Pregnenolone supplementation

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Info in this presentation => Pregnenolone

Pregnenolone: General info

Anamnesis: Actual complaints of pregnenolone deficit

Physical exam => Physical signs

Low pregnenolone levels assoc. with disease

Lab tests => Serum, 24-hour urine

Pregnenolone supplementation

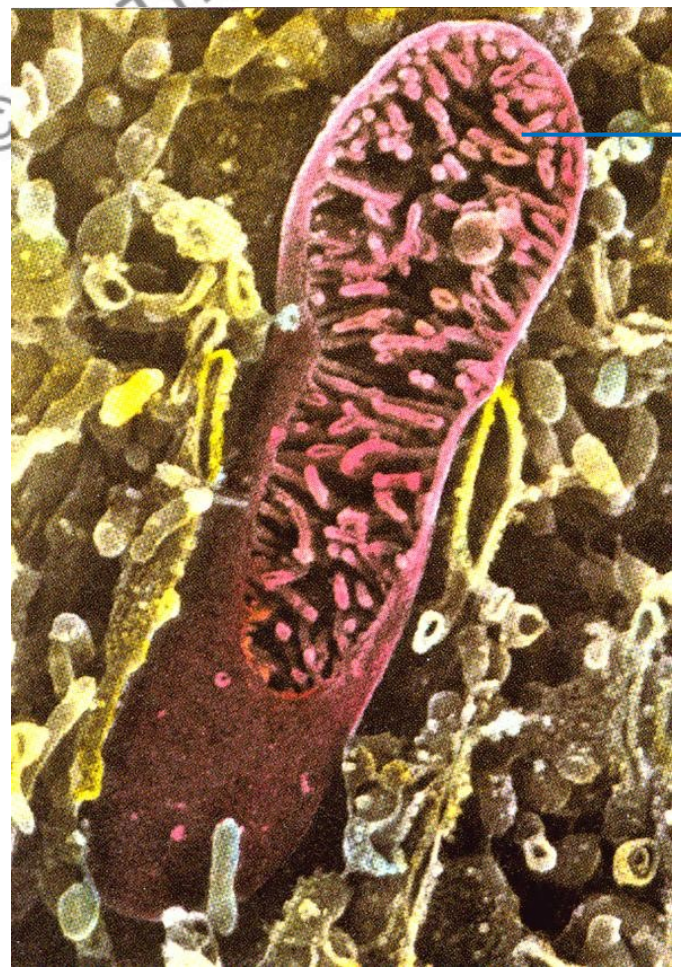
Diseases

Pregnenolone

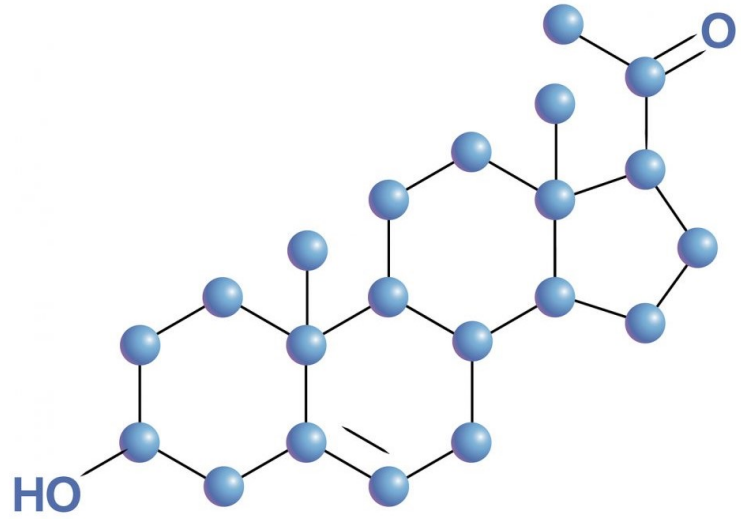
=> Origin

Mitochondria => produce steroid hormones, incl. pregnenolone

Mitochondrium

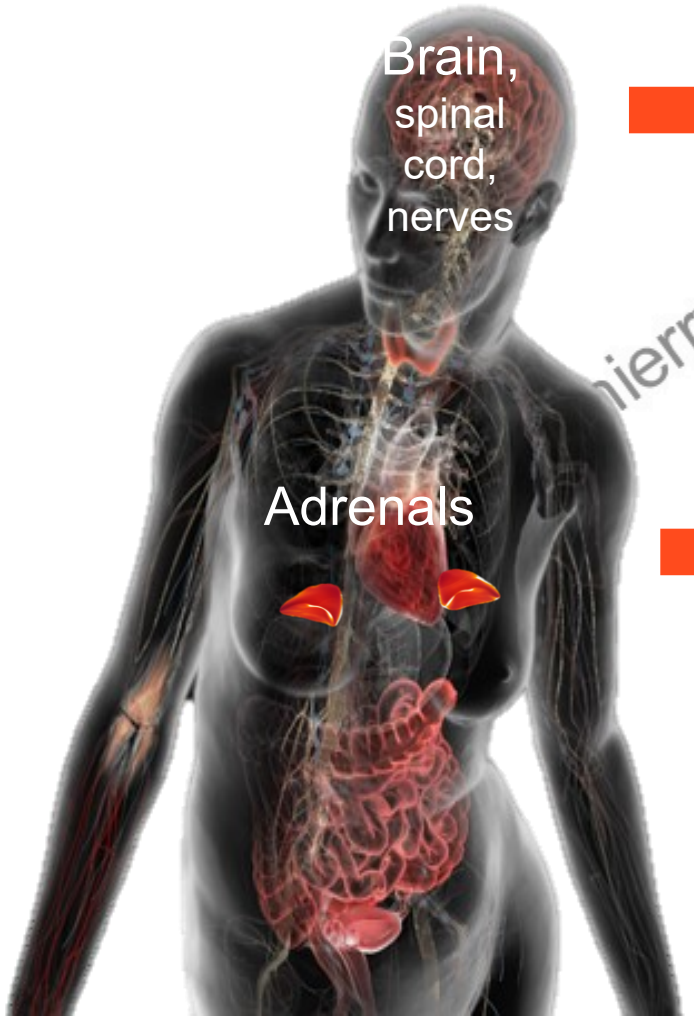


Pregnenolone



synthesized from cholesterol

Pregnenolone production sites



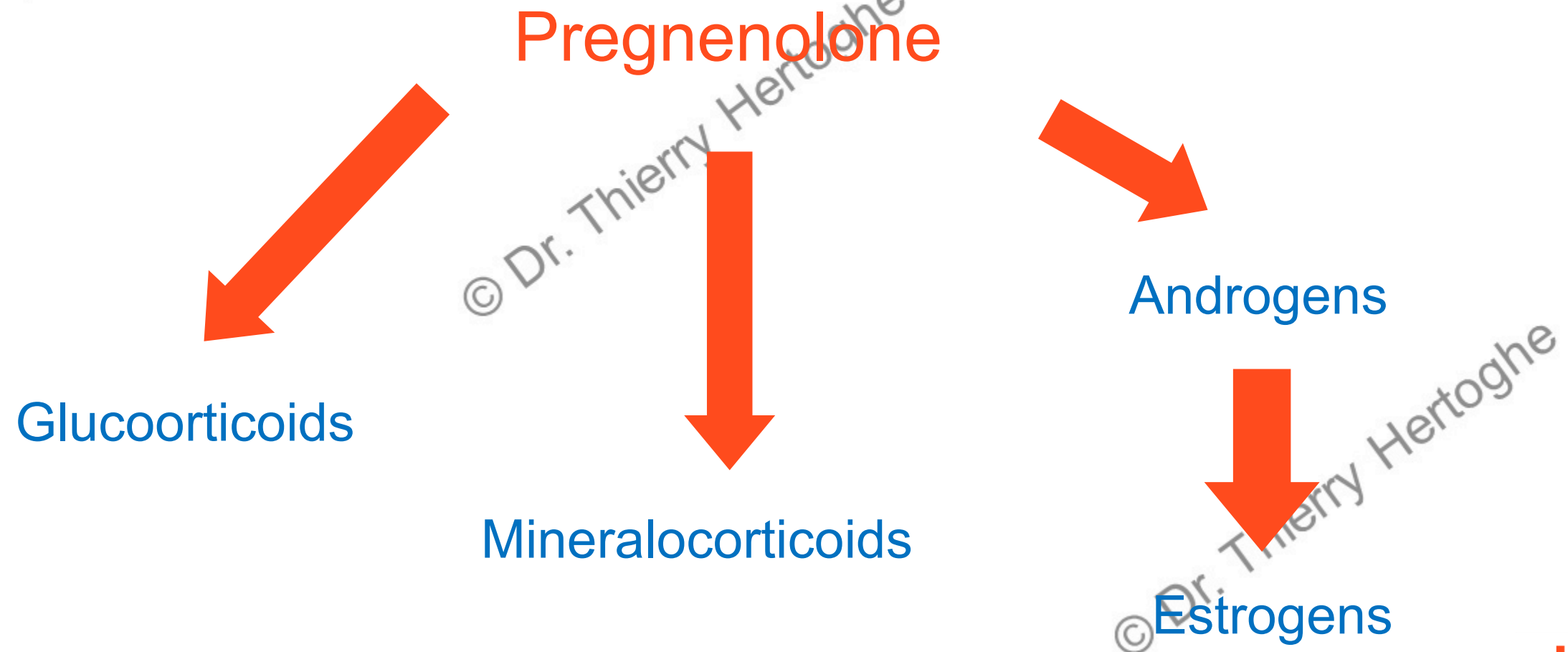
Pregnenolone

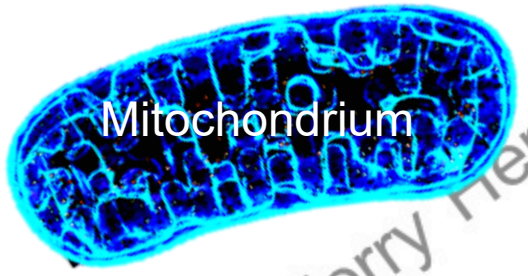
Pregnenolone

Pregnenolone

A major precursor?

Pregnenolone = Precursor to adrenal & sex hormones





Cholesterol

Pregnenolone

= mother hormone

Progesterone

DHEA

Androstenedione

Estrone

Testosterone

Estradiol

Aldosterone

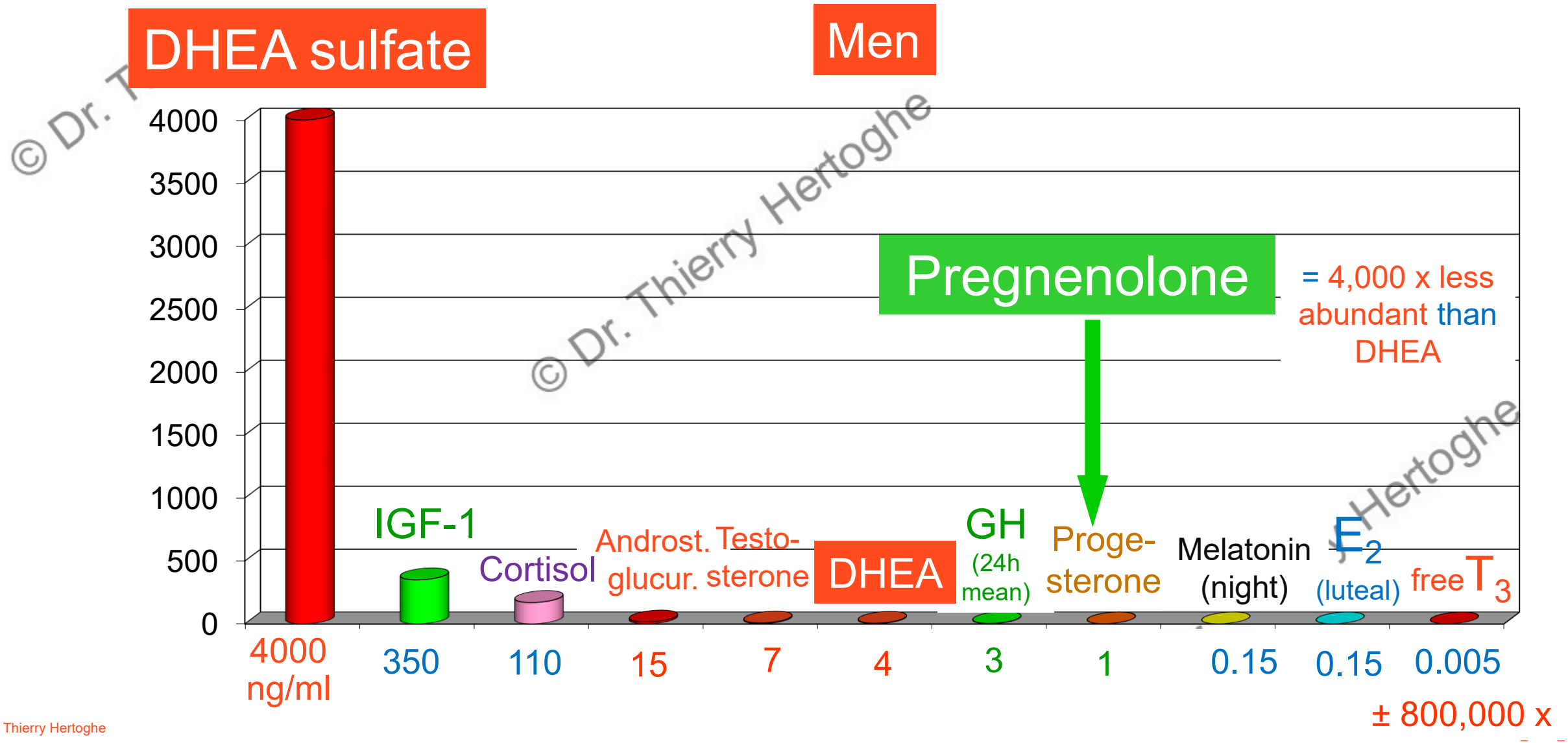
Cortisol

Dihydrotestosterone

Pregnenolone levels

How abundant in blood?

