Neurobiologiskt potpurri

Dan Larhammar
Inst f Neurovetenskap
Dan.Larhammar@neuro.uu.se

UPPSALA UNIVERSITET
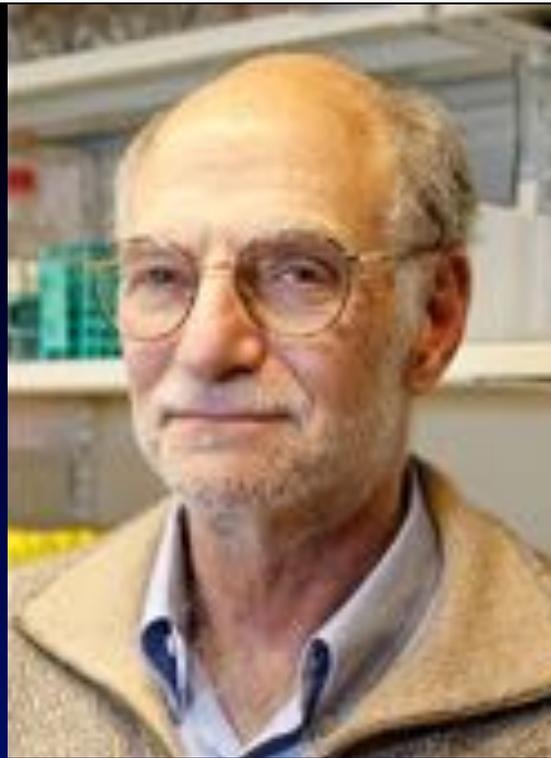
Nobelpriset i
fysiologi eller medicin
2017

