Age Management AMMG Medicine Group

DRA. PAULA MARTIN-MARFIL

# STRESS MANAGEMENT MEDICINE

## ”Improving Cognitive High Performance: Cognitive Enhancement , Smart Drugs, Brain Stimulators, Wearables, etc”.

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## LEARNING OBJETIVES

- Learn about stress and its consequences on cognitive function.
- Learn about how stress management medicine can comprehensively treat the reversible cognitive decline as a consequence of stress and improve cognitive function.
- Learn the benefits of using new emerging technologies in the field of cognitive enhancement

1. STRESS MANAGEMENT MEDICINE
2. STRESS PHSYOPATHOLOGY
3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT
4. BRAIN STIMULATORS
5. COGNITIVE WEARABLES

STRESS MANAGEMENT MEDICINE

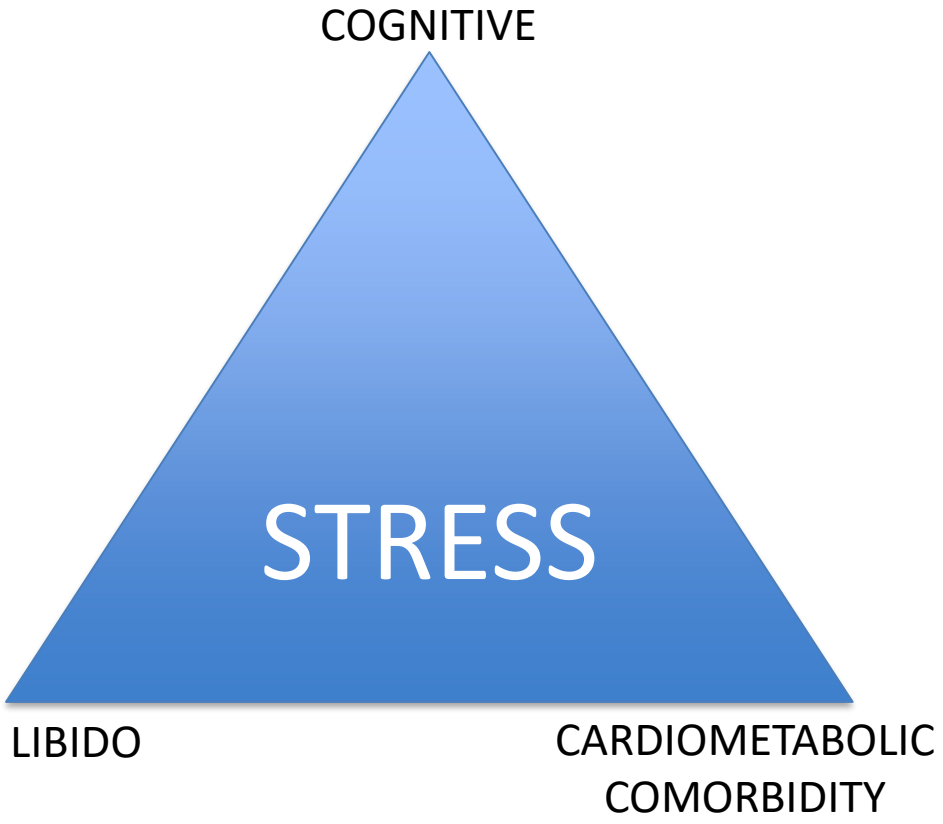
LIFESTYLE:
- Nutrition
- Exercise
- Brain Trainning
- Stress Relief Techniques

ORAL/IV SUPPLEMENTS

HORMONAL OPTIMIZATION

NEURO/BIOFEEDBACK

PSYCHOTHERAPY (EMDR)



# 1. STRESS MANAGEMENT MEDICINE

1) Stress consequences Treatment

2) Pre/Post Surgery Treatment

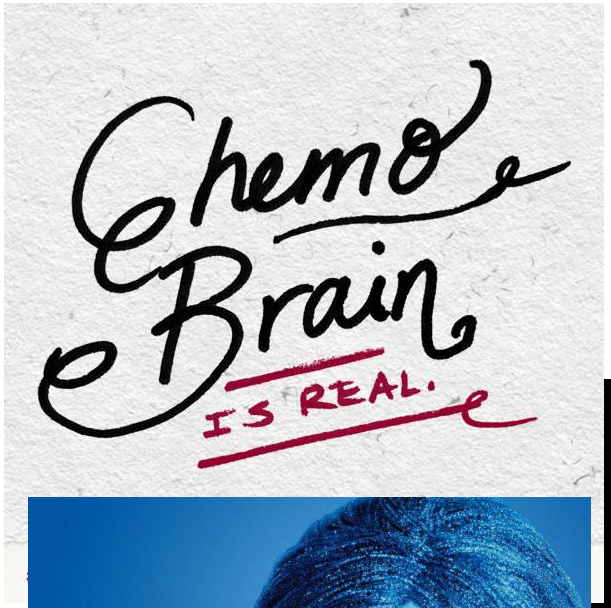
3) Psychotherapeutic process enhancement

4) Cognitive enhancement

5) Preventive Treatment

1. Stress consequences Treatment

Traumatic Brain Injury, PTSD, BurnOut, ChemoBrain, Psychiatry Disorders, etc.