Serum pregnenolone levels in men

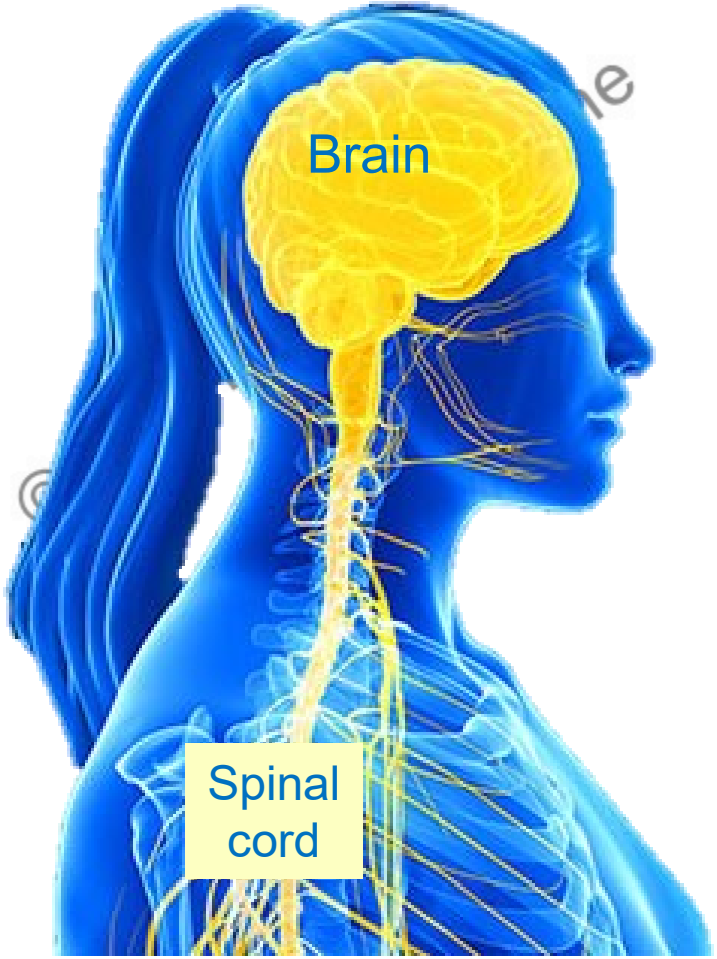


Pregnenolone levels

=> Abundant in the brain

Pregnenolone = Neurosteroid

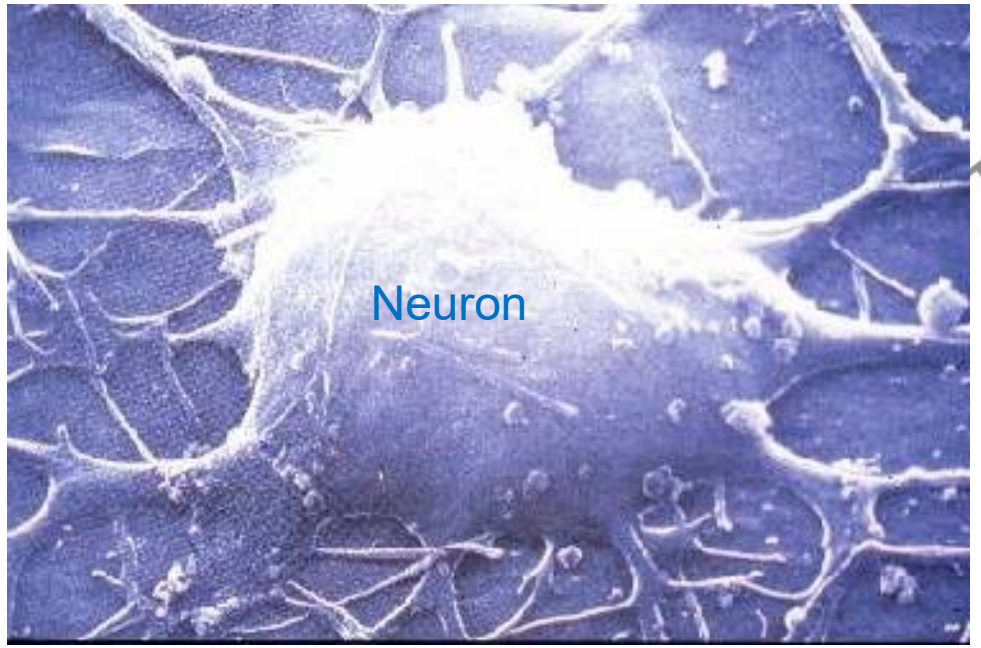
Pregnenolone = synthesized in



= Neurosteroid

Peripheral nerves

Pregnenolone = neurosteroid



Pregnenolone = synthesized in the

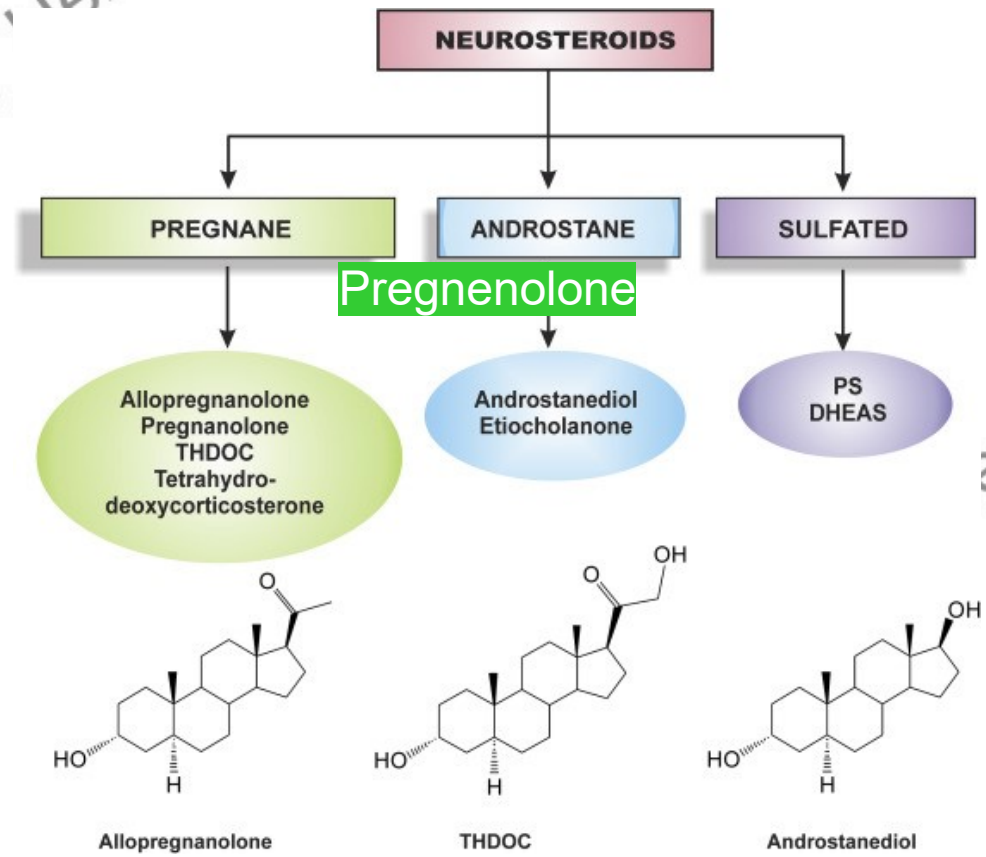
mainly by:

- neurons
- macroglial cells, incl. astrocytes
- oligodendroglial cells
- Schwann cells

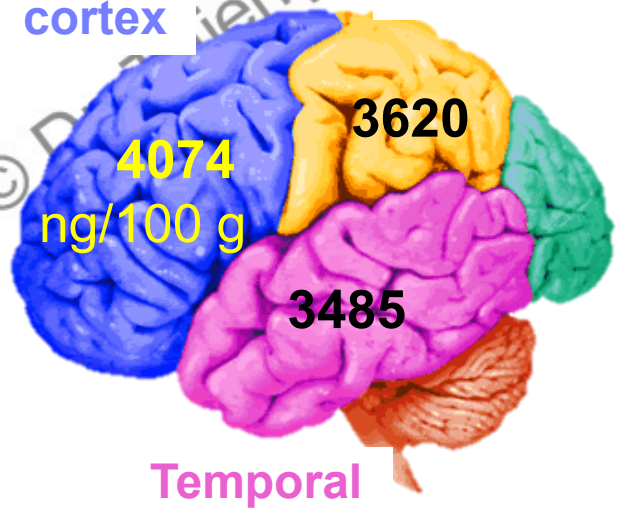
Pregnenolone = neurostimulating “neurosteroid”

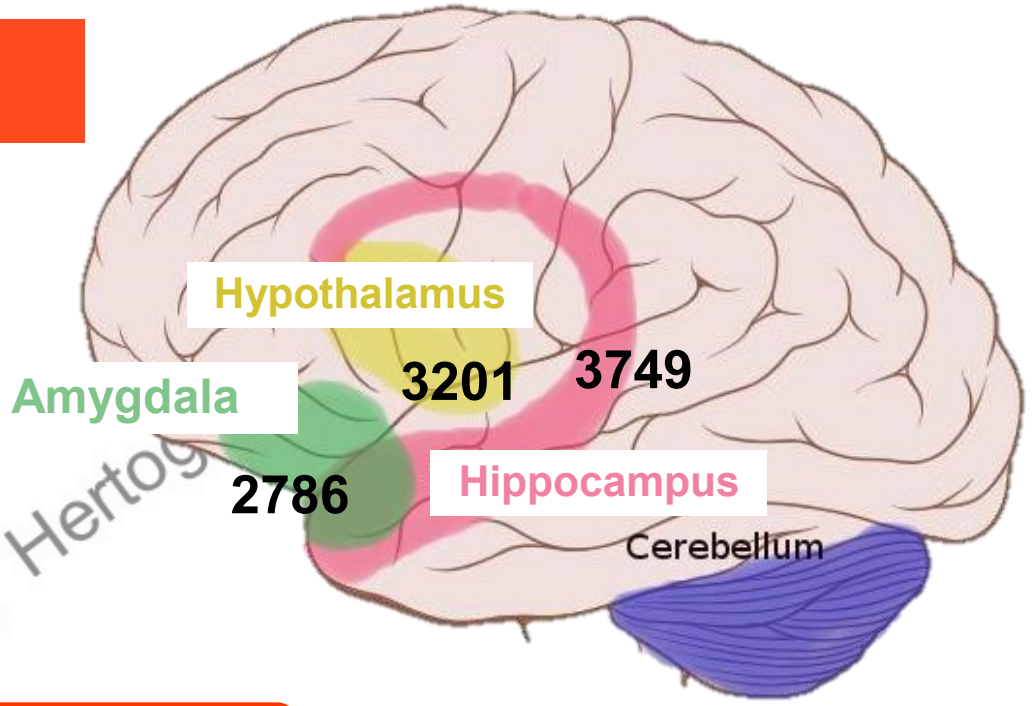
Pregnenolone = Neurosteroid

= Steroids synthesized in the nervous system



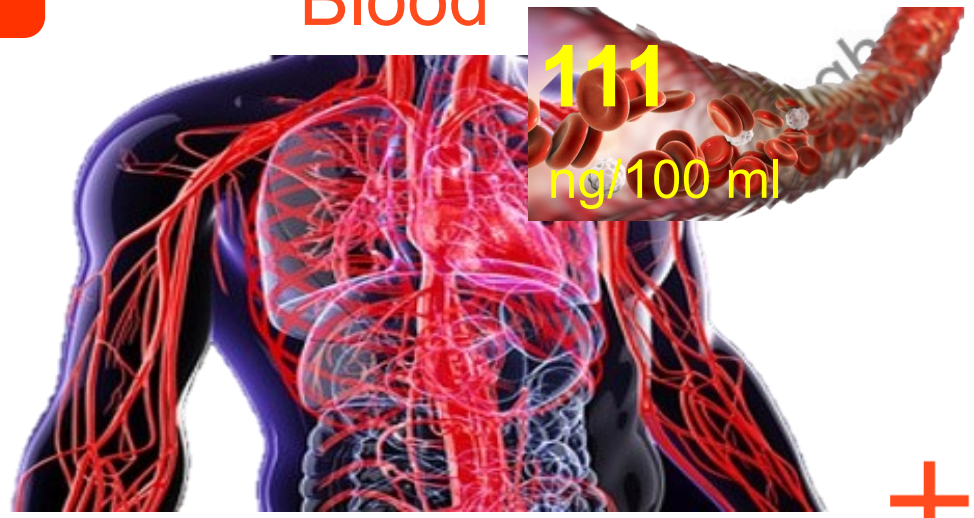
Brain Pregnenolone





25x to 35x ↑ levels in brain than in blood

Blood



Pregnenolone in several regions of human brain *(Lanthier A et al., J Steroid Biochem, 1986, 25: 445-449)*, comparison w/ blood levels *(Roberts E et al., 1990, in the Biological Role of DHEA, eds Kalimi M & Regelson W (de Gruyter, Berlin), p 43-63)*