Jeffrey Hall
Michael Rosbash
Michael Young

Dan Larhammar
Inst f Neurovetenskap
Dan.Larhammar@neuro.uu.se

Jeffrey C. Hall
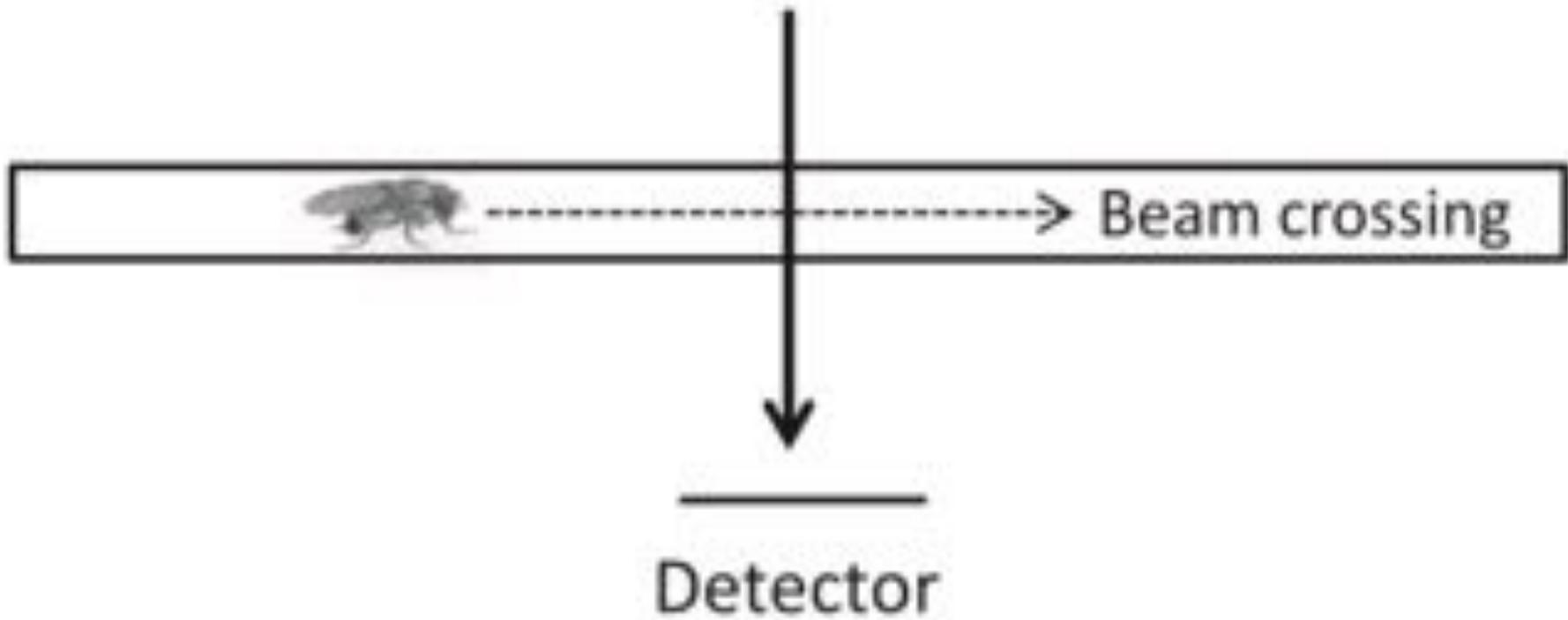Brandeis Univ.
1944

Michael Rosbash
Brandeis Univ.
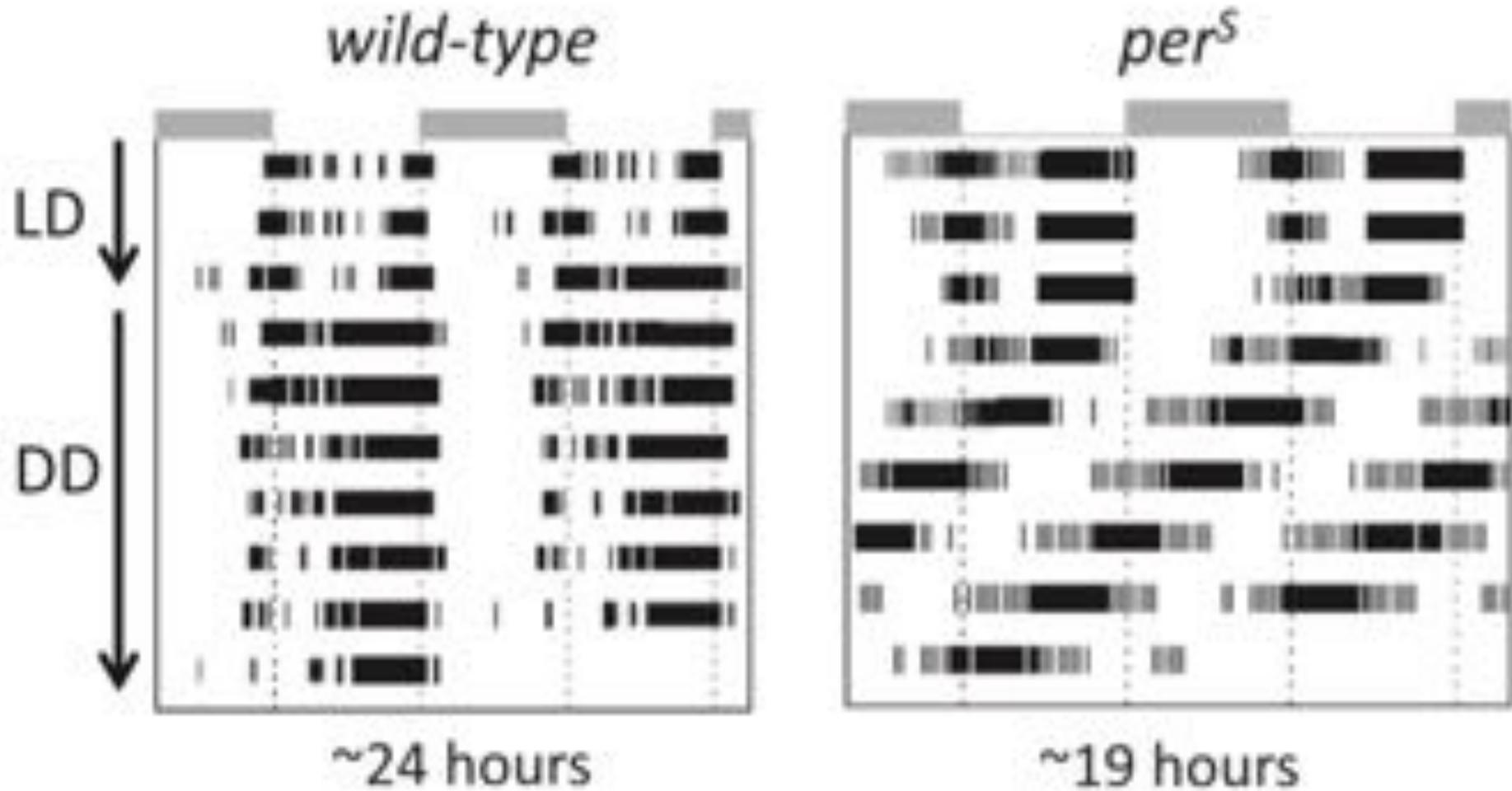1945