2. Pre/Post Surgery Treatment:
Intensive Immunonutrition Pre;Surgery
Intensive Healing Repair PostSurgery.

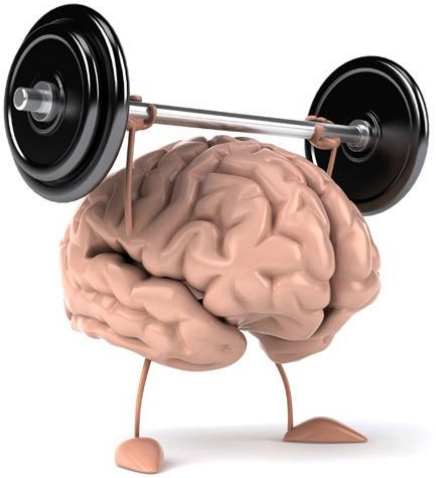


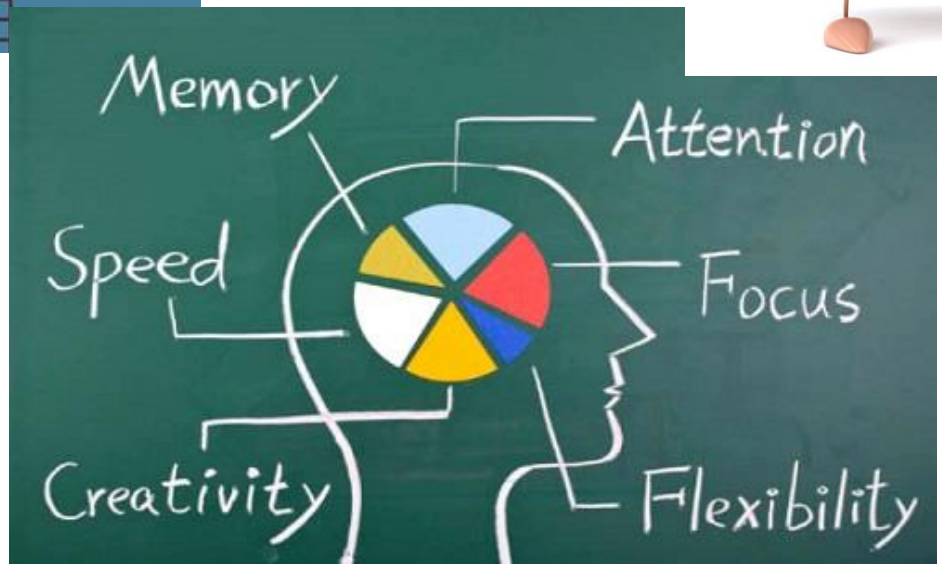
3. Psychotherapeutic process enhancement



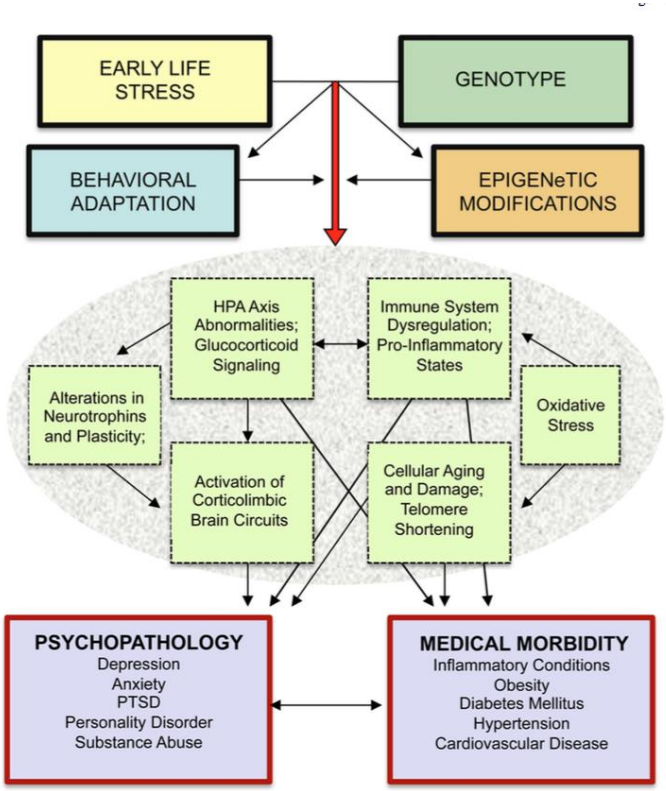
## 4. Cognitive enhancement



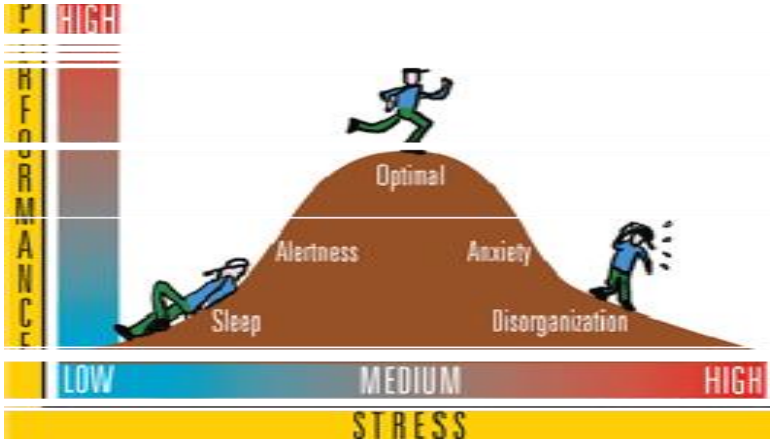


## 5. Preventive Treatment

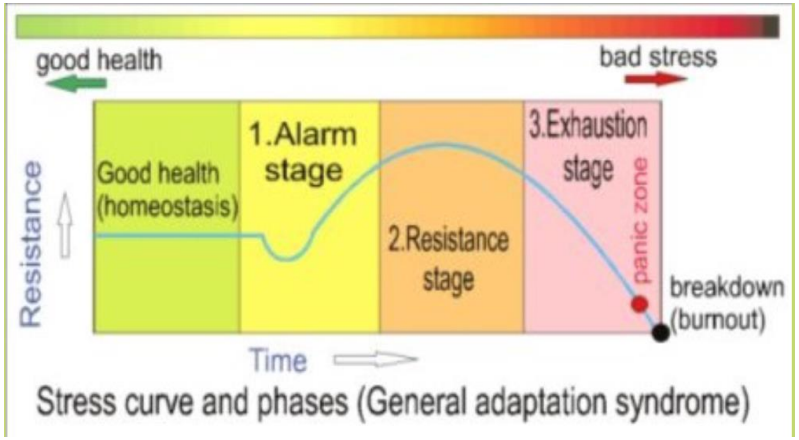





- Stress
  - A sum of biological reactions to stimul or events that we perceive as challenging or threatening (= stressors) that tends to disturb the homeostasis
    - "Positive" stress (eustress) –
    - "Negative" stress (disstress)
- Stressor
  - any factor disturbing body homeostasis
    - type: physical, mental, emotional
    - source: external or internal