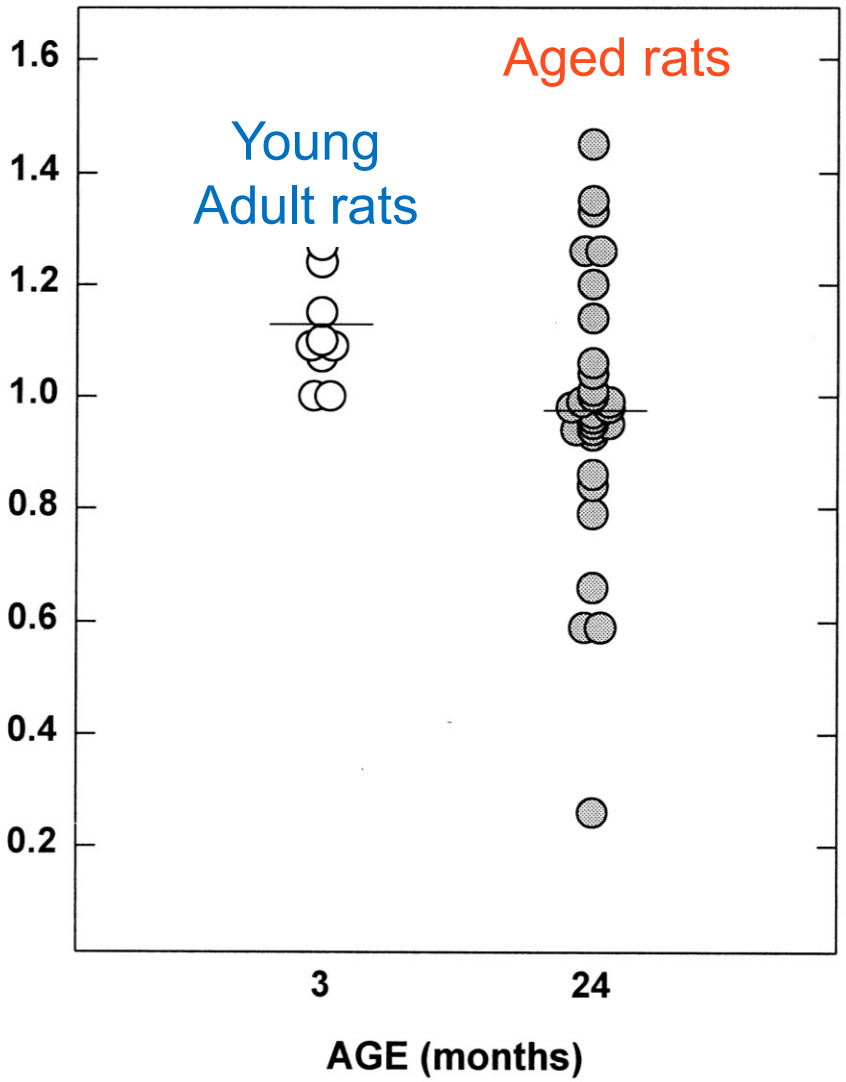
Pregnenolone levels

Aging => Progressive ↓

Aging => ↓ Pregnenolone sulfate in the hippocampus aged rats

Pregnenolone sulfate Levels

(log ng/g tissue)



Pregnenolone sulfate levels (log ng/g tissue) in the hippocampus of young adult (3 month old, *n* = 12) & aged (24 month old, *n* = 28) rats

Valleacute, Monique et al. (1997) Proc. Natl. Acad. Sci. USA 94, 14865-14870

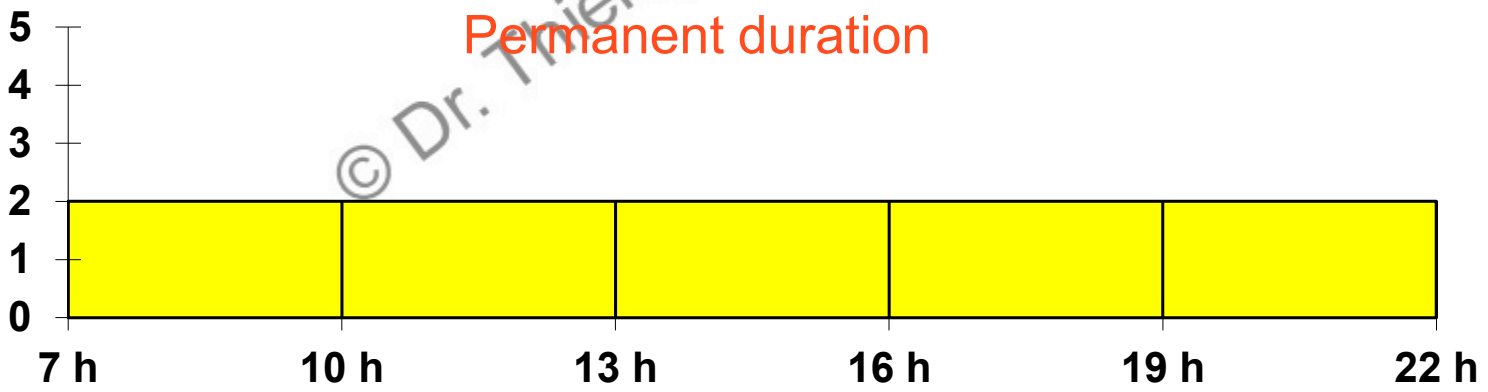
Pregnenolone deficiency: Diagnosis

Pregnenolone deficiency

=> Complaints

Complaints due to ↓ pregnenolone

↓ Pregnenolone



Pregnenolone deficiency

Attention difficulties

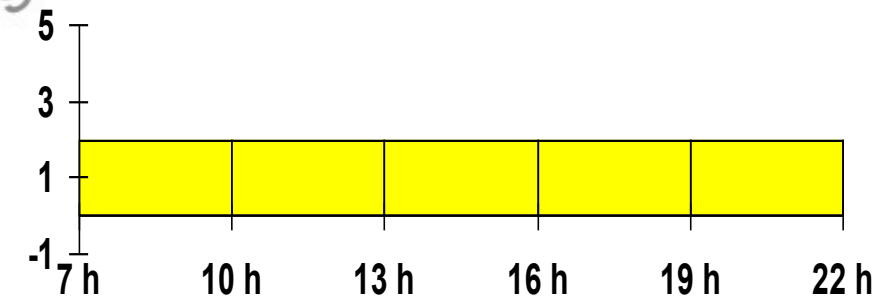
Memory loss

Distraction

Pregnenolone deficiency

Memory loss

Permanent:



Short –term: when you think your memory loss is due to

- being too busy
- or not sufficiently interested to memorize things.

Memory loss

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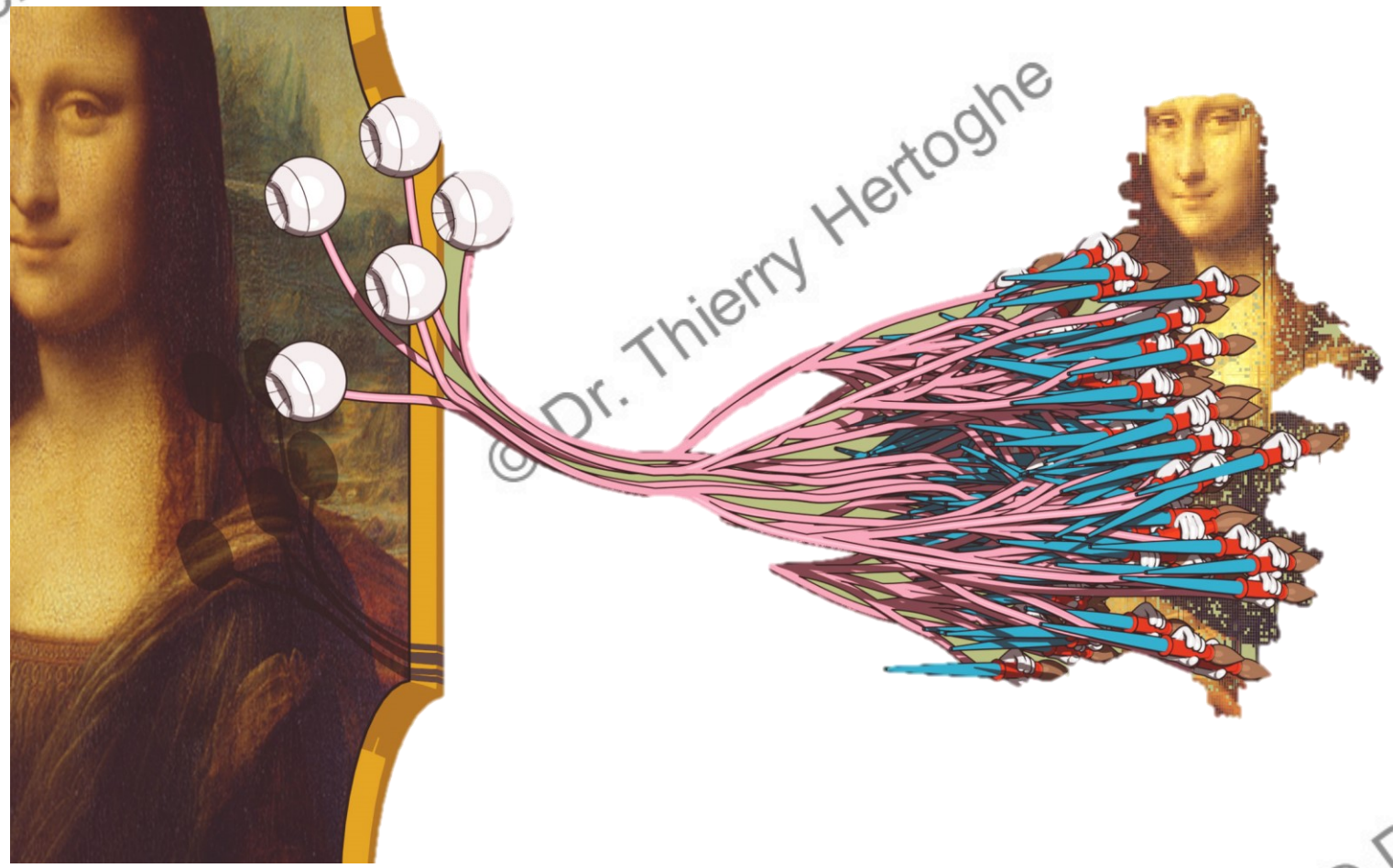
© Dr. Thierry Hertoghe

Pregnenolone deficiency

Loss of color vision & artistic perception



Preg may ↑ visual color vision & artistic perception *(Sayhelian, 1997)*

Pregnenolone deficiency

Anxiety

Pregnenolone deficiency

=> Physical signs

Pregnenolone deficiency = Physical signs

Physical signs of pregnenolone deficiency

= Signs of adrenal cortex & gonadal hormone deficiencies

Pregnenolone deficiency

Cortisol deficiency

Inflammation

Aldosterone deficiency

Low BP

Estrogen, Progesterone deficiencies

Sexual regression/underdevelopment

DHEA, Testosterone, DHT deficiencies

Dry skin, weak muscles

Physical signs of pregnenolone deficiency since childhood

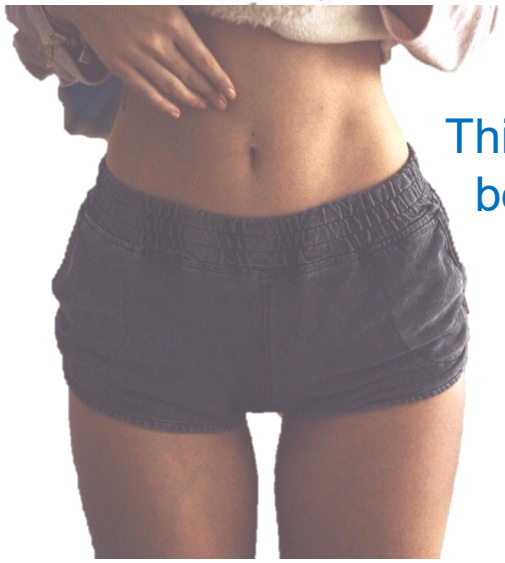
Pregnenolone deficiency since childhood => ↑ Severity of physical signs

Signs of

adrenal cortex hormone deficiencies

Since childhood

Thinner, narrower face



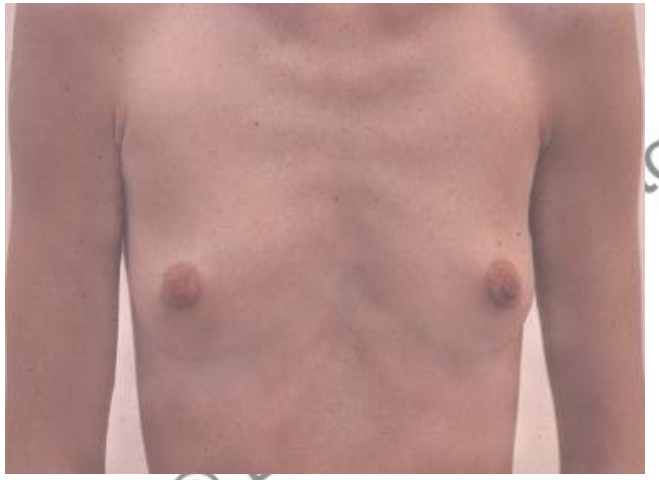
Thinner body

Signs of

sex hormone deficiencies

Since puberty

Sexual under-development



Pregnenolne deficiency appearing in adulthood => Often moderate physical signs

Pregnenolone deficiency appearing later during adulthood => More moderate physical signs

Signs of

adrenal cortex hormone deficiencies

Since adulthood

Fuller, larger face & body

may have become more hollow

Signs of

sex hormone deficiencies

Since adulthood (after puberty)

Muscle hypotrophy

Normal sexual development, but in regression

Pregnenolone deficiency

=> Complaints & Physical signs: Summary

Pregnenolone deficiency => Complaints & Physical signs

Mental & psychological complaints

- Attention deficit, lack of concentration
- Distraction
- Short-term memory loss, too busy or not sufficiently interested to remember
- Anxiety
- ↓ Color vision
- ↓ Artistic perception

Physical signs of adrenal cortex hormone deficiencies

- Thin face & underweight body
- Pigment spots, dark circles under the eyes
- Low BP
- Armpit & pubic hair loss, etc.