Michael Young
Rockefeller Univ.
1949

Bananfluga
Drosophila melanogaster

Infraröd ljusstråle
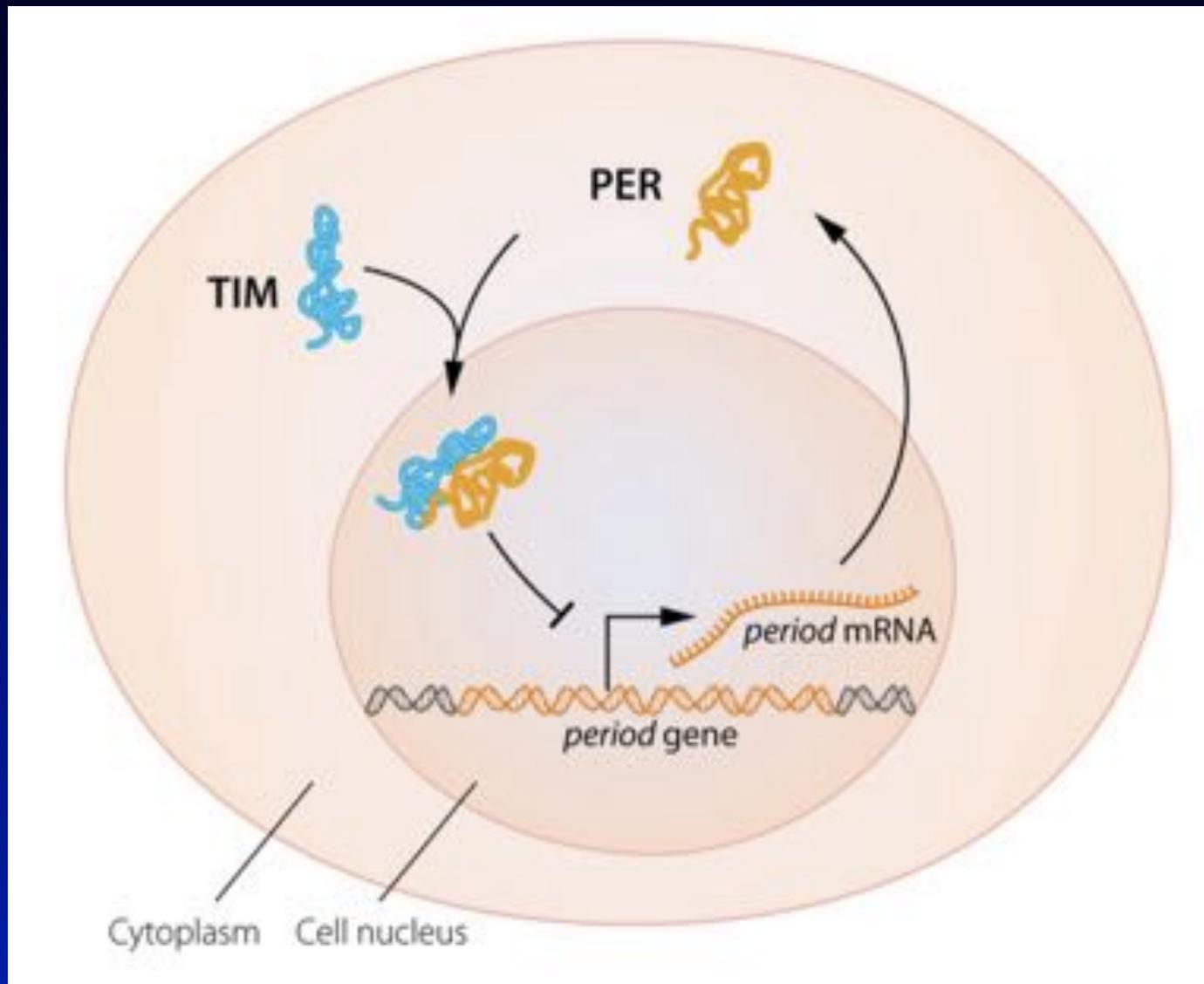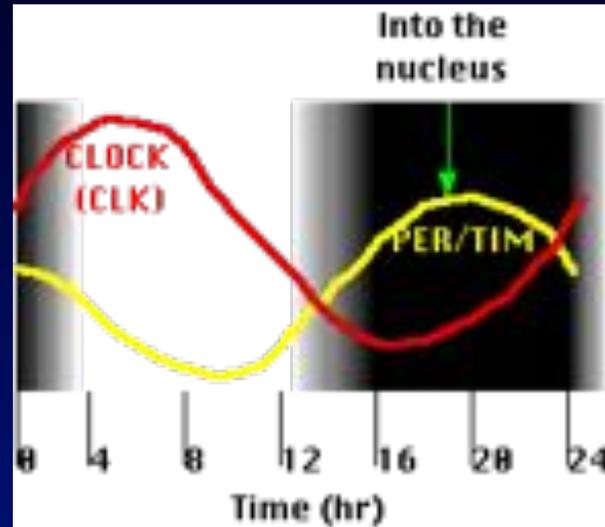
Beam crossing

Detector

Aktivitetsdiagram

Period-genen:

Protein som varierar i mängd under dygnet
Reglerar sig själv och andra gener

Fler komponenter:
Clock
Cycle
Cryptochrome
Doubletime

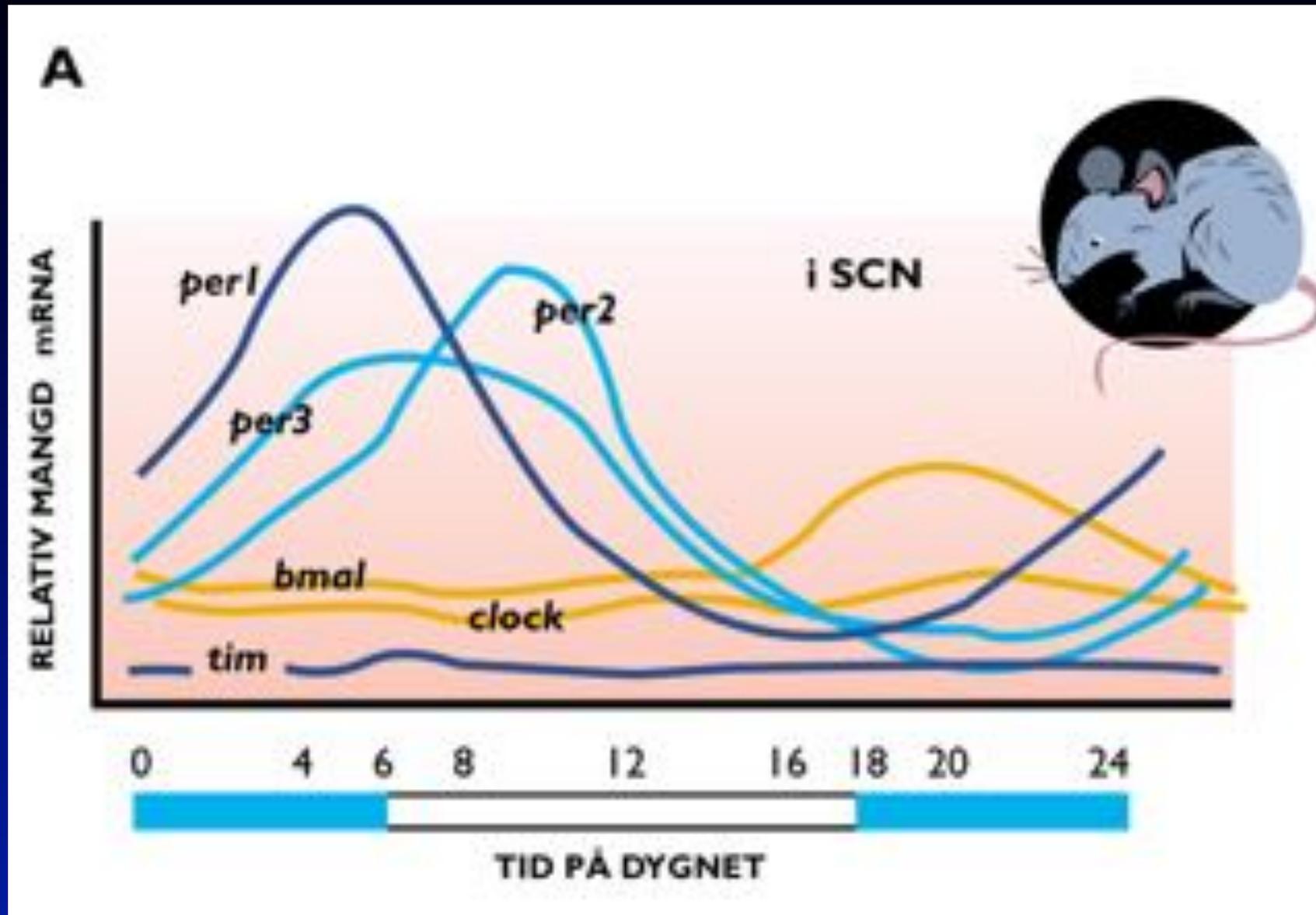Däggdjur: Tre gener för PER

Öga – hypothalamus – tallkottkörteln (melatonin)