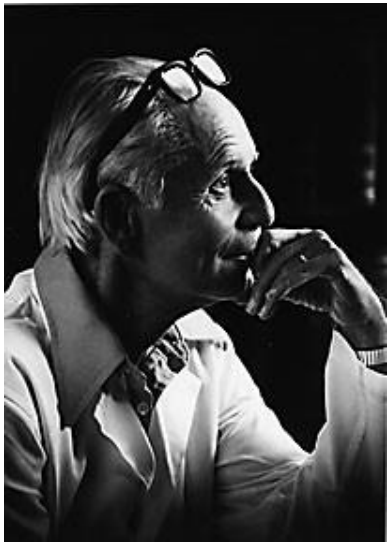


- **GAS represents a three-stage reaction or ways of coping with stress.**
  - **(1) general** - because it is produced only by agents which have a general effect upon large portions of the body.
  - **(2) adaptive** - because it stimulates defence
  - **(3) syndrome** - because its individual manifestations are coordinated and largely dependent upon each other



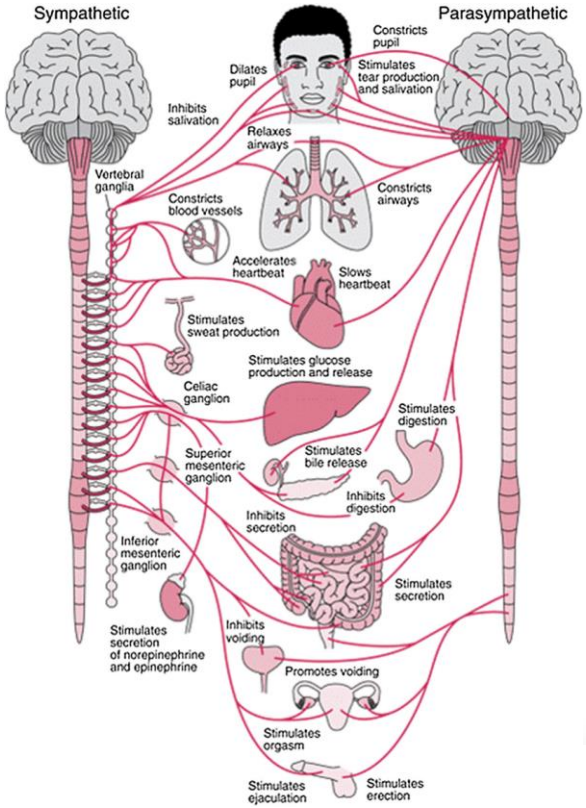
Stress curve and phases (General adaptation syndrome)

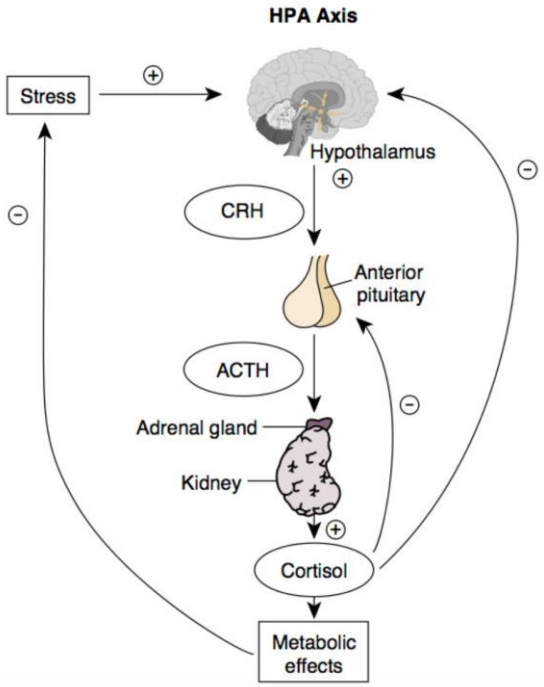
HANS SELYE



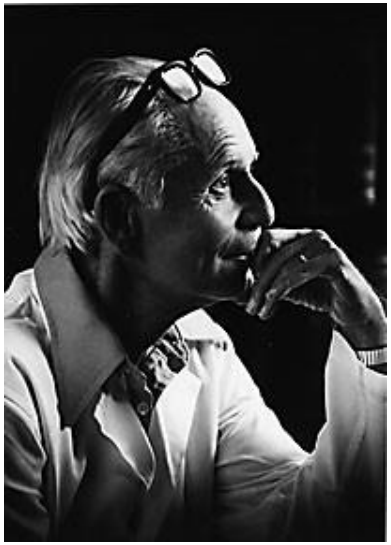
Austrian-born physician (1907-1982) who emigrated to Canada in 1939 born in Hungary, studied in Prague

- **GAS involves 2 major regulatory systems of the body**
  - Autonomic nervous system (ANS), mainly sympathetic
  - Endocrine system – hypothalamo-pituitary-adrenal axis