Physical signs of sex hormone deficiencies

- Sexual underdevelopment or regression
- Muscle loss
- Premature aging, etc.

↓ Pregnenolone levels

=> ↑ Disease

↓ Pregnenolone levels

=> ↑ Attention deficit disorder

Attention deficit hyperactivity disorder => ↓ Serum pregnenolone

29 boys aged 7-15 yrs + DSM-IV criteria of attention deficit-hyperactivity disorder

Observational study

↓ Serum pregnenolone

↑ Symptoms of attention deficit hyperactivity disorder in all,

esp. evident in boys with less severe ADH disorder

(sign. inverse association)

Pregnenolone may protect against ADHD symptoms

Strous RD, et al. Int J Neuropsychopharmacol. 2001 Sep;4(3):259-64

↓ Pregnenolone levels

=> ↑ Anxiety disorder

Generalized anxiety disorder => ↓ Serum pregnenolone sulfate

8 Men with generalized anxiety disorder

vs 8 healthy control men

Sign. ↓ serum pregnenolone sulfate

Semeniuk T, al. J Neuropsychiatry Clin Neurosci. 2001 Summer;13(3):396-8

Pain

=> ⬇ Pregnenolone

Severe pain => ↓ Serum pregnenolone

50 patients with severe, constant pain

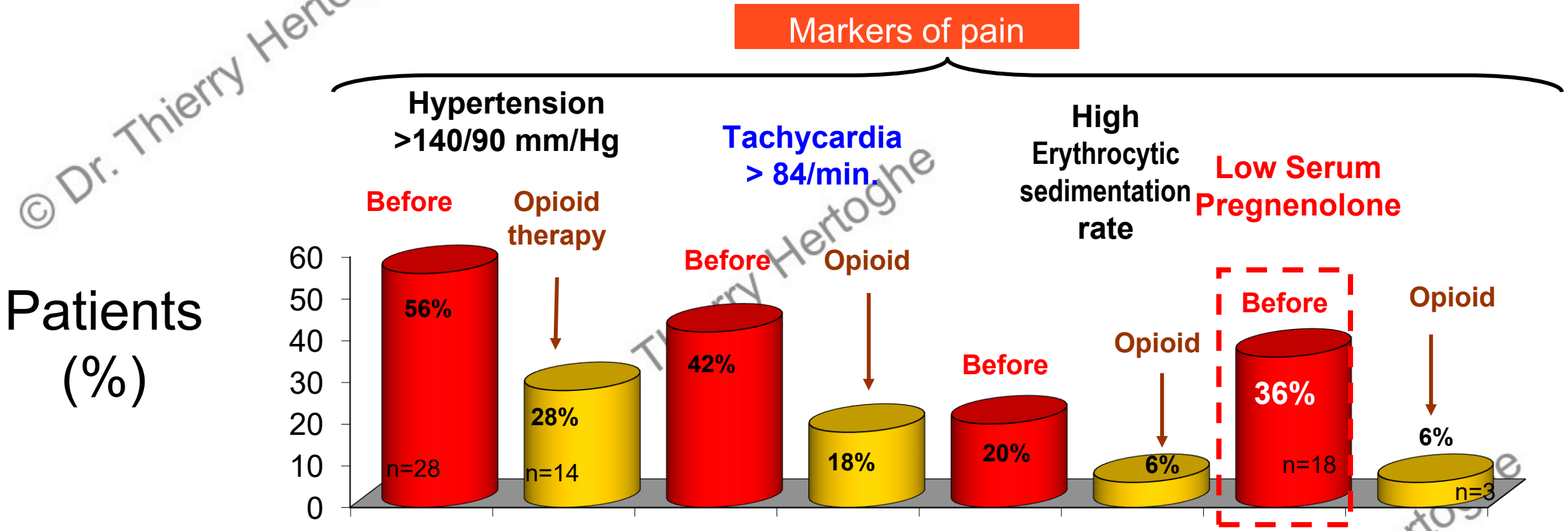
Severe, intractable pain

↓ Serum pregnenolone

= marker of pain

[No authors listed] Physiologic abnormalities as biologic markers in severe, intractable pain. Pain Med. 2002 Jun;3(2):183-184

↓ Serum pregnenolone = Biological marker of pain



Mean blood pressure, pulse rate, ESR, & pregnenolone that were abnormal in many patients with constant, excruciating pain demonstrated positively & sign. ($p<.05$) improvement under 3 months combined short- & long-acting painkillers.

Pain Med. 2002 Jun;3(2):183-184

↓ Pregnenolone levels

=> ↑ Alzheimer’s disease

Alzheimer's disease => ↓ Serum pregnenolone

6 Alzheimer patients

Alzheimer patients

↓

vs healthy older adults

2.5x ↓ Serum pregnenolone

(43.6 vs 111 ng/ml)

All Alzheimer patients => ↓ pregnenolone levels than the control group

Roberts E et Fitten LS, 1990, in the Biological Role of DHEA, eds Kalimi M & Regelson W (de Gruyter, Berlin), p 43-63

Alzheimer's disease => ↓ Brain pregnenolone

Alzheimer patients

↓

vs non-demented contrls

-20 to – 90% ↓ Brain pregnenolone levels

↓

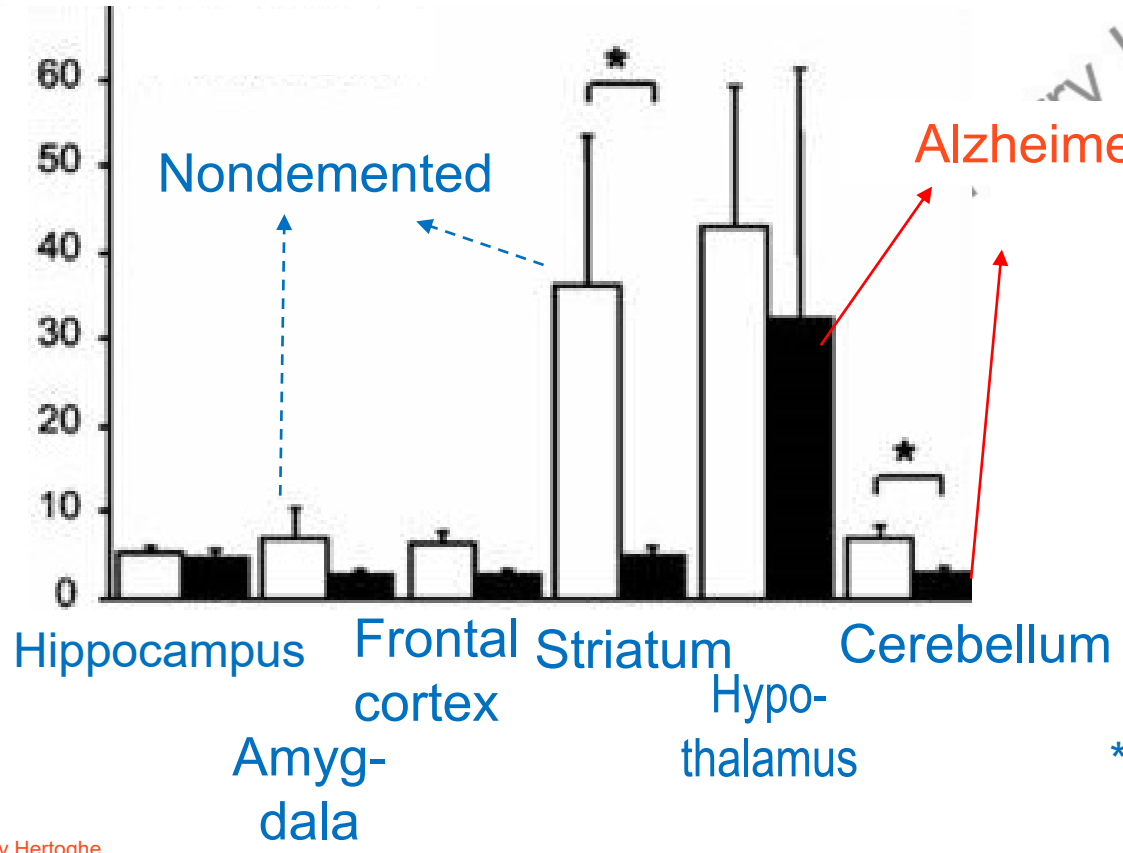
↓ Striatum & cerebellum pregnenolone sulfate levels
=> ↑ beta-amyloid peptide levels in the brain cortex
(significant negative correlation)

Weill-Engerer S, et al. J Clin Endocrinol Metab. 2002 Nov;87(11):5138-43

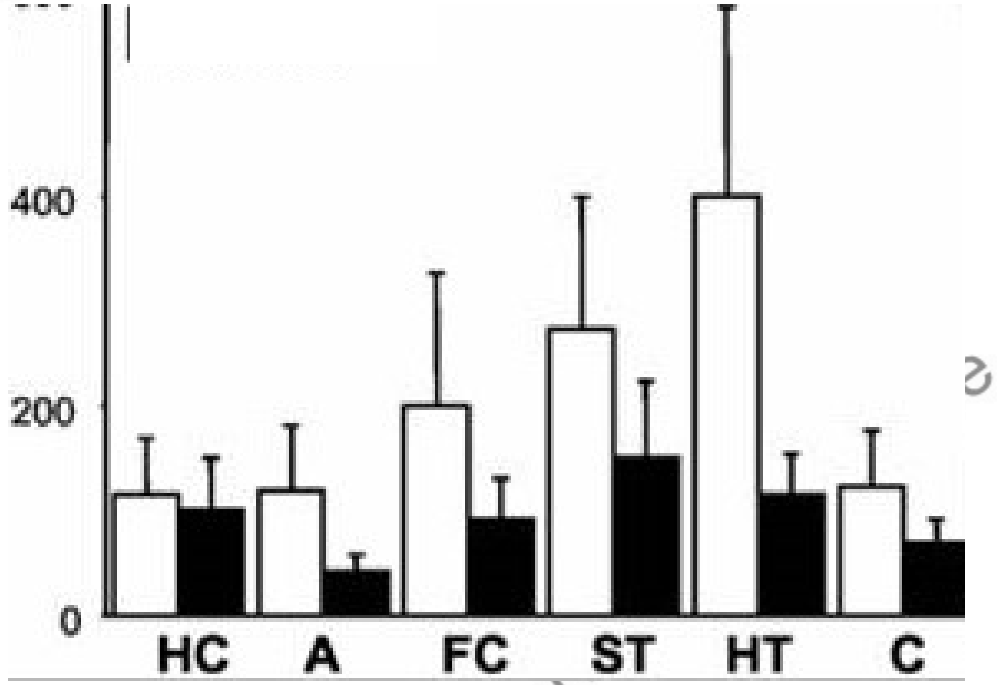
Alzheimer's disease => ↓ Brain pregnenolone (sulfate)eg s

↓ levels of pregnenolone in 6 brain regions of Alzheimer disease patients compared to non-demented.

Serum pregnenolone sulfate



Serum Pregnenolone



*, $P < 0.05$

Weill-Engerer S, et al. J Clin Endocrinol Metab. 2002 Nov;87(11):5138-43.