Ljusreceptor i ögat justerar dygnsrytm: melanopsin
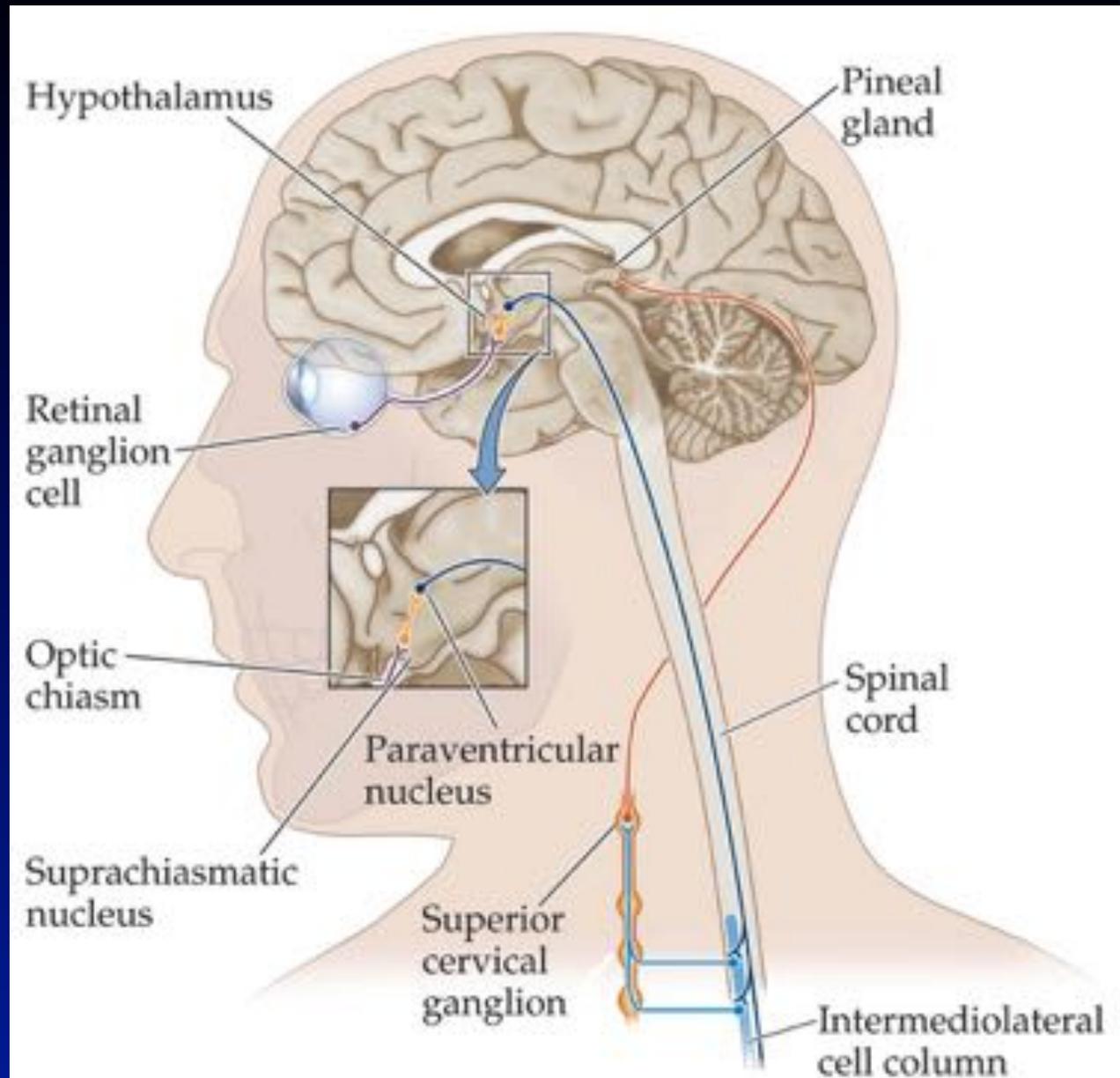
Circadiansk rytm
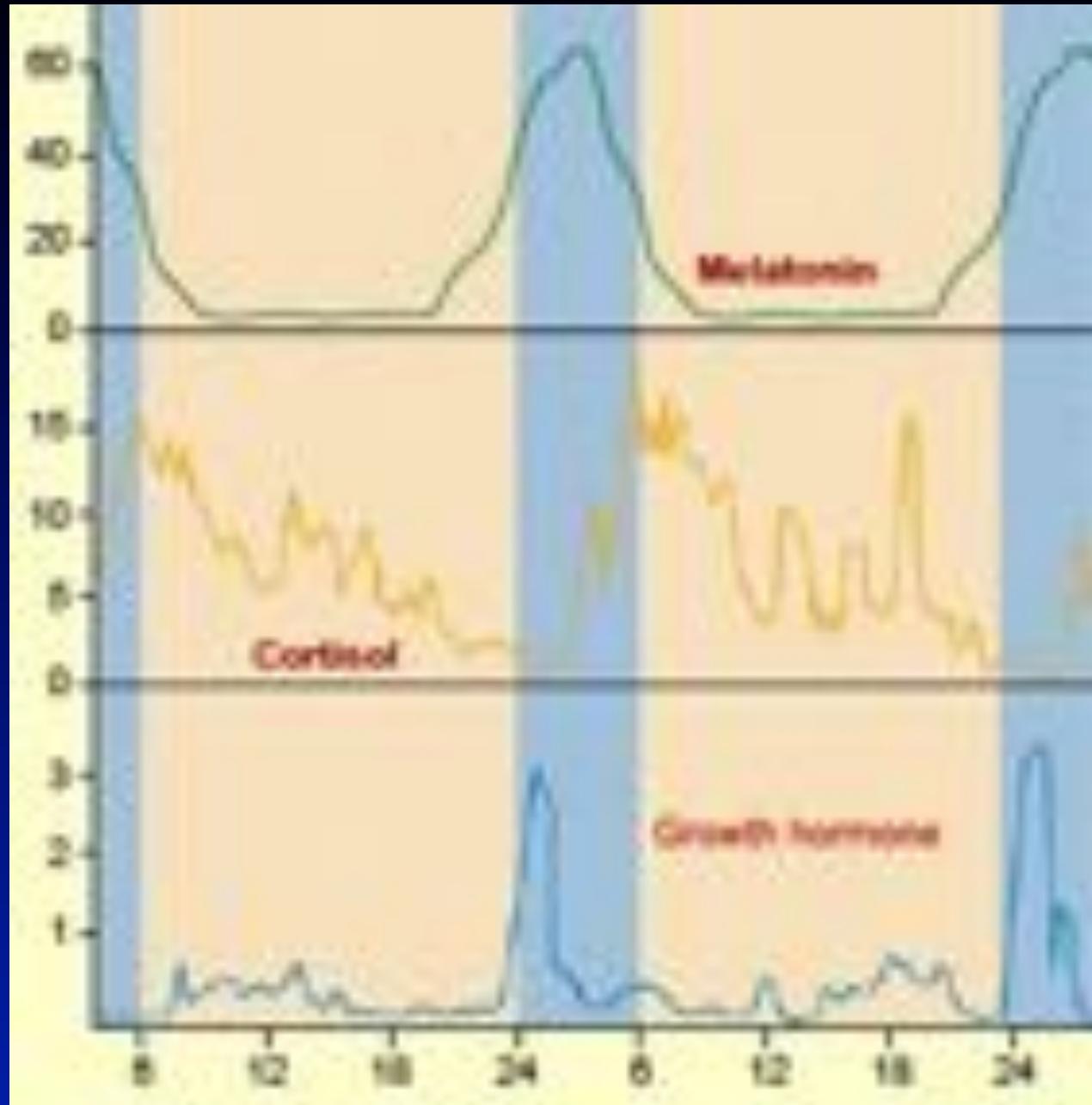
SCN i hypothalamus
är den centrala klockan