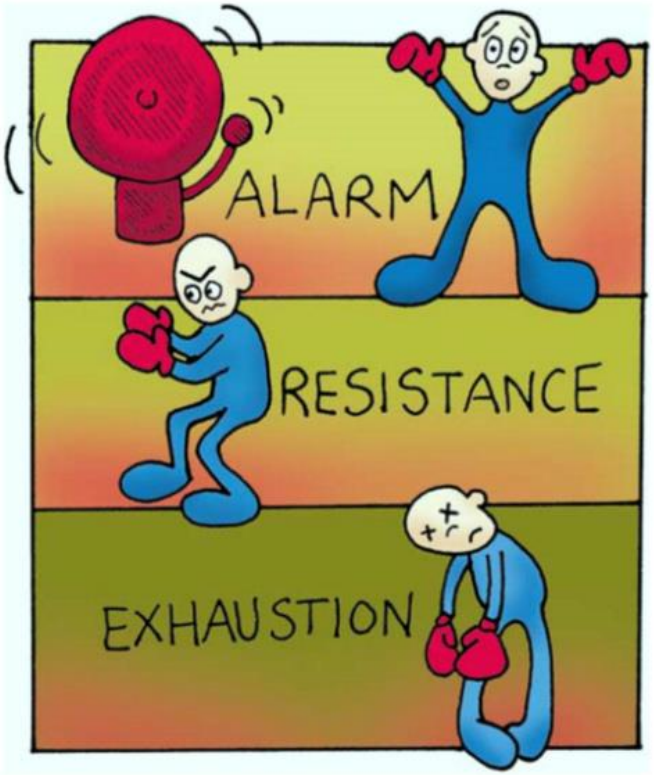




HANS SELYE



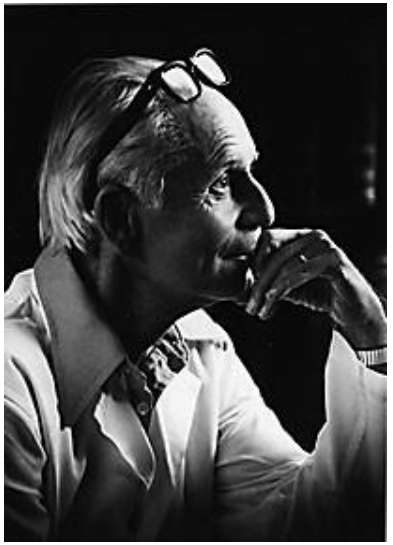
Austrian-born physician (1907-1982) who emigrated to Canada in 1939 born in Hungary, studied in Prague

- **3 distinctive stages in the syndrome's evolution**
  - **Alarm reaction** (already described by Walter B. Cannon in 1914 and 1935)
  - **Stage of resistance**
  - **Stage of exhaustion**




Three reactions or stages of stress

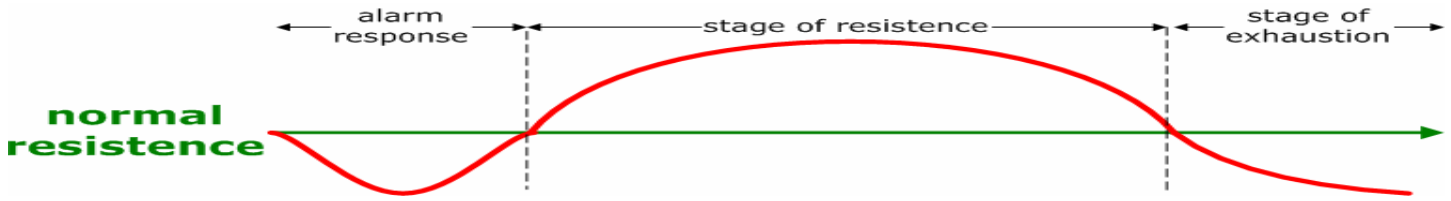
HANS SELYE



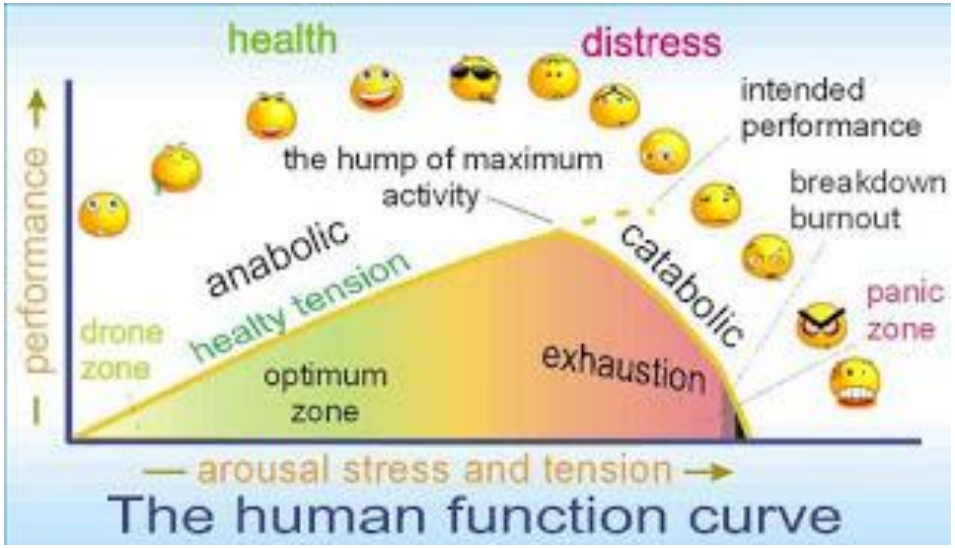
Austrian-born physician (1907-1982) who emigrated to Canada in 1939 born in Hungary, studied in Prague

- **(1) alarm reaction (AR)**
  - –fright → fight or flight (F&F or Cannon´s emergent reaction)
  - –The body's **resistance** to physical damage **drops** for a short-time so that organism can rearrange its priorities to cope with the stressor.
    - Use of available body sources for energy (glycogen), redistribution of blood to maintain higher blood pressure by increase of the peripheral resistance, increased oxygenation by bronchodilation, increased muscle, coronary and brain perfusion in order to act
  - –If the stressor no longer exists the body returns to its normal level of resistance.
  - –Extreme catabolism, immunodeficiency, cardiovascular consequences of metabolic derangements.

- **(2) stage of resistance (SR)**
  - –If the stressor persists ("we can't fight or flee from it or, rather, we are unable to apply counteracting psychosocial resources"), level of **resistance increases** beyond normal, relaxed levels → quite energy-consuming state
    - increased energy demands covered by adipo- and proteo-catabolism, blood pressure maintained by Na retention, …
  - –This stage is an example of **allostasis** (= achieving stability through change, active process).
  - –extreme catabolism, immunodeficiency, cardiovascular consequences of metabolic derangements, …