Lab tests

for pregnenolone

Pregnenolone lab tests

Blood

24h urine

Pregnenolone deficiency

=> Serum tests

© Dr. Thierry Hertoghe

Pregnenolone deficiency => Serum

→ Serum pregnenolone sulfate

Optimal: 100 ng/mL

Deficiencies: 0 - 70

Ref.: 4 – 120 ng/mL

Pregnenolone deficiency => Serum

→ Serum pregnenolone

= 50x ↓ concentration than serum pregnenolone sulfate

Optimal: 150 ng/dL= 1.5 ng/mL

Deficiencies: 0 - 80

Ref.: 0.1-2 ng/mL

Pregnenolone deficiency

=> 24-hour urine tests

© Dr. Thierry Hertoghe

Pregnenolone deficiency

24h urine pregnantriol = pregnenolone metabolite

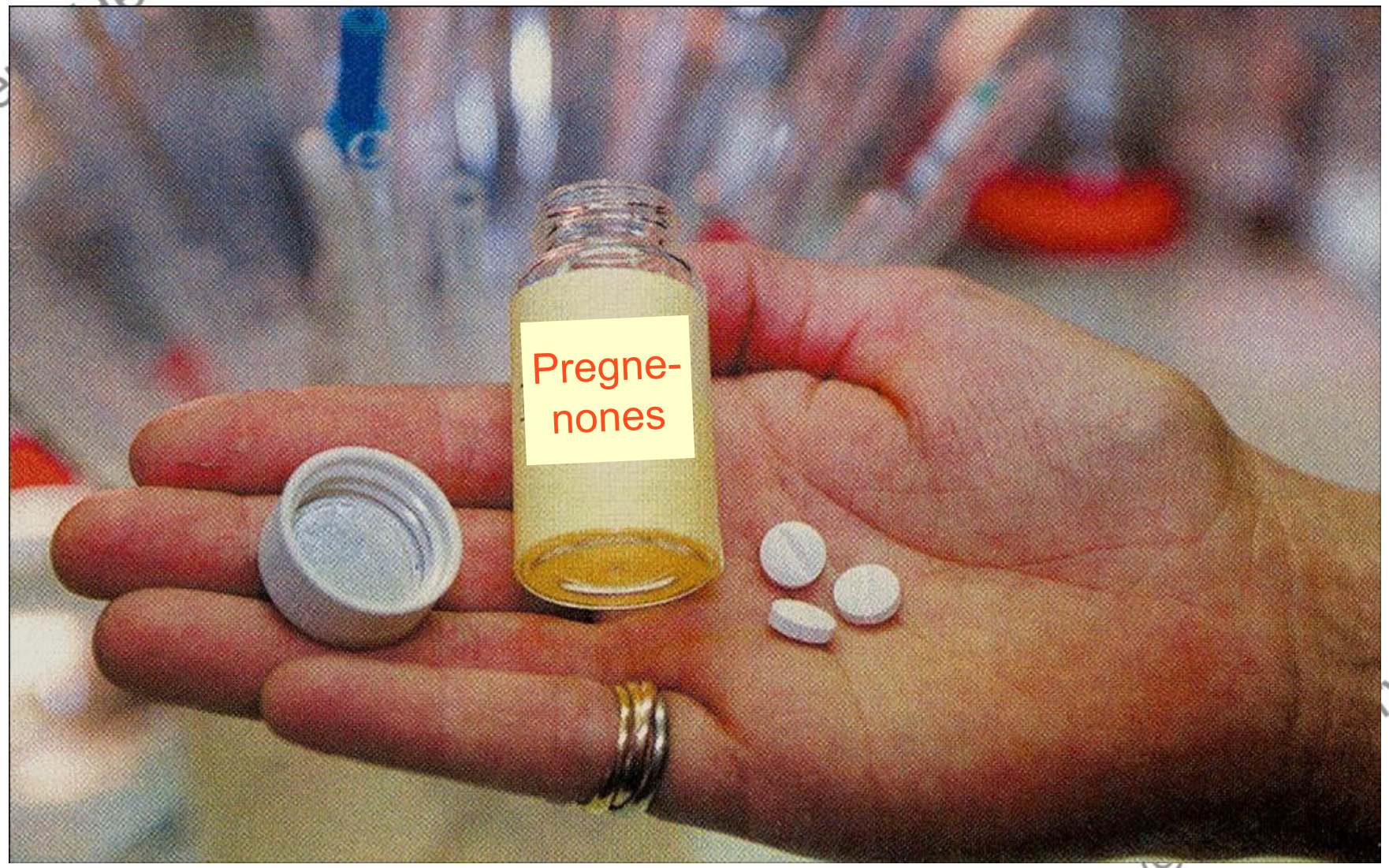
Optimal: 1 mg/g creatinine

Deficiencies: 0-0.7

Ref.: 0.4-1.1 mg/g creatinine

Pregnenolone supplementation

Pregnenolone supplementation



Pregnenolone treatment

Oral, sublingual

Pregnenolone therapy => Doses

Pregnenolone supplementation:	Dose
Pregnenolone deficiencies	
• Small children	10 mg / day
• Adolescents	25 mg / day
• Adults	50 mg / day
• Severe memory loss	100-150 mg / day

To take upon awakening

Pregnenolone treatment

=> To improve short-term memory

Pregnenolone treatment

Pregnenolone Oral

- 100 mg/day in the upon awakening during 4 months, then 50 mg/day orally
- Slow progress: improvement of short-term memory after 3-4 months in ± 3 on 4 patients

Pregnenolone treatment

=> Speed of memory improvement

How long before first improvement with hormone therapy?

Memory improvement

	First improvement	Last improvement
Cortisol	24 hours	2-3 months
Pregnenolone	2-4 months	6 months
Thyroid	2-4 months	8-12 months
Testo E2	2-4 months	8-12 months
GH	2-4 months	12-36 months
DHEA	4-6 months	8 months

Pregnenolone at 30-50 mg/day

=> Well-tolerated

Pregnenolone at 30 mg/day

Pregnenolone

at 30 mg/day

= well tolerated,

Meieran SE, et al. Psychoneuroendocrinology. 2004 May;29(4):486-500

Pregnenolone treatment

=> Problems

Doesn't work, no difference

- Cause:

1. Insufficient dose

- Treatment :

1. ↑ dose of pregnenolone

Pregnenolone at 30 mg/day

Pregnenolone

at 30 mg/day

= well tolerated,

but may be too low to improve memory

Meieran SE, et al. Psychoneuroendocrinology. 2004 May;29(4):486-500

Pregnenolone at 50 mg/day

Pregnenolone

at 50 mg/day

= efficient to improve memory

Doesn't work, no difference

Cause:

1. Insufficient dose
2. Intake in the evening
3. Inactive brand
4. Intestinal malabsorption (bloating belly, loosy stools, diarrhea)

Treatment:

1. ↑ Pregnenolone dose
2. Take preg in the morning
3. Change brand, control levels of pregnenolone
4. Correct digestion: better food choice (Paleo diet, void milk products, sweets & cereals)

Oily skin

Cause:

- Overdose: doses ≥ 200 mg/day
- Pregnenolone excess with excessive conversion to androgens => excessively stimulate the sebum secretion => oily skin

Treatment:

↓ Pregnenolone dose

Pregnenolone supplementation

=> Benefits on diseases

Pregnenolone supplementation

=> ↑ Short term Memory in humans

(visual & spatial)

8 weeks of 50 mg/day Preg => ↑ Memory & visual attention in schizophrenia

60 patients with schizophrenia

Pregnenolone 50 mg/day for 8 weeks

vs initial condition

- Sign. ↓ deficits in visual attention measured with the Matching to Sample Visual Search task (p=0.002), with moderate effect sizes (d=0.42)
- Sign. ↓ deficits in sustained attention (Rapid & Information Processing, p=0.038)
- Sign. ↑ executive functions (Stockings of Cambridge, p=0.049)
- Sign. ↑ spatial working memory (p<0.001)

- Placebo: No improvements among subjects

Kreinin A, Bawakny N, et al. Winter 2017;10(4):201-210

8 weeks of 500 mg/day Preg => ↑ Memory in schizophrenia

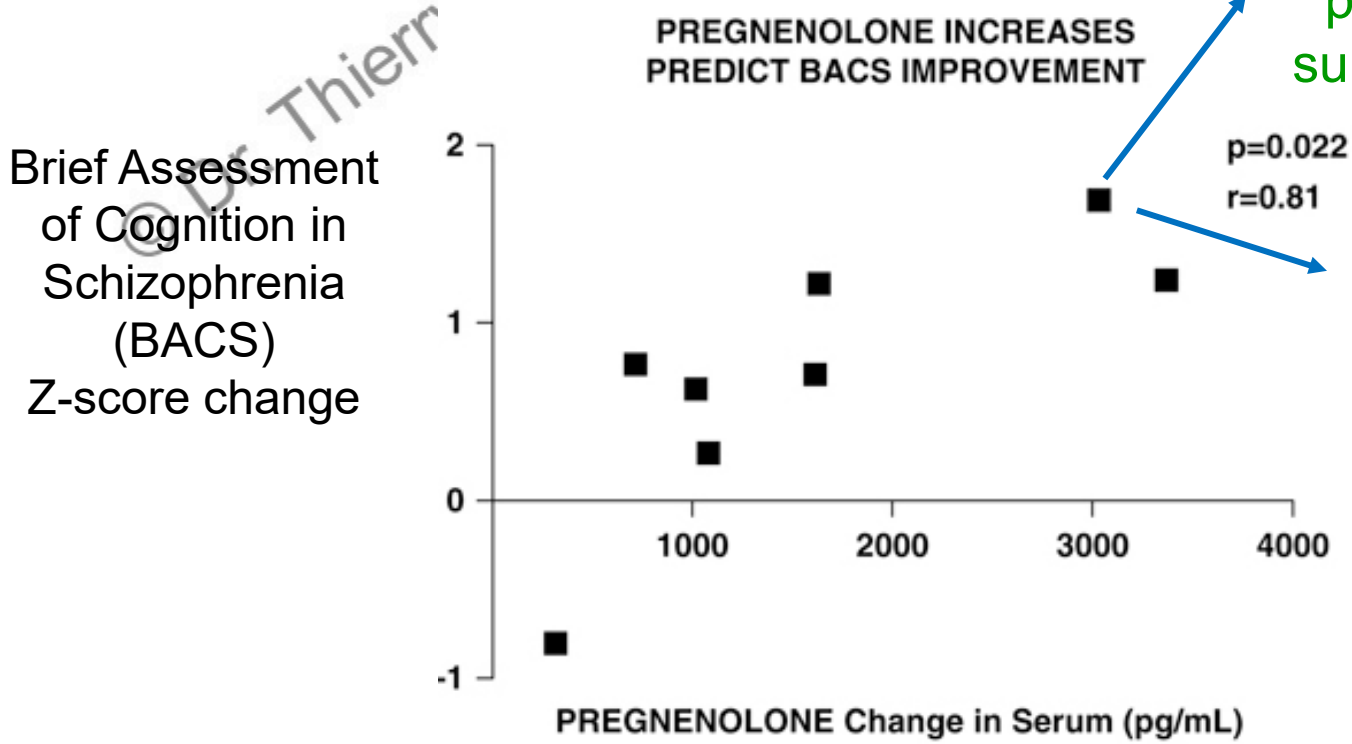
18 patients with schizophrenia

Pregnenolone fixed escalating doses to 500 mg/day for 8 weeks (9 patients)

vs placebo (9 patients)

Sign. ↑ cognition

↑ Serum pregnenolone with pregnenolone supplementation



Brief Assessment of Cognition in Schizophrenia (BACS) Z-score change

↑ BACS scores at 8 weeks (p=0.022)

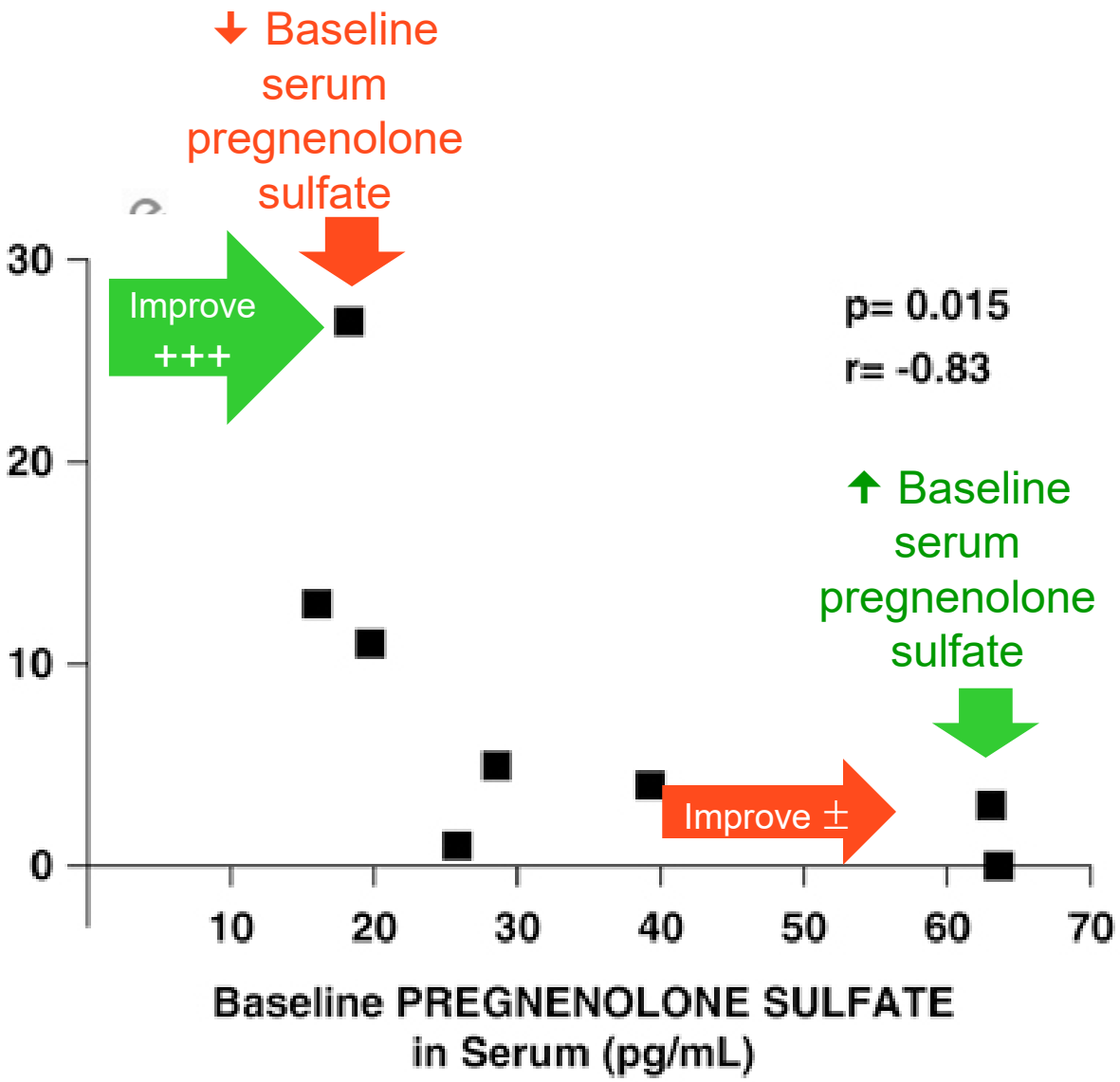
Marx CE, et al. Neuropsychopharmacology. 2009 Jul;34(8):1885-903

