LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN
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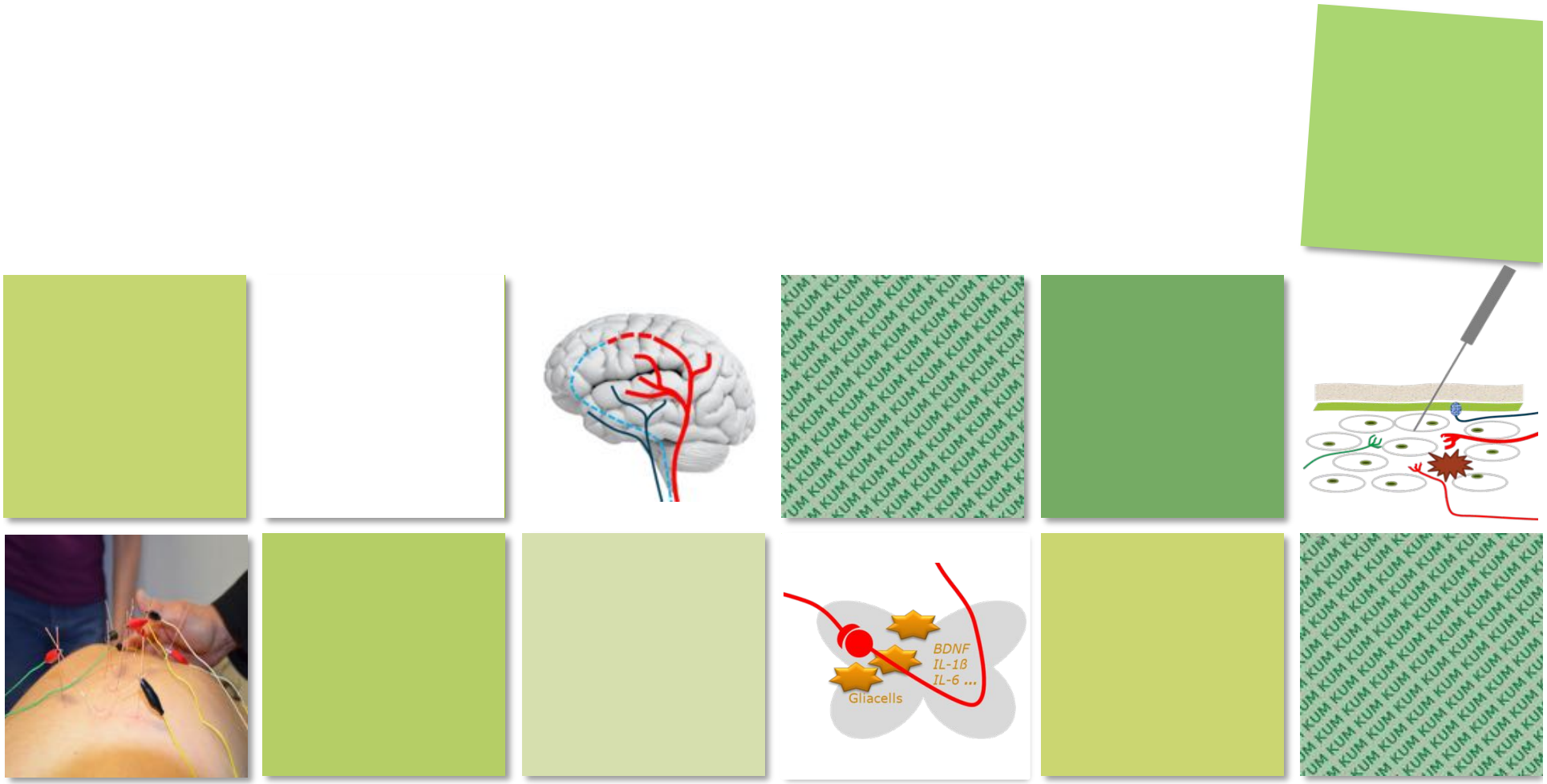