Sömnsjukdomar

Narkolepsi: signalsubstansen hypokretin/orexin
(påverkar även aptit)

DSPS delayed sleep phase syndrome

ASPS advanced sleep phase syndrome

Aptit och mättnad i hjärnan

Hypothalamus
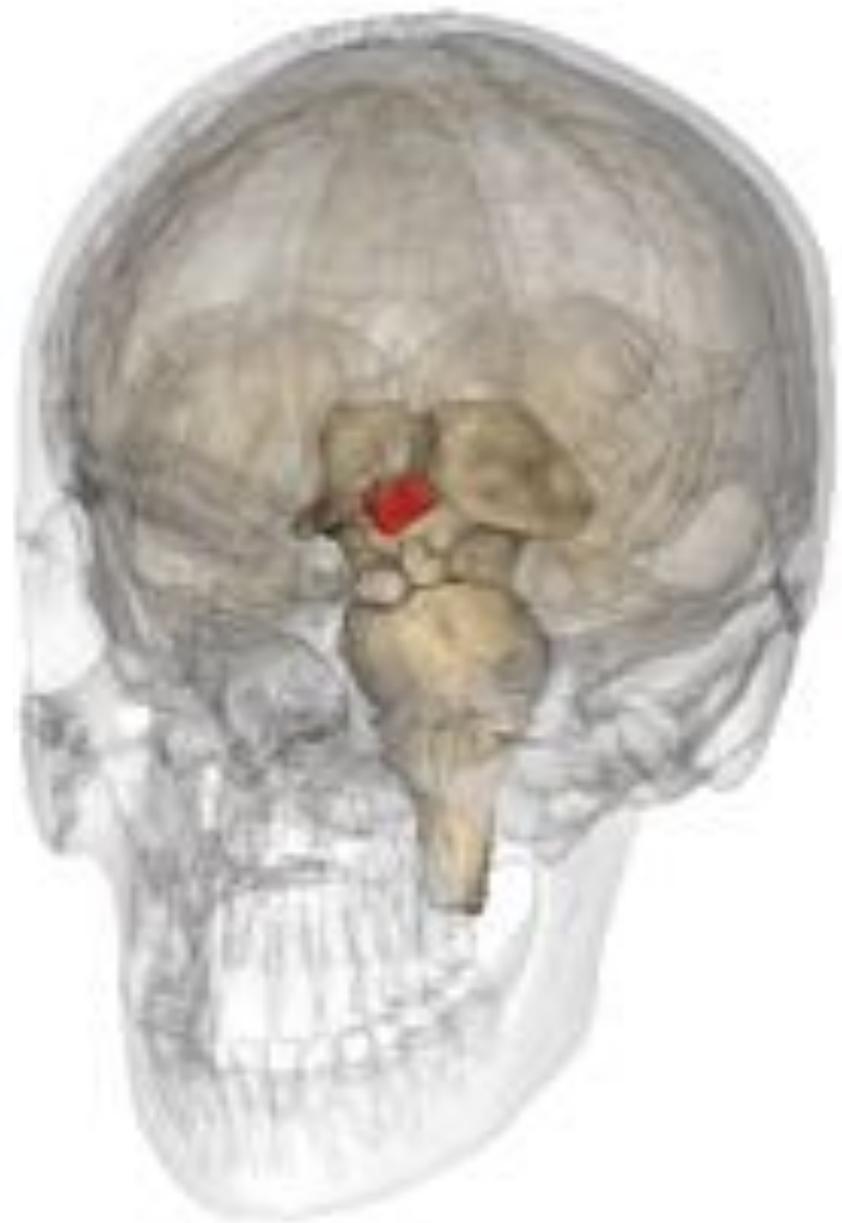
Leptin system (leptos = thin)

ob (obese) = leptin

Jeff Friedman
Rockefeller Univ.

ob/ob mouse

normal (wildtype) mouse

<u>Leptin</u>: secreted from adipocytes
146 amino acids
Zhang et al., Jeff Friedman
Nature 1994

Picture by Jordan Rehm
Science & Medicine 1997

Leptin deficiency

Before leptin treatment
3.5 years old

8 years old

Before leptin treatment at age 5 years
and after 4 years of therap at 9.

Jean Marx
Science 7 Feb. 2003

Gibson et al.
J Clin Endocrinol Metab 2004

Average plasma ghrelin, insulin and leptin concentrations during a 24-hour period in 10 human subjects consuming breakfast (B), lunch (L), and dinner (D) at the times indicated (08.00, 12.00, and 17.30, respectively).