8 weeks of 500 mg/day Preg => ↑ Memory & visual attention in schizophrenia

18 patients with schizophrenia

↓ Baseline serum pregnenolone & pregnenolone sulfate

↑ Improvements in cognition with pregnenolone supplementation (improvements in Matrics Consensus Cognitive Battery (MCCB) composite scores, sign. Inverse associationP: (r(s)=-0.76, p=0.037), PS: (r(s)=-0.83, p=0.015))



Marx CE, et al. Neuropsychopharmacology. 2009 Jul;34(8):1885-903

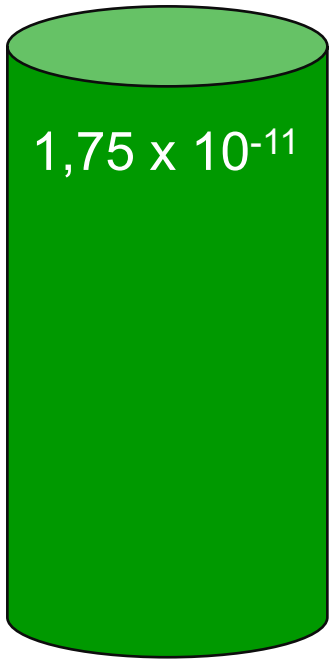
Pregnenolone supplementation

=> ↑ (Short-tem) memory in animals

Pregnenolone => ↑ Memory

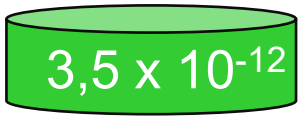
Doses sufficient to reverse the amnesia caused by DMSO?

Testosterone



DHEA

5x ↓ dose



Pregnenolone

500x ↓ dose → Pregnenolone shows ↑ efficacy

3,5 x 10-14

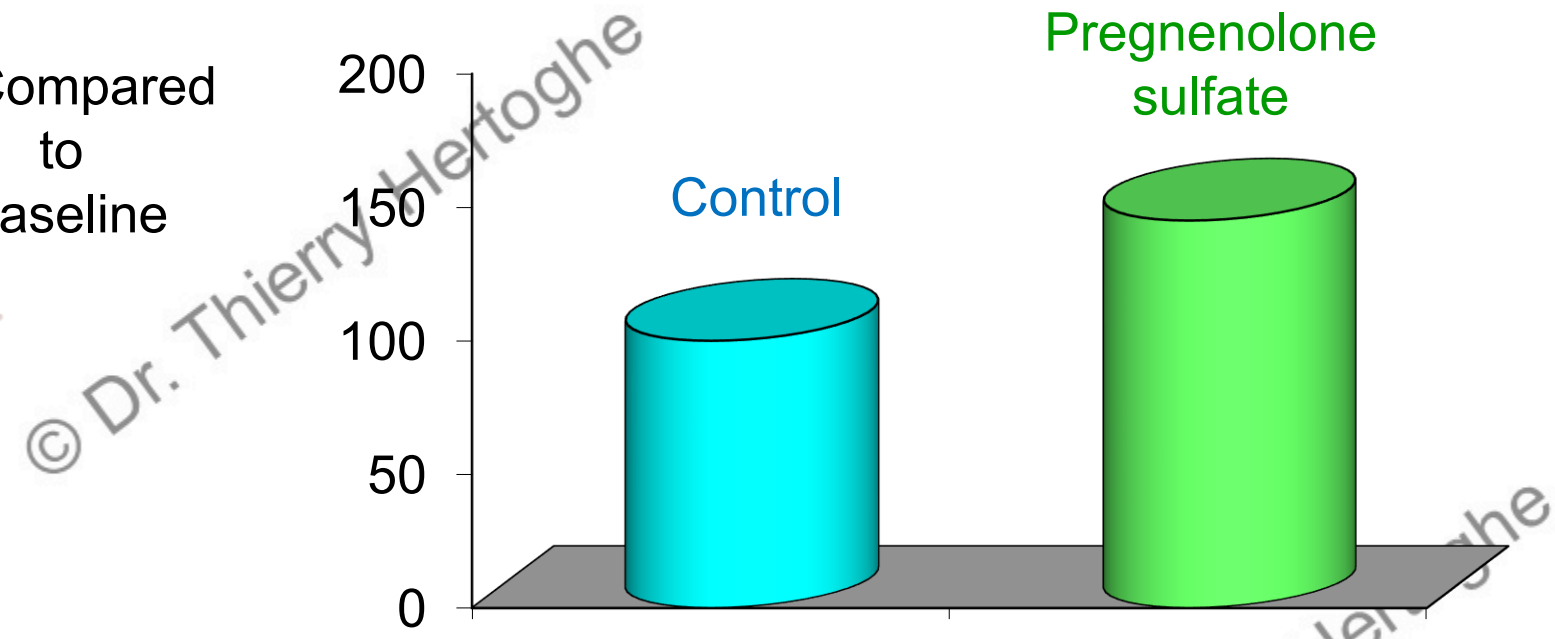
Flood JF et al., Proc Natl Acad Sci USA, 1992, 89: 1567-71

Pregnenolone supplementation

=> ↑ Spatial memory

Pregnenolone sulfate => ↑ Spatial memory in rats

Spatial memory
(recognition of familiar environment)



Pregnenolone sulfate infusion into the rat medial septum improved recognition memory of a familiar environment. The septo-hippocampal pathway could be involved in preg's promnesic properties.

Darnaudery M, et al.. Brain Res. 2002;951(2):237-42

Pregnenolone

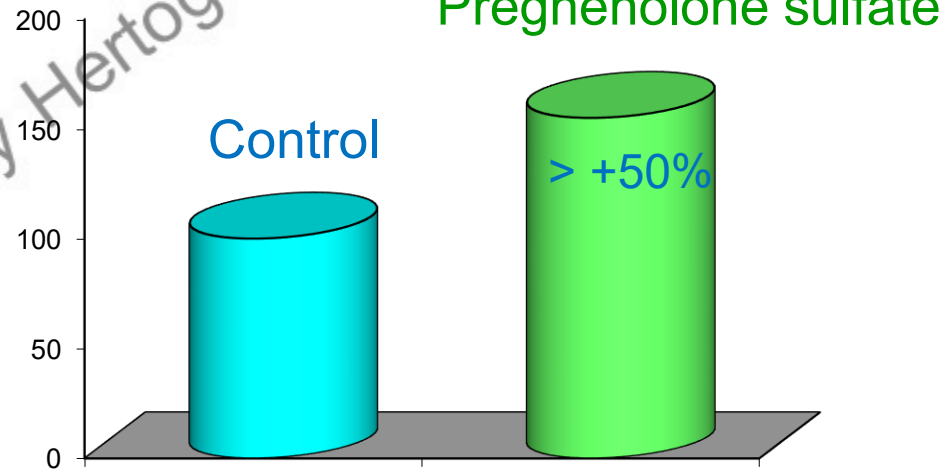
(Mechanisms of memory enhancement)

=> ↑ Acetylcholine in hippocampus

Pregnenolone sulfate => ↑ Acetylcholine in hippocampus of rats

% Compared to baseline

Acetylcholine release
in hippocampus



Pregnenolone sulfate infusion into the rat medial septum ↑ acetylcholine release by >50% of baseline . The septo-hippocampal pathway could be involved in preg's promnesic properties.

Darnaudery M, et al. Brain Res. 2002;951(2):237-42

Pregnenolone

(Mechanisms of memory enhancement)

=> ↑ Arousal, & thus attention

Pregnenolone => ↓ Sedation by Benzodiazepines

11 adults + single dose

of diazepam (0.2 mg/kg)

± 14 mg for
70 kg person

4-wks' of with 30 mg/day pregnenolone (5 adults)

vs 6 aduylts + placebo

Pregnenolone pretreatment:

1. Signif. ↓ diazepam's sedation ($p<0.03$) => clinical. apparent
2. Non-signif. ↓ diazepam's amnesia
3. No effect on anxiety ratings

Chronic treatment with pregnenolone may:

1. Antagonize certain acute effects of BNZ
2. ↑ Arousal via antagonist or inverse agonist actions at the benzodiazepine/GABA(A) receptor complex

Meieran SE, Reus VI, et al. 2004 May;29(4):486-500.

Pregnenolone

(Mechanisms of memory enhancement)

⇒Protects neurons

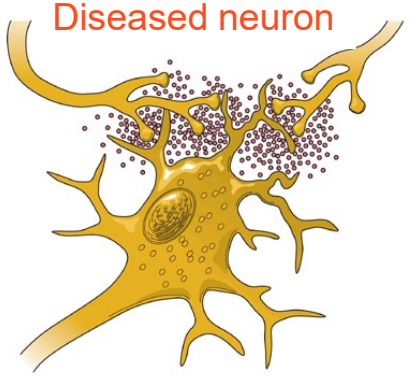
⇒↓ Amyloid-beta & glutamate neurotoxicity

Pregnenolone => protects mice hippocampal neurons against cell death & ↓ nuclear glucocorticoid receptors

Glutamate

↓

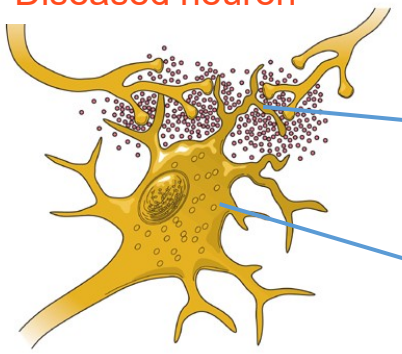
Diseased neuron



Amyloid Beta protein

↓

Diseased neuron



Hippocampal neurons from mouse origin

24 hrs: Pregnenolone pretreatment (500 nM)
=> 20 hrs: glutamate or amyloid beta protein

↓

Neuro-protective

↓↓ Neuron death

↓↓ Nucleus (glutamate toxicity)
↑↑ glucocorticoid receptors

Gursoy E, et al. Neurochem Res. 2001 Jan;26(1):15-21

Pregnenolone supplementation

=> ↓ Anxiety

1x 400 mg/day Preg => ↓ Anxiety in healthy adults

31 healthy adults

Pregnenolone 1x 400 mg/day (16 patients)

↓

vs placebo (15 patients)

↓

Sign. ↓ self-reported anxiety

↓

↑ Serum allopregnanolone

↓

↑ Connectivity between the amygdala & dorsal medial prefrontal cortex, an effect => ↓self-reported anxiety

Sripada RK, et als. Biol Psychiatry. 2013 Jun 1;73(11):1045-53

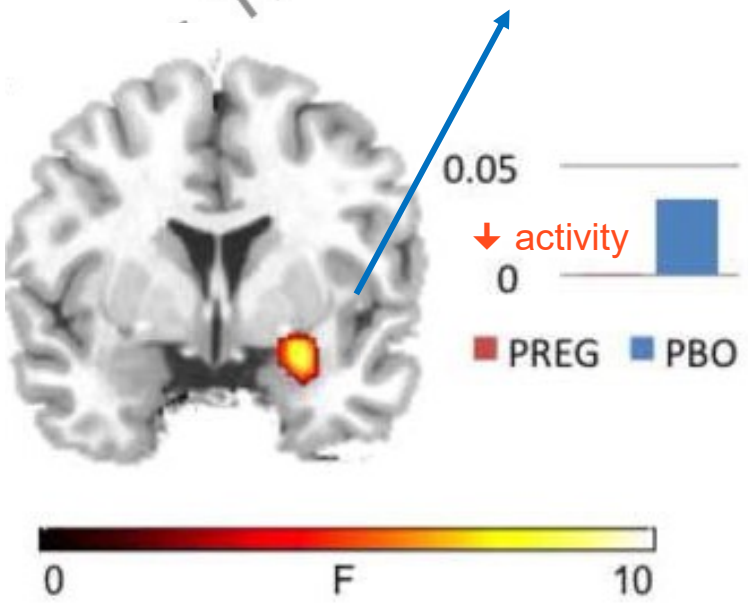
1x 400 mg/day Preg => ↓ Anxiety in healthy adults