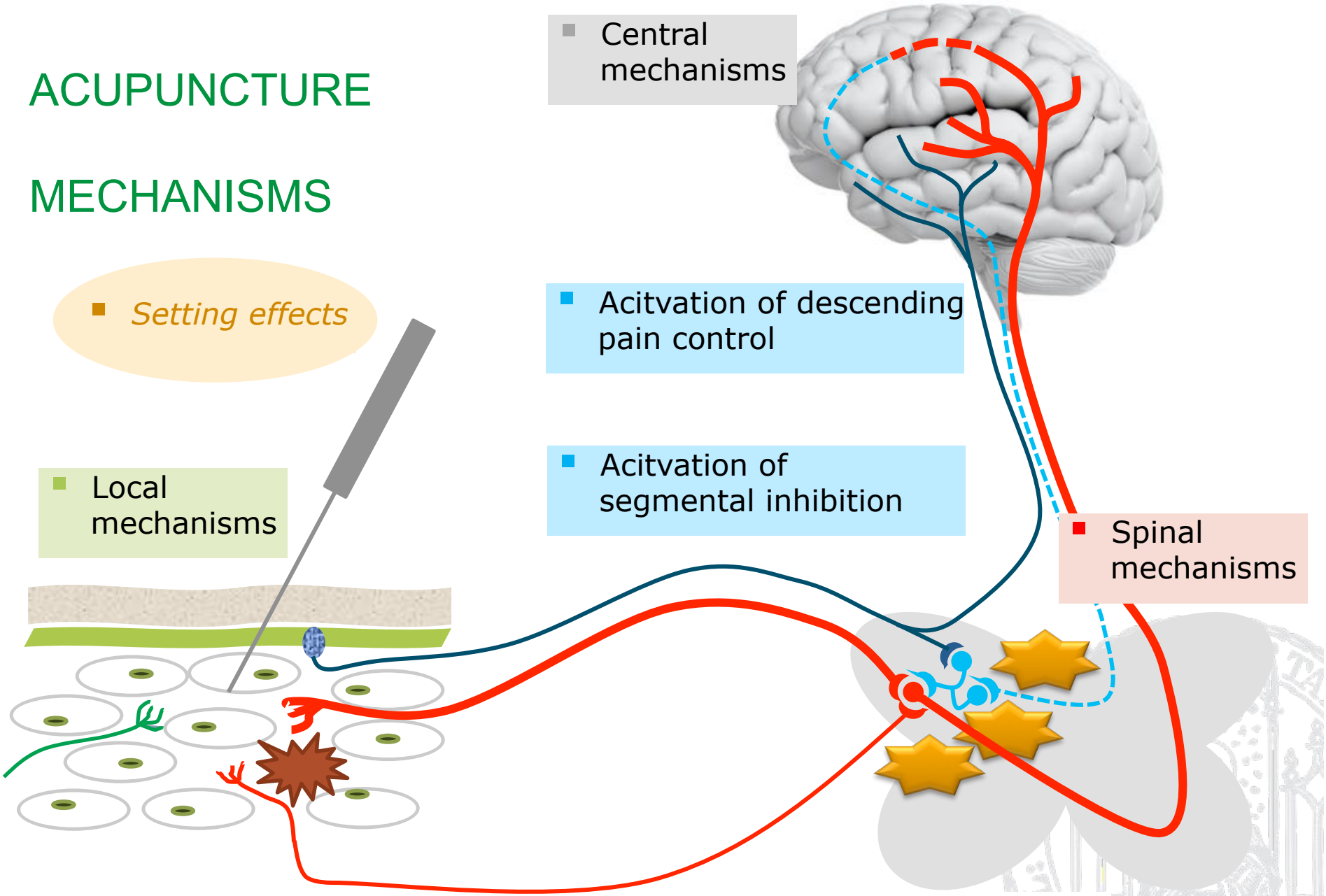
MULTIDISCIPLINARY PAIN CENTRE
DEPARTMENT OF ANAESTHESIOLOGY
UNIVERSITY OF MUNICH

