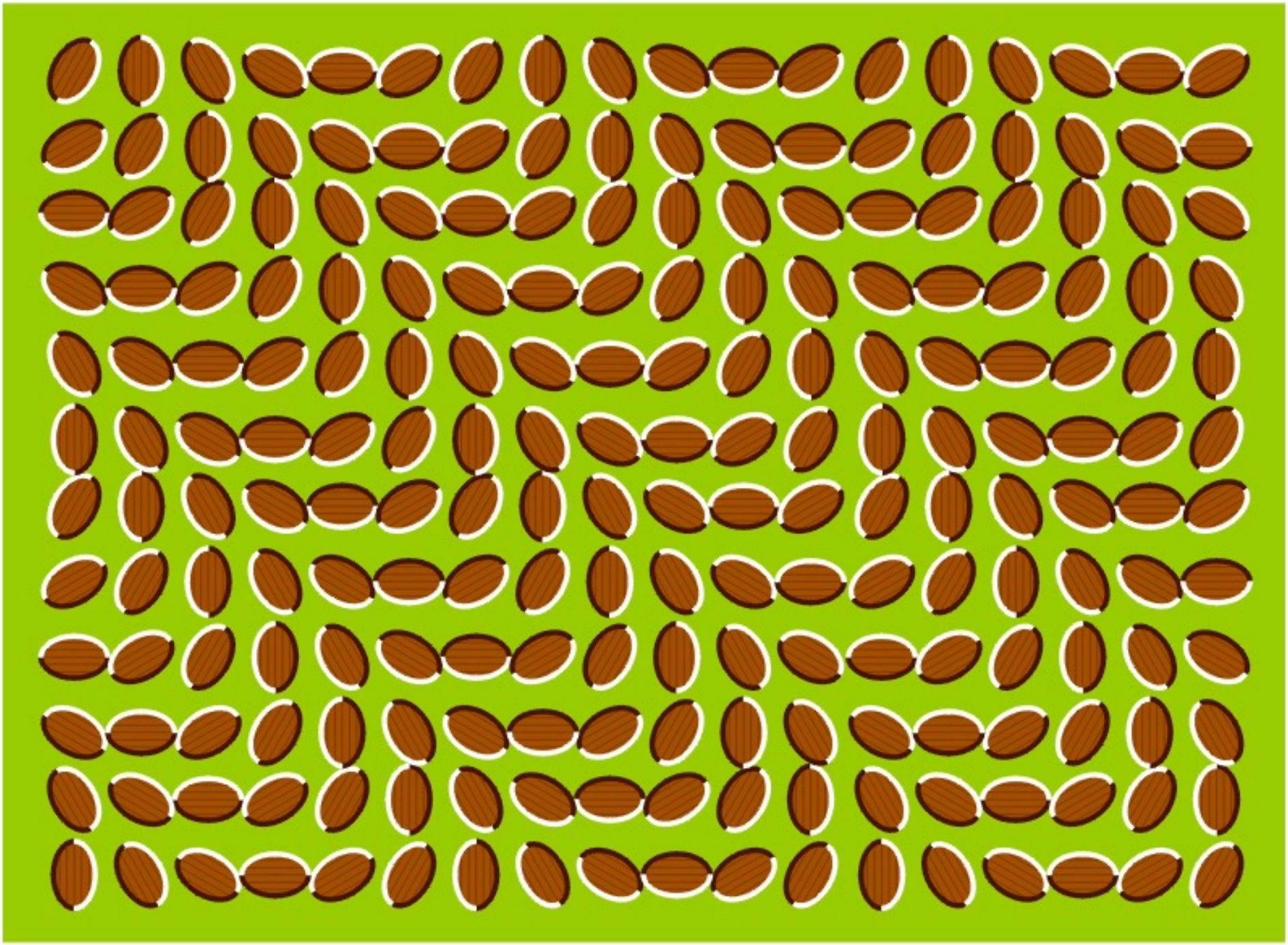
- The concept of the exposome has emerged as a new strategy for studying all environmental exposures throughout an individual□s life and their impact on human health.
- To propose the term **Psychoexposome** in line with the concept of the exposome from the field of environmental sciences.
- Psychology may take advantage from both exposome and omic sciences to create an integrated psychoexposome approach that may help in deciphering the etiology of psychological disorders and improving people's mental health.