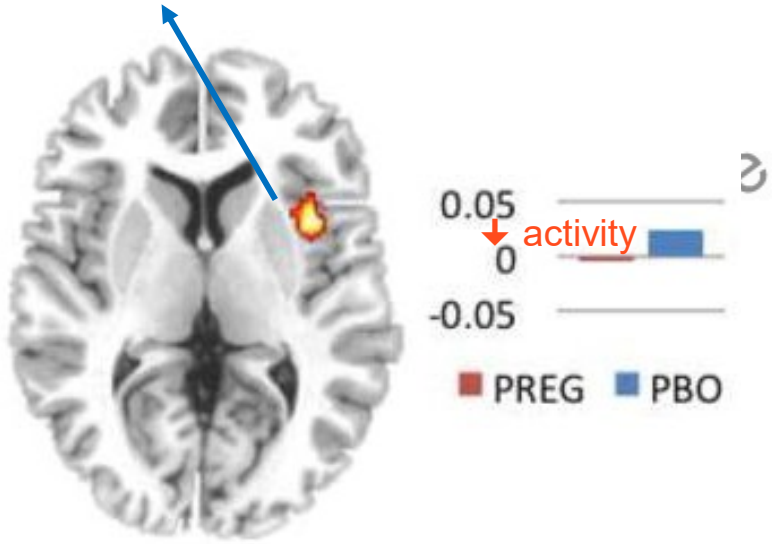
31 healthy adults

Pregnenolone 1x 400 mg/day (16 patients)

vs placebo (15 patients)

Sign. ↓ activity in right amygdala & right insula
across all conditions (vs placebo)





Sripada RK, et als. Biol Psychiatry. 2013 Jun 1;73(11):1045-53

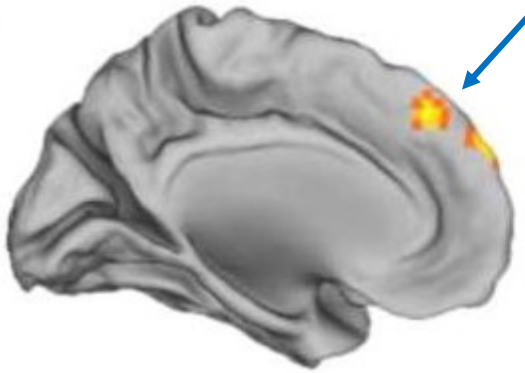
1x 400 mg/day Preg => ↓ Anxiety in healthy adults

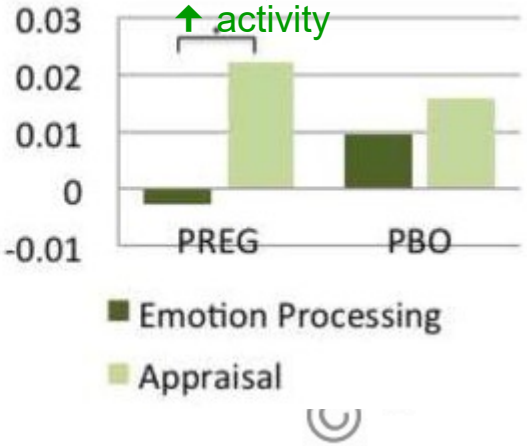
31 healthy adults

Pregnenolone 1x 400 mg/day (16 patients)

vs placebo (15 patients)

Sign. ↑ activity in the dorsal medial prefrontal cortex during appraisal





Sripada RK, et als. Biol Psychiatry. 2013 Jun 1;73(11):1045-53

12 weeks of 500 mg/day of Preg => ↓ Anxiety in bipolar disorder

73 patients with bipolar disorder (DSM-IV)

Pregnenolone titrated to 500 mg/day for 12 weeks

↓

vs placebo

↓

- Sign. ↓ anxiety

↓

- ↑ Serum pregnanolone levels
- ↑ serum allopregnanolone, a metabolite of pregnenolone ()

↓

Sign. baseline-to-exit ↓ Hamilton Rating Scale for Anxiety (HRSA) scores (negative correlations: r(22)=-0.48, p=0.019 & r(22)=-0.43, p=0.036, resp.)

Ritsner MS, et al. J Clin Psychiatry. 2010 Oct;71(10):1351-62

Pregnenolone

=> ↓ Depression

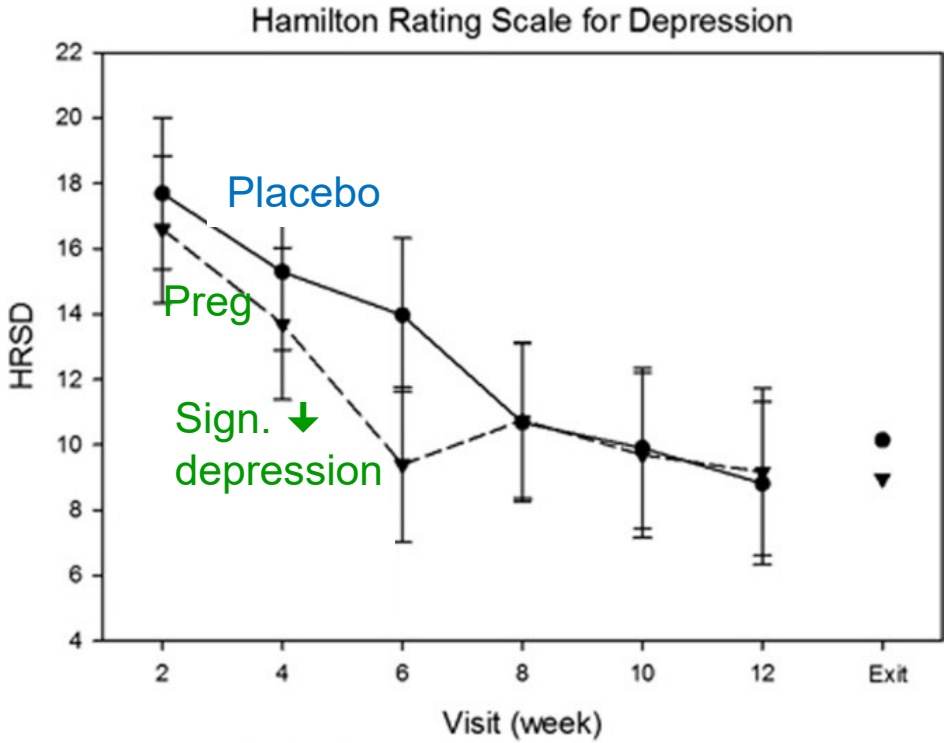
12 weeks of 500 mg/day of Preg => ↓ Depression in bipolar disorder

73 patients with bipolar disorder (DSM-IV)

Pregnenolone titrated to 500 mg/day for 12 weeks

↓ vs placebo

- Sign. ↓ depression (↓ the 17-item Hamilton Rating Scale for Depression (HRSD) scores, p=0.025)



- Sign. ↑ depression remission rates (61% vs 37%, as assessed by the Inventory of Depressive Symptomatology-Self-Report (IDS-SR, p=0.046)
- Pregnenolone was well tolerated

Ritsner MS, et al. J Clin Psychiatry. 2010 Oct;71(10):1351-62

Pregnenolone supplementation

=> ↓ Schizophrenia symptoms

Schizophrenia

Positive Symptoms

- Hallucinations
- Delusions

Negative Symptoms

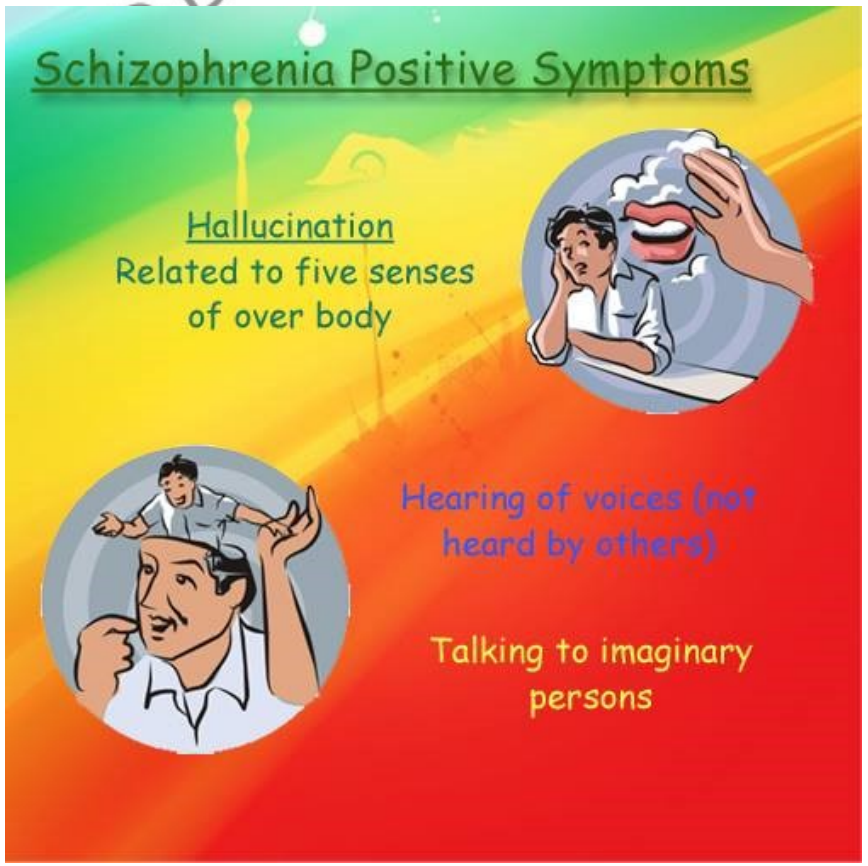
- Anhedonia
- Amotivation
- Social Withdrawal
- Flat affect

Cognitive Symptoms

- Poor short/long-term memory
- Speech/Communication Difficulties
- Inattention

8 weeks of 30 mg/day of Preg => ↓ Positive symptoms of schizophrenia

44 chronic schizophrenia or schizoaffective disorder patients (DSM-IV)



Pregnenolone 30 mg/day for 8 weeks

↓ vs placebo

- Sign. ↓ positive symptoms of schizophrenia
  (↓ positive symptom scores, improved more than in patients receiving DHEA)

  Positive symptoms = excess of activity, such as hallucinations, delusions)

- Sign. ↓ extrapyramidal side effects (improved less than in patients receiving DHEA)
- Sign. ↑ attention & working memory performance (p=0.048)
- NO effect on negative symptoms
- No effect of placebo or 200 mg/day of pregnenolone

Ritsner MS, et al. J Clin Psychiatry. 2010 Oct;71(10):1351-62

8 weeks of 500 mg/day Preg => ↓ Negative symptoms of schizophrenia

18 patients with schizophrenia

Pregnenolone fixed escalating doses to 500 mg/day for 8 weeks (9 patients)

↓

vs placebo (9 patients)

- Sign. ↓ negative symptoms of schizophrenia

  4x more ↑ improvements in the Scale for the Assessment of Negative Symptoms (SANS) scores (mean change = 10.38 vs 2.33 in patients receiving placebo, p=0.048)

  Negative symptoms = absence of activity, such as a lack of concern for one's appearance, & lack of language & communication skills)

- **Placebo**: No improvements among subjects

Marx CE, et al. Neuropsychopharmacology. 2009 Jul;34(8):1885-903

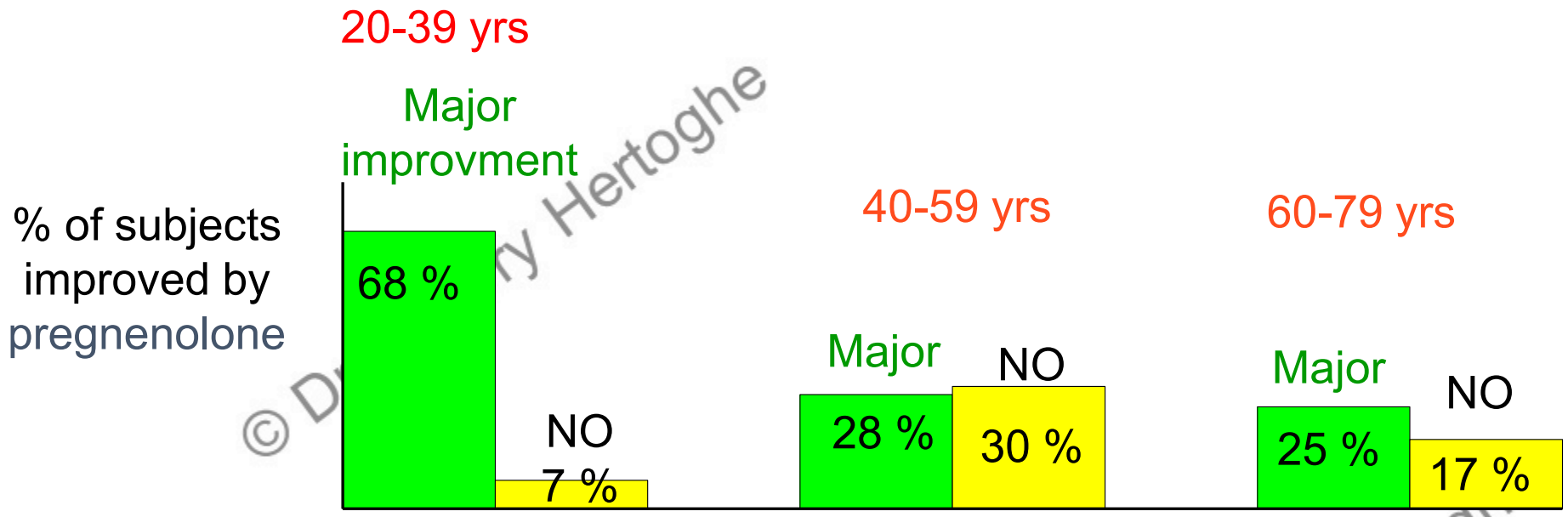
High doses of pregnenolone

=> ↓ Pain of rheumatoid diseases

Pregnenolone therapy => ↑ Improvement of rheumatoid arthritis in young adults

68 arthritis adults
(17 men & 47 women)

- mean age = 47.5 yr
- mean duration of disease = 9.7 years,
- 45 had moderate to severe degree of arthritis by X-ray examination).