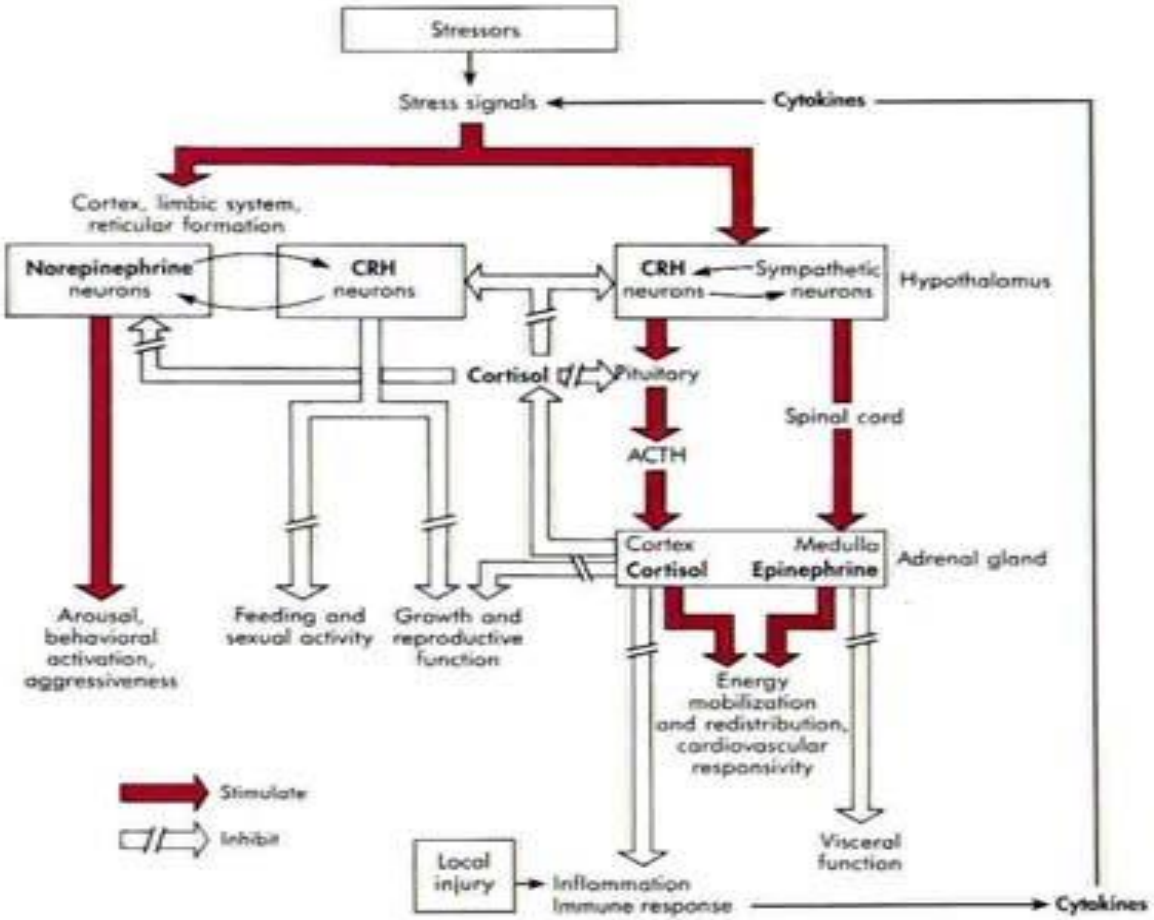


- **(3) stage of exhaustion (SE)**
  - if the exposure to stressor continues (**allostatic overload**) for a long time (weeks – years) body resistance collapses due to the inability to meet energy demands and due to side effects of extreme or exaggerated stress reactions → **diseases of adaptation**
  - extreme catabolism, immunodeficiency, cardiovascular consequences of metabolic derangements, …



- Adaptive, enabling surveillance by alteration of metabolism, cardiovascular & respiratory functions, decreasing pain perception (analgesia) and, at the same time, inhibition of processes decreasing surveillance chance such as reproductive functions and food intake and processing
  - **Metabolic alterations** → increase of glycemia using catecholamines (CAT) and glucocorticoids (GC)
    - ↓ insulin-stimulated glucose uptake
    - ↓ protein, fatty acid and glycogen synthesis
    - ↑ lipolysis and proteolysis (incl. part of the immune systems which is "sacrificed" in order to to gain AA)
    - ↑ glycogenolysis by CAT (short-term effects on glycemia)
    - ↑ gluconeogenesis by GC (long-term effects on glycemia)

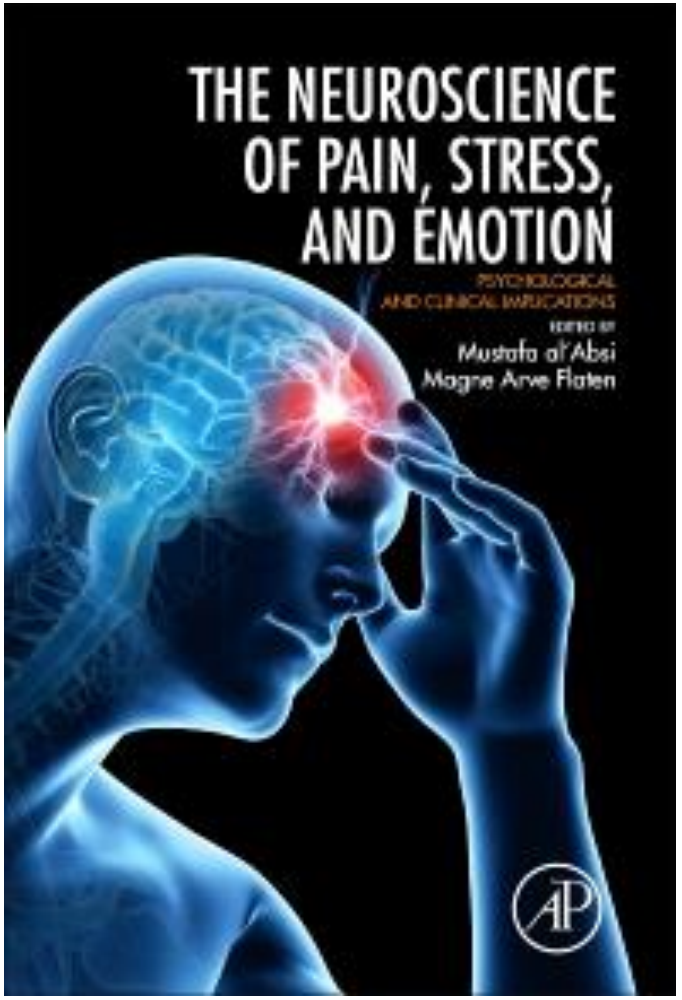
- Adaptive, ena… &
  respiratory fu… ime time,
  inhibition of … functions
  and food inta…
  - **Metabolic**… AT) and
    glucocortic…
    - ↓ insulin-…
    - ↓ protein…
    - ↑ lipolysi…
      systems…
    - ↑ glycoge…
    - ↑ gluconeo…
      glycemia…