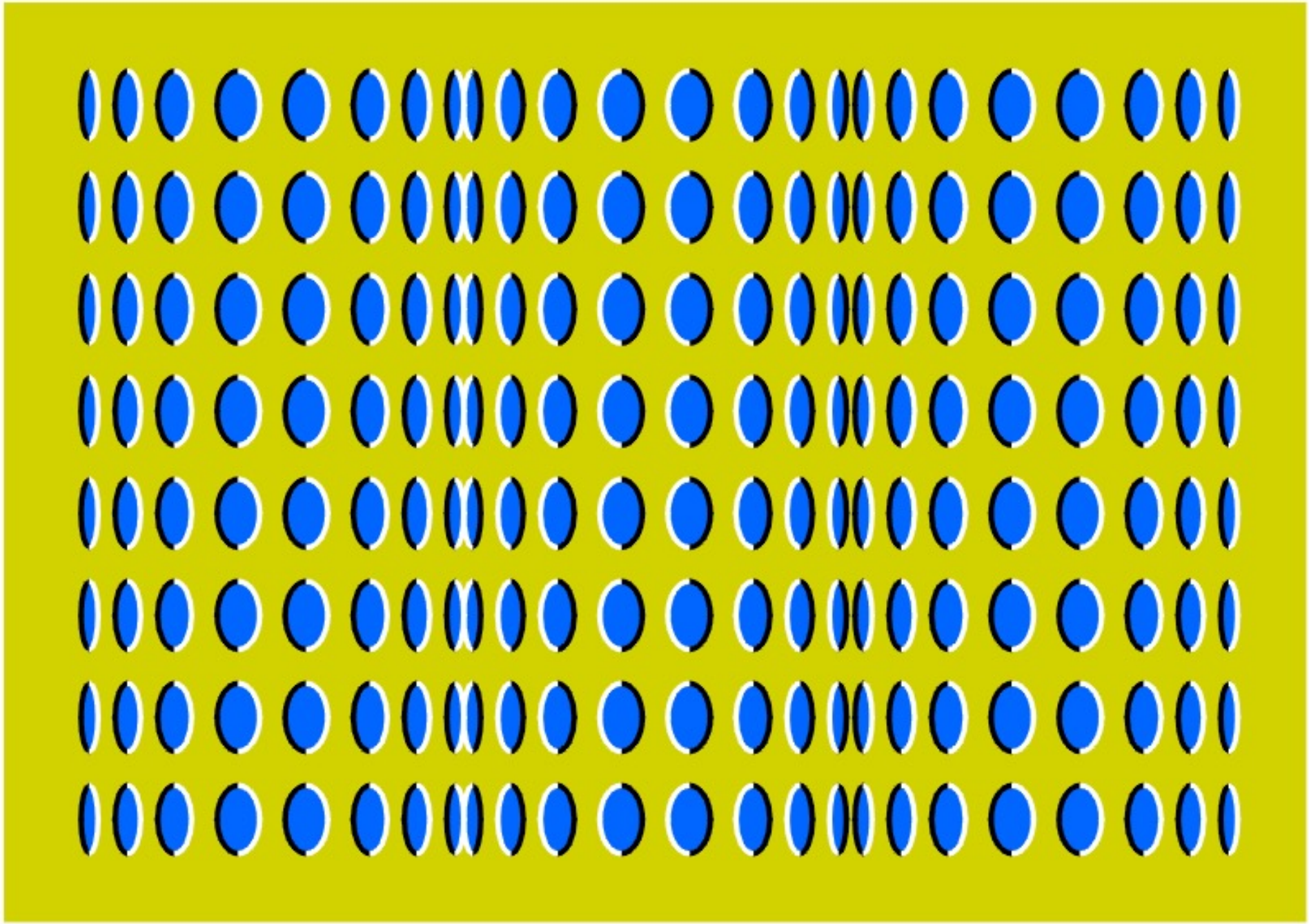
Pred kraj mali test:

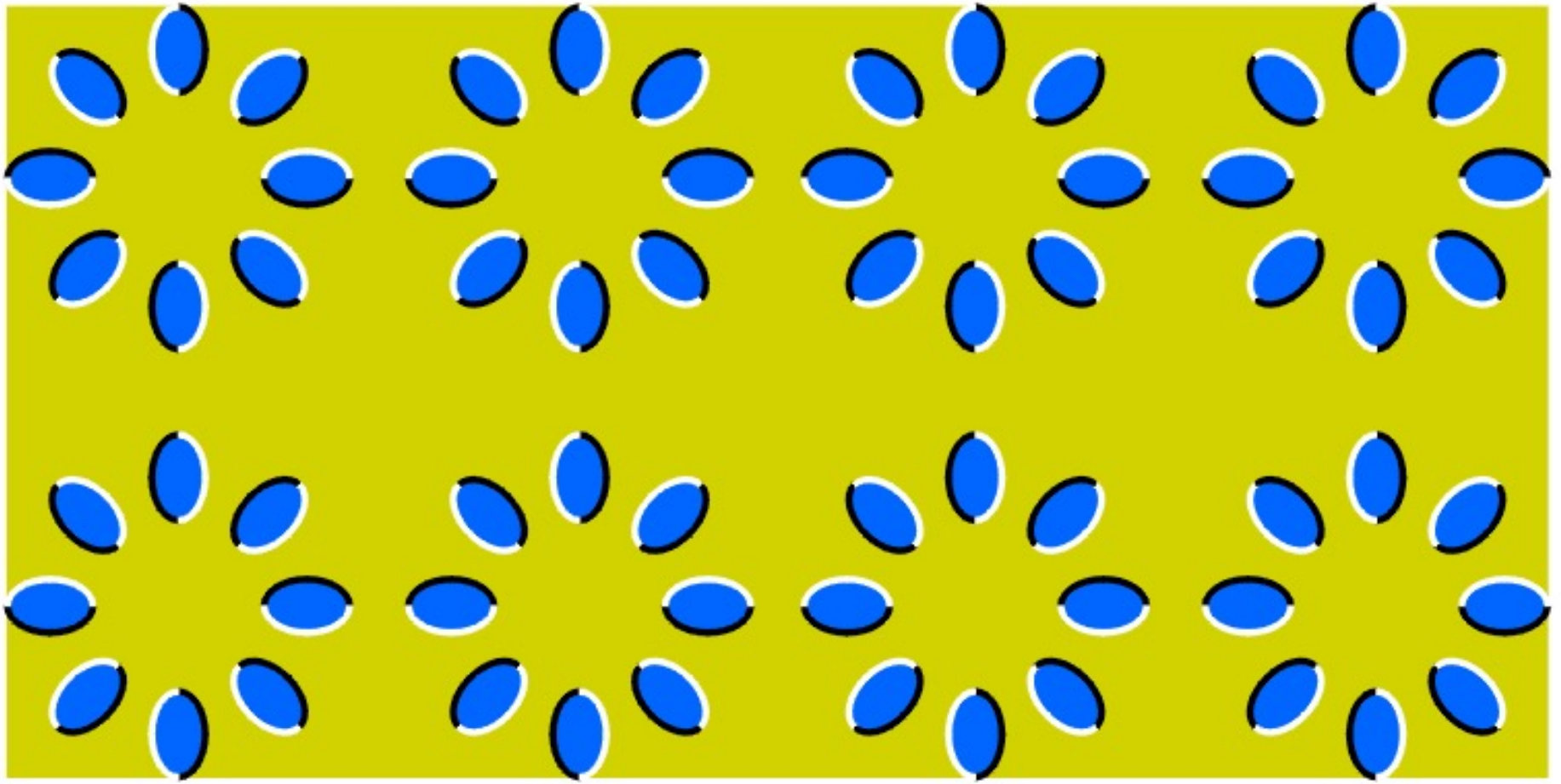
Kažu da ćete promatranjem ovih slika jednostavno ustanoviti kolikoj ste količini stresa izloženi.

Što ste više pod stresom to će vam se slike više činiti u pokretu.

Nemojte zaboraviti da djeca ove slike vide nepomičnima!







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