Pregnenolone therapy (500 mg/day … 2 to 30 weeks)

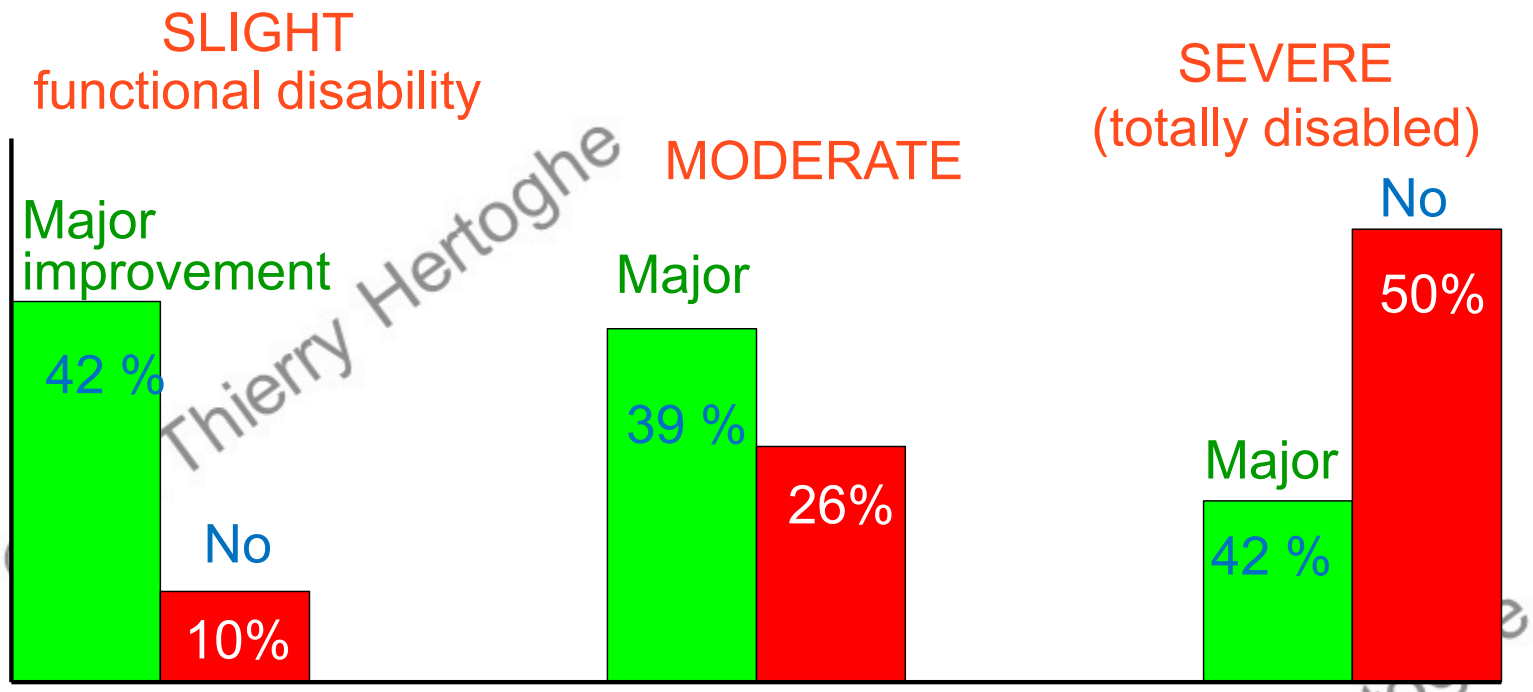
- Smaller doses were found to be less satisfactory
- Better results in the younger age group.
- Improvement occurs usually by the end of 2 weeks

Freeman H et al, J Clin Endocrinol, 1950, 10, 1503-1532

Pregnenolone therapy => ↑ Improvement of rheumatoid arthritis with mild functional disability

68 arthritis patients

% of subjects improved by pregnenolone



Pregnenolone therapy (500 mg/day … 2 to 30 weeks)

- Better results in the patients with slight functional disability

Freeman H et al, J Clin Endocrinol, 1950, 10, 1503-1532

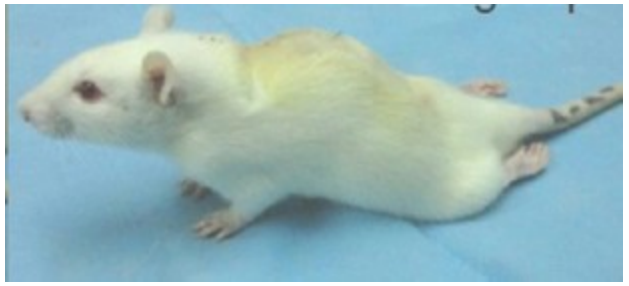
Pregnenolone supplementation

=> Improves nerve/spinal cord repair

Pregnenolone
=> ↑ Recovery of spinal injury

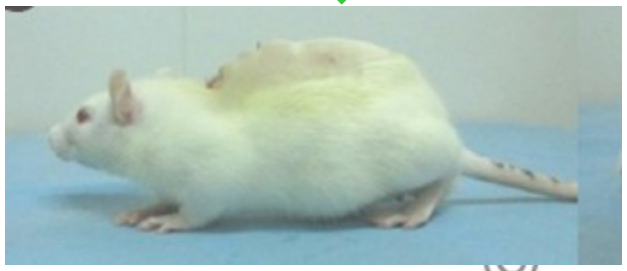
Rats => spinal injury

Spinal injury alone



Spinal injury + Pregnenolone
+ indomethacine (anti-inl.)
+ bacterial lipopolysaccharide (stimulator of cytokine secretion) immediately after the injury

- Highly sign. ↓ damage
- ↓ Histopathological changes
- Spared tissue from secondary injury
- ↑ Restoration of motor function.
- Remarkably, 11 of 16 of the rats treated with the above combination were able to stand & walk at 21 days after injury, 4 of them almost normally.



Results far superior to those obtained in controls or in rats to which the substances were given separately or in combinations of two.

Guth L, et aljury. Proc Natl Acad Sci U S A. 1994 Dec 6;91(25):12308-12.

Lower magnif.

Characteristic central canal dilatation

Higher magnification

Control

Lesion

Lesion

Control

Largest cavities are dorsal to the level of the central canal

PREG/LPS

PREG/LPS

Thin rim of residual spinal tissue at the ventral margin of the lesion (arrow)

Sparing of white matter

PREG/LPS/ indomethacine

PREG/LPS/ Indometh.

Sparing of white matter with typical myelinated nerve fibers

Ependymal cells migrating into the lesion from the central canal

Blood vessels in gray matter

PREG/LPS/ indomethacine

(greater magnific.)

PREG/LPS/ indomethacine

(greater magnific.)

Myelinated nerve fibers

Spared white matter = longi-tudinally oriented nerve fibers

Guth L, et al. Proc Natl Acad Sci U S A. 1994 Dec 6;91(25):12308-12.

Pregnenolone supplementation

Evidence-based

Pregnenolone: 15 placebo-controlled trials – all in adults

Healthy adults

Emotions: the reduction of brain connectivity (in amygdala region) with pregnenolone treatment in healthy volunteers

1. Sripada RK, Welsh RC, Marx CE, Liberzon I. The neurosteroids allopregnanolone and dehydroepiandrosterone modulate resting-state amygdala connectivity. Hum Brain Mapp. 2014 Jul;35(7):3249-61.

Anxiety: the improvement (reduction) with pregnenolone treatment in healthy volunteers

1. Sripada RK, Marx CE, King AP, Rampton JC, Ho SS, Liberzon I. Allopregnanolone elevations following pregnenolone administration are associated with enhanced activation of emotion regulation neurocircuits. Biol Psychiatry. 2013 Jun 1;73(11):1045-53.

Benzodiazepine-sedation: the sedation reduction with pregnenolone treatment

1. Meieran SE, Reus VI, Webster R, Shafton R, Wolkowitz OM. Chronic pregnenolone effects in normal humans: attenuation of benzodiazepine-induced sedation. Psychoneuroendocrinology. 2004 May;29(4):486-500.

Pregnenolone: 15 placebo-controlled trials – all in adults

Patients with psychological disorders

Substance abuse: the different metabolism of pregnenolone treatment (pharmacology)

1. Kashani L, Shams N, Moazen-Zadeh E, Karkhaneh-Yousefi MA, Sadighi G, Khodaie-Ardakani MR, Rezaei F, Rahiminejad F, Akhondzadeh S. Pregnenolone as an adjunct to risperidone for treatment of women with schizophrenia: A randomized double-blind placebo-controlled clinical trial. J Psychiatr Res. 2017 Nov;94:70-77.
2. Mason BL, Van Enkevort E, Filbey F, Marx CE, Park J, Nakamura A, Sunderajan P, Brown ES. Neurosteroid Levels in Patients With Bipolar Disorder and a History of Cannabis Use Disorders. J Clin Psychopharmacol. 2017 Dec;37(6):684-688.

Obsessive-compulsive disorder: nonsignificant improvement with pregnenolone treatment

1. Kellner M, Nowack S, Wortmann V, Yassouridis A, Wiedemann K. Does pregnenolone enhance exposure therapy in obsessive-compulsive disorder? - A pilot, interim report of a randomized, placebo-controlled, double-blind study. Pharmacopsychiatry. 2016 Mar;49(2):79-81.

Bipolar disorder: the improvement (reduction) of depression with pregnenolone treatment

1. Daftary S, Yon JM, Choi EK, Kim YB, Bice C, Kulikova A, Park J, Sherwood Brown E. Microtubule associated protein 2 in bipolar depression: Impact of pregnenolone. J Affect Disord. 2017 Aug 15;218:49-52.
2. Brown ES, Park J, Marx CE, Hynan LS, Gardner C, Davila D, Nakamura A, Sunderajan P, Lo A, Holmes T. A randomized, double-blind, placebo-controlled trial of pregnenolone for bipolar depression. Neuropsychopharmacology. 2014 Nov;39(12):2867-73.
3. Osuji IJ, Vera-Bolaños E, Carmody TJ, Brown ES. Pregnenolone for cognition and mood in dual diagnosis patients. Psychiatry Res. 2010 Jul 30;178(2):309-12.

Pregnenolone: 15 placebo-controlled trials – all in adults

Patients with psychological disorders

Schizophrenia: the improvement with pregnenolone treatment

1. Marx CE, Lee J, Subramaniam M, Rapisarda A, Bautista DC, Chan E, Kilts JD, Buchanan RW, Wai EP, Verma S, Sim K, Hariram J, Jacob R, Keefe RS, Chong SA. Proof-of-concept randomized controlled trial of pregnenolone in schizophrenia. Psychopharmacology (Berl). 2014 Sep;231(17):3647-62..
2. Ritsner MS, Bawakny H, Kreinin A. Pregnenolone treatment reduces severity of negative symptoms in recent-onset schizophrenia: an 8-week, double-blind, randomized add-on two-center trial. Psychiatry Clin Neurosci. 2014 Jun;68(6):432-40.
3. Ritsner MS, Gibel A, Shleifer T, Boguslavsky I, Zayed A, Maayan R, Weizman A, Lerner V. Pregnenolone and dehydroepiandrosterone as an adjunctive treatment in schizophrenia and schizoaffective disorder: an 8-week, double-blind, randomized, controlled, 2-center, parallel-group trial. J Clin Psychiatry. 2010 Oct;71(10):1351-62.
4. Marx CE, Keefe RS, Buchanan RW, Hamer RM, Kilts JD, Bradford DW, Strauss JL, Naylor JC, Payne VM, Lieberman JA, Savitz AJ, Leimone LA, Dunn L, Porcu P, Morrow AL, Shampine LJ. Proof-of-concept trial with the neurosteroid pregnenolone targeting cognitive and negative symptoms in schizophrenia. Neuropsychopharmacology. 2009 Jul;34(8):1885-903.
5. Kreinin A, Bawakny N, Ritsner MS. Adjunctive pregnenolone ameliorates the cognitive deficits in recent-onset schizophrenia: An 8-week, randomized, double-blind, placebo-controlled trial. Clin Schizophr Relat Psychoses. Winter 2017;10(4):201-210.

Schizophrenia: the improvement with combined pregnenolone with L-theanine therapies

1. Kardashev A, Ratner Y, Ritsner MS. Add-on Pregnenolone with L-theanine to antipsychotic therapy relieves negative and anxiety symptoms of schizophrenia: An 8-week, randomized, double-blind, placebo-controlled trial. Clin Schizophr Relat Psychoses. Spring 2018;12(1):31-41.

Thank you for your attention!

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Dr HERTOGHE MEDICAL SCHOOL

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