Note that ghrelin and insulin curves are virtually reciprocal.

While insulin is a fast feedback reporter of food ingestion (along with PYY3-36 and PP), leptin is a long-term reporter of adipocyte mass.

(Glucagon curve is similar to insulin, i.e., released upon meals, stimulated by amino acids, especially L-Arg, and by low glucose. However, the level of glucagon increases only by 50%.)
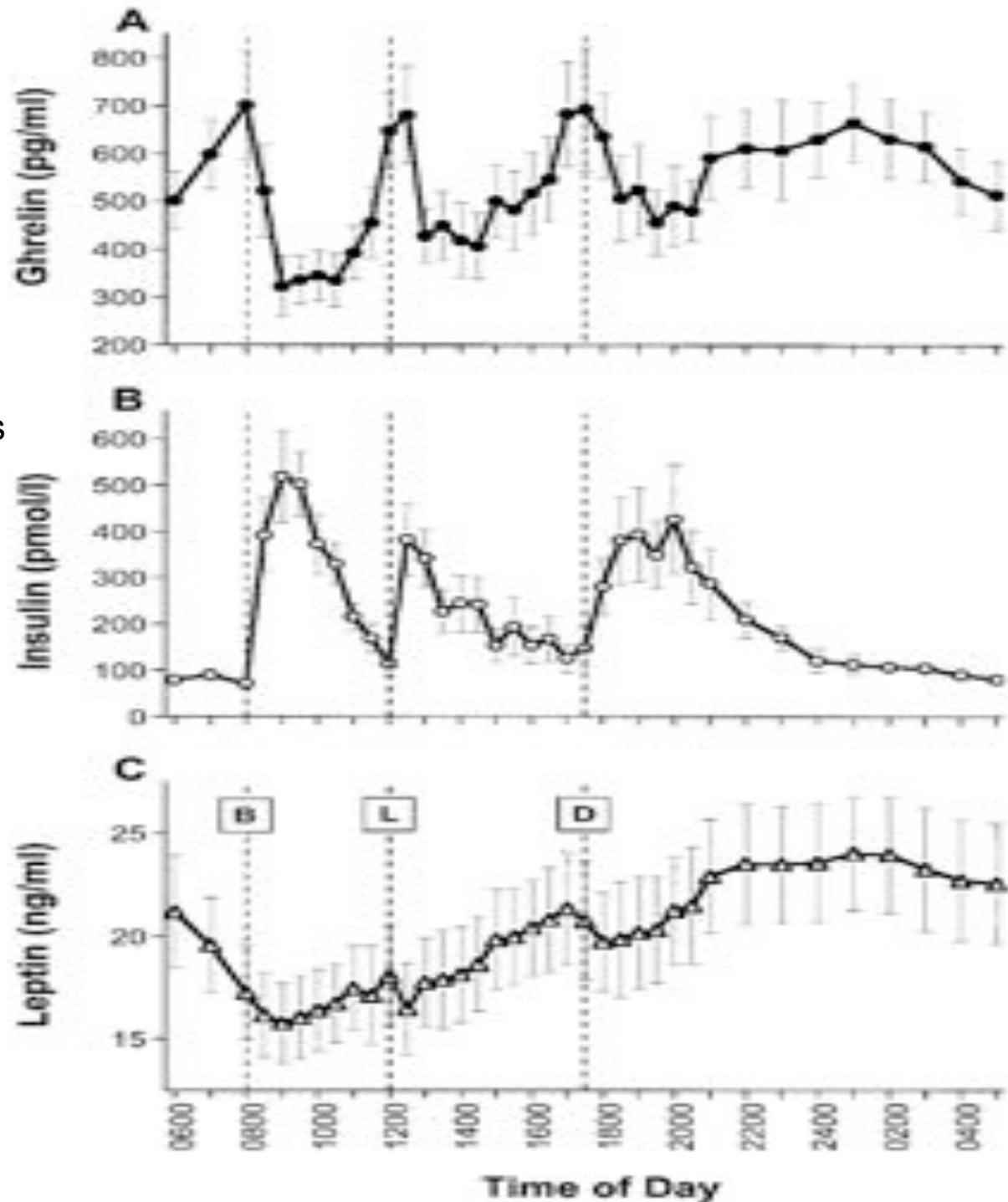
Cummings et al. Diabetes 2002

Leptin reduces appetite:

- Direct stimulation of α-MSH
- Direct inhibition of NPY and AGRP release
- Also insulin and GLP-1 contribute.
- Inhibition of NPY neurons may be via stimulation of GABA-ergic inhibitory neurons.

NPY acts on receptors Y1 and Y5 in PVN.
α-MSH acts on receptor MC4 in PVN.
AGRP is antagonist on MC4.
CART action is unknown.