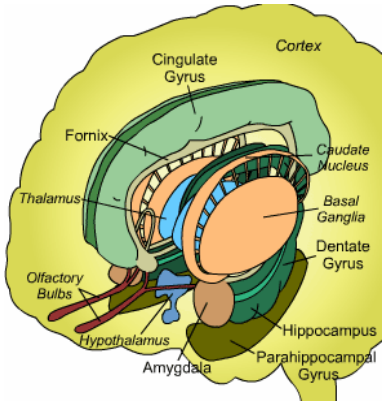
- **Cardiovascular and respiratory alterations** → glucose and oxygen traffic to muscles, heart and brain using CAT, GC and ADH
  - Apart from CAT effects on cardiovascular and respiratory functions and effect of GC on Na retention in the kidney there is also release of ADH to help ↑ circ. Volume.

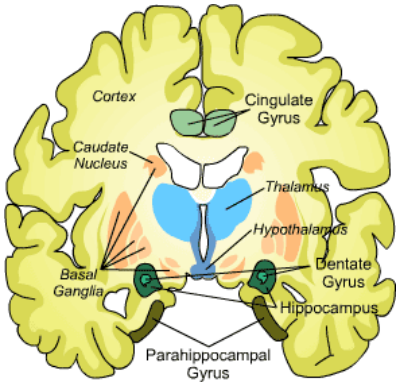


- **Stress-induced analgesia** (SIA) → decrease of pain perception by 2 ways
  - opiates-dependent SIA: enkephalins and β-endorphines
  - opiates independent SIA: glutamate
- **Cognitive and emotional alterations**
  - ↑ motivation, arousal, vigilance, anxiety by ↑ delivery of NE to CNS structures

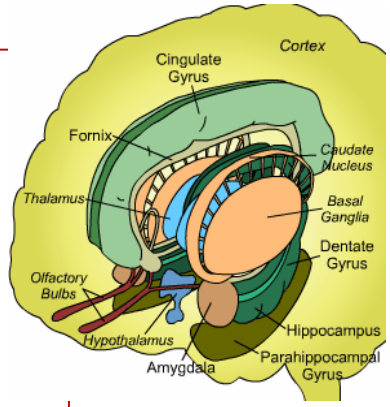


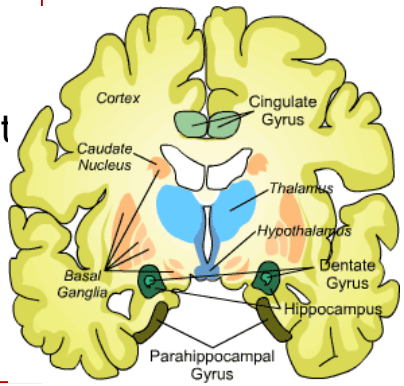
- (1) Analysis of the potentially threatening situation
  - higher cognitive areas – **prefrontal cortex**
    - major connections to amygdala and LC, however, gives us a voluntarily option to modify automatic responses (conscious control over anxiety)!
      - ~ process of extinction = stimulus that triggers a conditioned fear gradually loses this effect
      - ~ involved in the final phase of confronting a danger, = after the initial automatic, emotional reaction, the action that is best for us is chosen (people whose frontal cortex is damaged - "frontal syndrome" can't plan the simplest task)



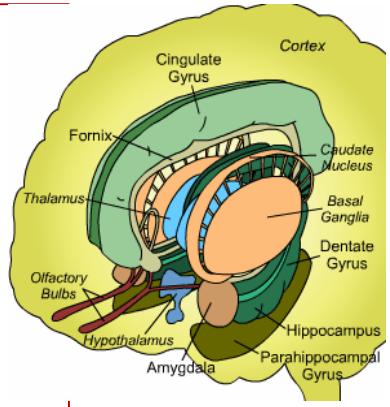



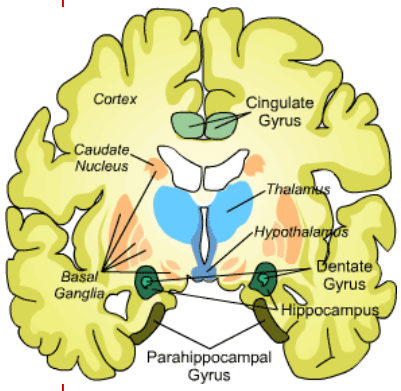
- (2) Respective autonomic and neuroendocrine reactions
  - –limbic system
    - **hippocampus**
      - ~ memory (storage and retrieving), connections to amygdala → origin of strong emotions triggered by particular memories
      - ~ processing of the context of a situation
      - ~ connections to hypothalamus
    - **amygdala**
      - ~ essential for decoding emotions, and in particular stimuli that are threatening to the organism
      - ~ many inputs converge in the amygdala directly from the sensory thalamus or from various sensory cortexes



- **thalamus**
  - sensory information to amygdala
- **hypothalamus**
  - activated by the structures of the limbic system
  - controls activity of pituitary and ANS (LC)
- **brain stem**
  - pons
    - ~ **locus coeruleus** (LC) – afferentation from hypothalamus, controls activity of the SNS and other CNS parts by NE release → increase of cognitive functions (prefrontal cortex), motivation, HPA activity (↑ CRH), SNS activation
  - medulla oblongata – n. tractus solitarii