PYY3-36 via Y2 inhibits NPY release.
PP via Y4 stimulates α-MSH release.
Ghrelin stimulates NPY release.
NPY neurons inhibit α-MSH release.
Thus, PYY3-36 reduces this inhibition from
    NPY neurons (disinhibition)
NPY in the arcuate nucleus reduces α-MSH
    release via Y1.
Other neuropeptides are also
involved, e.g.:
- MCH (melanin-conc. hormone)
- Orexins (=hypocretins)
- Galanin

Ascending pathways drawn on one side and frontal section descending on the other.
Reality has perfect bilateral symmetry!
PVN = paraventricular nucleus
LHA = lateral hypothalamic area

PVN

MC4   Y1 Y5

α-MSH   NPY

AGRP

LHA

MCH Orexins

3rd vent.

NPY AGRP

α-MSH

Orexins Galanin

To NTS in brain stem

CRF TRH to pit.

NPY

PP via Y4

Insulin Leptin GLP-1

Input from brain stem

PYY3-36 via Y2

ghrelin

Arcuate nucleus

Long-Term Persistence of Hormonal Adaptations to Weight Loss

Priya Sumithran, M.B., B.S., Luke A. Prendergast, Ph.D.,
Elizabeth Delbridge, Ph.D., Katrina Purcell, B.Sc., Arthur Shulkes, Sc.D.,
Adamandia Kriketos, Ph.D., and Joseph Proietto, M.B., B.S., Ph.D.

50 overweight or obese patients.
10-week weight-loss program.
Mean loss 13.5±0.5 kg

Hormone levels at 10 weeks:
Satiety hormones dropped significantly:
 leptin, PYY, CCK, insulin, amylin
Hunger hormones increased significantly:
 ghrelin, GIP
One satiety hormone increased:
 Pancreatic polypeptide
Appetite increased significantly.

Hormone levels one year later:
All hormone levels (except amylin)
were still altered!
Appetite was still increased.

These findings may explain why it is
difficult to maintain a reduced body
weight.

Conference: Knowledge resistance and how to cure it

September 6-9, 2017
Wenner-Gren Center, Stockholm

1. Knowledge resistance and widespread misconceptions in society

2. Knowledge resistance in academia

3. Cognitive and psychological causes of knowledge resistance

4. Types and spreading of knowledge resistance

5. How to counteract and cure knowledge resistance

Trump's White House Press Secretary
Sean Spicer

2009 Obama inauguration

2017 Trump inauguration

Left: Getty Images; right: 58th Presidential Inaugural Committee

WASHINGTON, DC   THE WHITE HOUSE

NBC NEWS

NBC's Meet The Press host
Chuck Todd

Trump advisor
Kellyanne Conway

I cannot tell a lie.
- George Washington

I cannot tell the truth.
- Richard Nixon

I cannot tell the difference.
- Donald Trump

www.kevinkarstens.blogspot.com

1. Knowledge resistance and widespread misconceptions in society

Christopher Chabris

(c) 2010 Daniel J. Simons

http://www.youtube.com/watch?v=vJG698U2Mvo

The Monkey Business Illusion
http://www.youtube.com/watch?v=IGQmdoK_ZfY

The colour changing card trick
http://www.youtube.com/watch?v=v3iPrBrGSJM&list=PLJkCi3vFE0ZUX95TyvQJClk_S9wqpao9d

Four things most people get wrong about memory

What people believe about how memory works:
a representative survey of the U.S. population
Daniel J. Simons & Christopher F. Chabris, PLoS
One 2011

Memory works like a video camera, recording the world around us onto a mental tape that we can later replay. (63%)

An unexpected occurrence is likely to be noticed – even when people's attention is alsewhere. (78%)

Hypnosis can improve memory – especially when assisting a witness in recalling details associated with a crime. (55%)

Amnesia sufferers usually cannot remember their identity or name. (83%)

Strategy for informing people who have been misinformed.

2012

John Cook
    Univ of Queensland
Stephan Lewandowsky
    School of Psychology, Univ of Western Australia
    Univ. of Bristol, UK

https://skepticalscience.com/docs/Debunking_Handbook.pdf
https://skepticalscience.com/docs/Debunking_Handbook_Swedish.pdf

the
DEBUNKING
handbook

- Present core facts
- Explicit warnings before describing myth
- Provide correct explanations that replace the myth
- Use graphics (if possible)

It's not just <u>what</u> people think that matters,
but <u>how</u> they think.

The best approach is to focus on the facts
you wish to communicate

A simple myth is more cognitively attractive
than an over-complicated correction

On the reception and detection of pseudo-profound bullshit

Gordon Pennycook*   James Allan Cheyne†   Nathaniel Barr‡   Derek J. Koehler†

Jonathan A. Fugelsang†

"Pseudo-profound bullshit": seemingly impressive assertions that are presented as true and meaningful but are actually vacuous, often consisting of buzzwords, organized into statements with syntactic structure but no discernible meaning.

Gordon Pennycook

Examples from Deepak Chopra:
"Imagination is inside exponential space time events"
"Nature is a self-regulating ecosystem of awareness"

"Those more receptive to bullshit are less reflective, lower in cognitive ability, are more prone to ontological confusions and conspiratorial ideation, are more likely to hold religious and paranormal beliefs, and are more likely to endorse complementary and alternative medicine."

"An understanding of more precisely nuanced meanings of words may reveal inconsistencies, incongruities, and conflicts among terms in bullshit statements."

Deepak Chopra