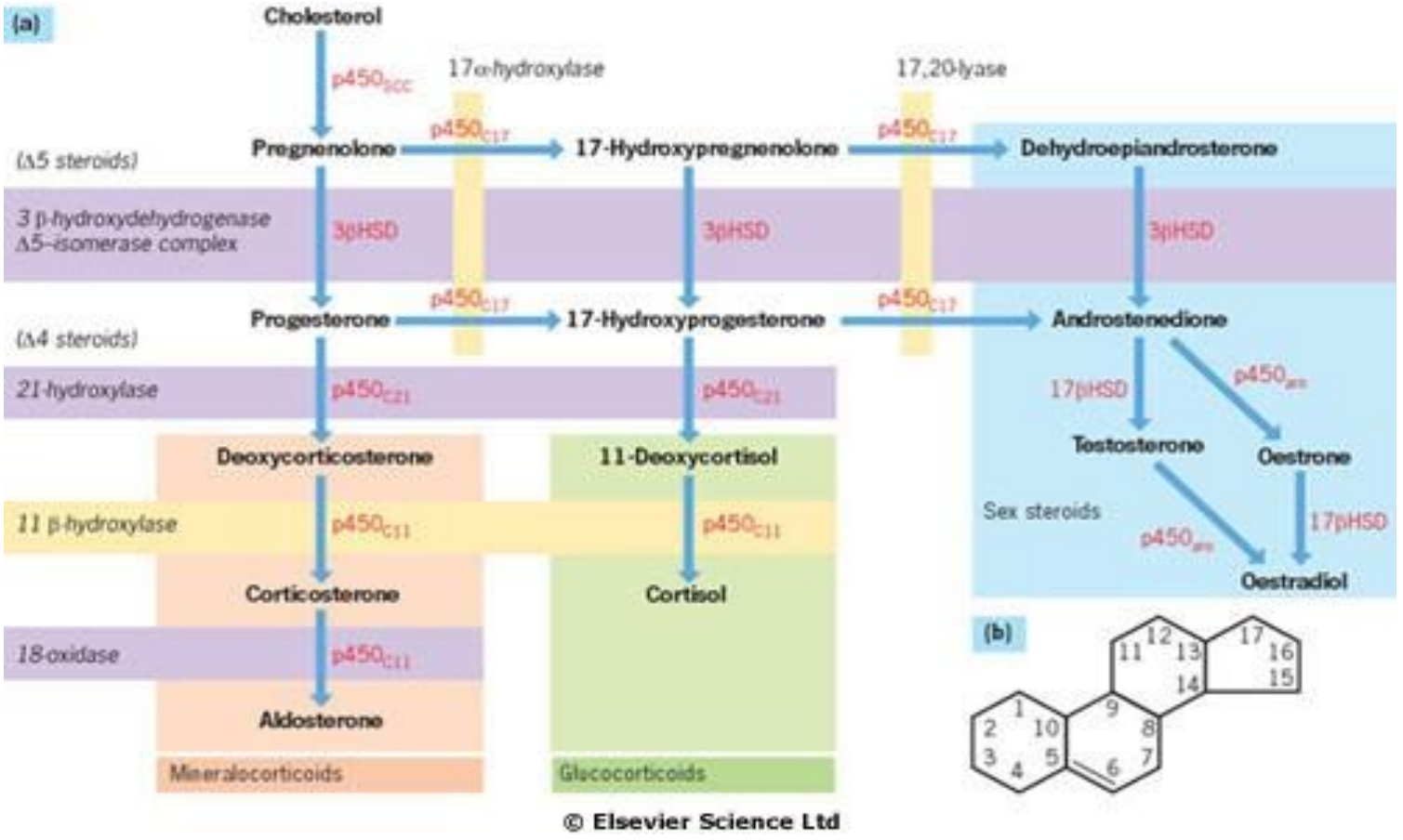


| | Adr | Cort | ACTH | DHEA | Test | Dop | Serot | GABA | Prog | Ac.Co |
|---|---|---|---|---|---|---|---|---|---|---|
| Acute Stress | ↑↑ | ↑ | — | — | — | ↑↑ | — | — | — | — |
| Chronic Stress | ↑ | ↑↑ | ↑↑ | ↓ | ↓ | ↑↑ | ↓ | ↑↑ | ↓ | ↓ |
| Exh | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ |

# 2. STRESS PHSYOPATHOLOGY

| | Adr | Cort | ACTH | DHEA | Test | Dop | Serot | GABA | Prog | Ac.Co |
|---|---|---|---|---|---|---|---|---|---|---|
| Acute Stress | ↑↑ | ↑ | — | — | — | ↑↑ | — | — | — | — |
| Chronic Stress | ↑ | ↑↑ | ↑↑ | ↓ | ↓ | ↑↑ | ↓ | ↑↑ | ↓ | ↓ |
| Exh | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ |


(a)
Cholesterol
p450scc
17α-hydroxylase
17,20-lyase
Pregnenolone
p450c17
17-Hydroxypregnenolone
p450c17
Dehydroepiandrosterone
(Δ5 steroids)
3 β-hydroxydehydrogenase
Δ5–isomerase complex
3βHSD
3βHSD
3βHSD
Progesterone
p450c17
17-Hydroxyprogesterone
p450c17
Androstenedione
(Δ4 steroids)
21-hydroxylase
p450c21
p450c21
17βHSD
p450aro
Deoxycorticosterone
11-Deoxycortisol
Testosterone
Oestrone
11 β-hydroxylase
p450c11
p450c11
Sex steroids
p450aro
17βHSD
Corticosterone
Cortisol
Oestradiol
18-oxidase
p450c11
Aldosterone
Mineralocorticoids
Glucocorticoids
(b)
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# 3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT

1. NEUROTRANSMITTERS
2. NEUROPERMISIVE ENVIRONMENT
    - INFLAMMATION
    - OXIDATIVE STRESS
    - MITOCHONDRIAL DISFUNCTION
    - NEUROESTEROIDS

SEROTONINE

• Tendency to mood variability.• Sadness / depression.• Food drive.• carbohydrates craving, preferably evening.• Sleep disturbances.• Personality changes.• Suicidal tendencies.• Tachycardia and / or precordalgia associated or not to headache. • Crisis of mania or hypomania.

5HTP
GRIFFONIA
ISRS

Schifano F, Orsolini L, Duccio Papanti G, Corkery JM (2015). "Novel psychoactive substances of interest for psychiatry". *World Psychiatry*. **14** (1): 15–26.

DOPAMINE

• Asthenia and adynamia.• Easy tiredness.• Lack of disposition.• Morning Apathy.• Decreased libido.• Desire to eat sugar.• Increased coffee needs.• Smoke more than before, if you smoke.• Decreased creativity

L-FENIALANINE
TIROSINE
MUCUNA PRURIENS
CoQ10
BUPROPIÓN

Schifano F, Orsolini L, Duccio Papanti G, Corkery JM (2015). "Novel psychoactive substances of interest for psychiatry". *World Psychiatry*. **14** (1): 15–26.

# 3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT

NORADRENALINE

• Salty foods craving.• Easy tiredness.• Lack of disposition.• Memory change.• migratory muscular pain. • Background of tpm if woman
• Tendency to depression

5HTP
L-FENILALANINE
VENLAFAXINE

Schifano F, Orsolini L, Duccio Papanti G, Corkery JM (2015). "Novel psychoactive substances of interest for psychiatry". *World Psychiatry*. **14** (1): 15–26.

# 3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT

GABA

• Irritability • Impatience• Aggression • Intolerance• Carbohydrates craving• Sleep disturbance• General eating disorders.• Dermal eruption or neurodermatitis

Teanina
Phenibut
Lacterum
Pregabaline
Gabapentine
Topiramate
Valproic acid

Schifano F, Orsolini L, Duccio Papanti G, Corkery JM (2015). "Novel psychoactive substances of interest for psychiatry". *World Psychiatry*. **14** (1): 15–26.

# 3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT

ACETILCOLINE

"Brain fog", poor short-term memory, Fatigue, especially fatigue that worsens with exertion, Constipation/gastroparesis, Dry eyes, Orthostatic hypotension, Flushing, Emotional instability, Chronic inflammation, Fast heart rate (tachycardia), Large pupils

FOSFATIDILSERINA
GPC
BACOPA
GINKO BILOBA
HUPERZINA A
VIMPOCETINA
DONEPEZILO
RIVASTIGMINA
PIRACETAM

Zhang YS, Li JD, Yan C. An update on vinpocetine: New discoveries and clinical implications. Eur J Pharmacol. 2018 Jan 15;819:30-34. doi: 10.1016/j.ejphar.2017.11.041. Epub 2017 Nov 26. Review. PubMed PMID: 29183836; PubMed Central PMCID: PMC5766389.

Schifano F, Orsolini L, Duccio Papanti G, Corkery JM (2015). "Novel psychoactive substances of interest for psychiatry". *World Psychiatry*. **14** (1): 15–26.

# 3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT

ANTIOXIDANTS

Pycnogenol
Lipoic Acid
Resveratrol
Vitamin E
Vitamin C
Q 10
NAC
Zinc

NEUROESTEROIDS

PREGNENOLONE
DHEA
TESTOSTERONE
PROGESTERONE/ESTROGEN

Gestuvo, M., & Hung, W. (2012). Common dietary supplements for cognitive health. *Aging Health*, *8*(1), 89–97. http://doi.org/10.2217/AHE.11.92

# 3. COGNITIVE ENHANCEMENT COMPREHENSIVE TREATMENT

INFLAMMATION

DHA
EPA
Cúrcuma

MODULATORS OF NEURAL ENERGETIC METABOLISM

Acetil L Carnitine
L Glutamine

MITOCHONDRIOGENIC

Resveratrol
PQQ
Melatonine

Gestuvo, M., & Hung, W. (2012). Common dietary supplements for cognitive health. *Aging Health*, *8*(1), 89–97. http://doi.org/10.2217/AHE.11.92

## HYPERBARIC OXYGEN THERAPY (HBOT)



Gao ZX, Rao J, Li YH. Hyperbaric oxygen preconditioning improves postoperative cognitive dysfunction by reducing oxidant stress and inflammation. Neural Regen Res. 2017 Feb;12(2):329-336. doi: 10.4103/1673-5374.200816. Review. PubMed PMID: 28400818; PubMed Central PMCID: PMC5361520.

## TRANSCRANIAL MAGNETIC STIMULATION (TMS)



Luber B, Lisanby SH. Enhancement of human cognitive performance using transcranial magnetic stimulation (TMS). Neuroimage. 2014 Jan 15;85 Pt 3:961-70.

## NEUROFEEDBACK



Frank Scharnowski, Nikolaus Weiskopf, Cognitive enhancement through real-time fMRI neurofeedback, Current Opinion in Behavioral Sciences, Volume 4, 2015,pages 122-127,
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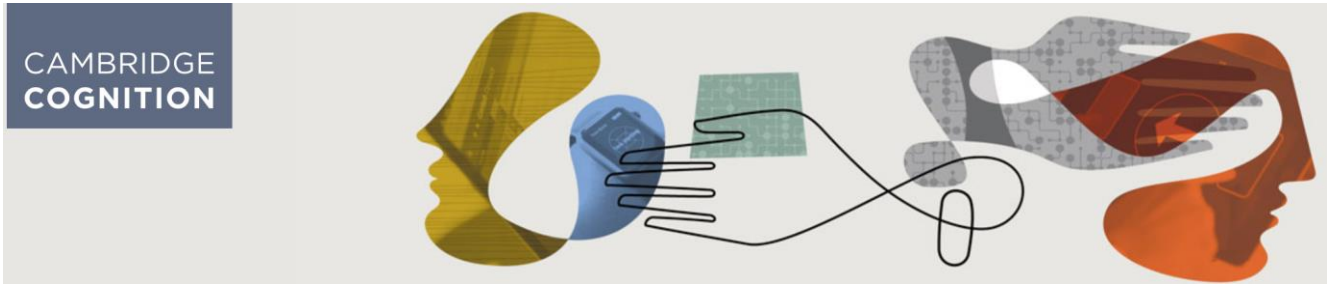
# 4. COGNITIVE WEARABLES









http://www.cambridgecognition.com/

# 5. CONCLUSIONS

Arnsten A. F. (2015). Stress weakens prefrontal networks: molecular insults to higher cognition. Nat. Neurosci. 18, 1376–1385. 10.1038/nn.4087

Buchanan T. W., Tranel D., Kirschbaum C. (2009). Hippocampal damage abolishes the cortisol response to psychosocial stress in humans. Horm. Behav. 56, 44–50. 10.1016/j.yhbeh.2009.02.011

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# 5. CONCLUSIONS

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# Thanks

My mission in life is not merely to survive,
But to thrive; and to do so with some passion,
Some compassion, some humor, and some style.

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