SCIENTIFIC REVIEW OF MECHANISMS OF ACUPUNCTURE



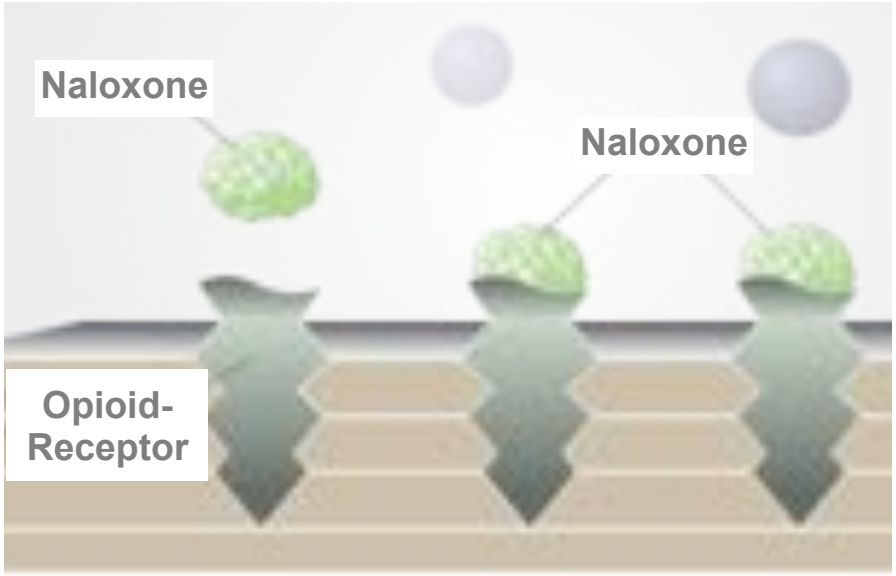
ACUPUNCTURE

MECHANISMS



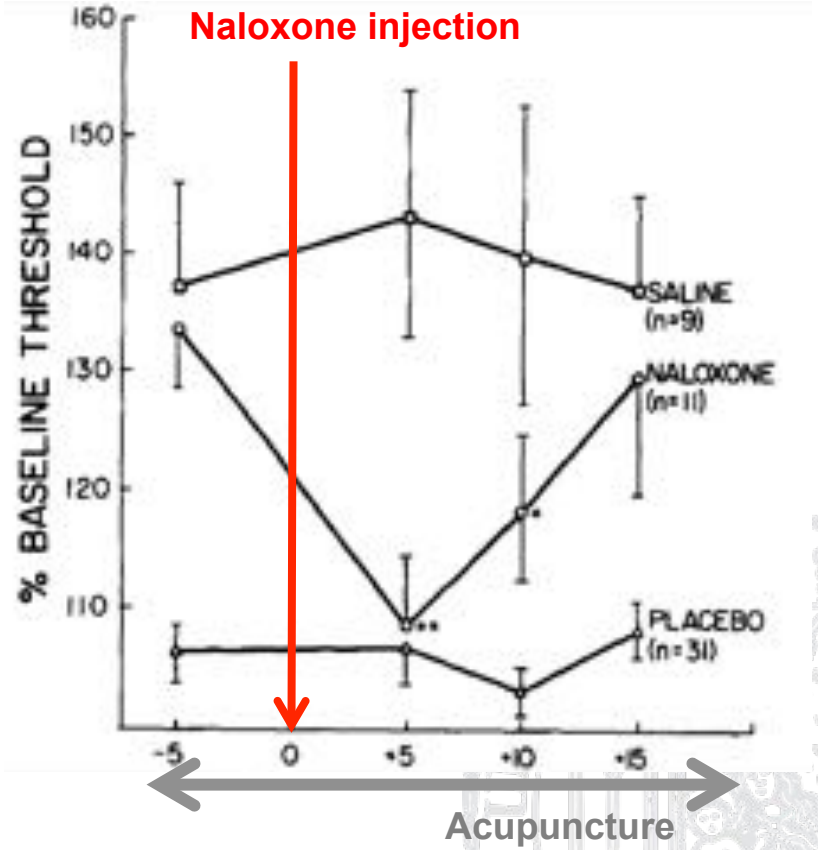
CENTRAL – RELEASE OF ENDOGENOUS OPIOIDS

LI 4



http://harmreduction.org (Graphics: Maya Doe-Simkins)

Mayer et al. Brain Res. 1977



NALOXONE INHIBITS ACUPUNCTURE ANALGESIA

- Mice

Pomernaz & Chiu Life Sci 1976
Cheng & Pomeranz Pain 1980
Martins et al. Pain Med 2012

- Rats

Chen et al. Behav Brain Res 1992
Koo et al. Pain 2002
Cidral Filoh Neuroscience 2011
Zeng et al. ECAM 2014

- Monkeys

Ha et al. Exp Neurol 1991

- Horses (Twitching)

Lagerweij et al. Science 1984

- Humans

Chapman et al. Pain 1980 / 1983
Abrams et al. Anesth Analg 1981
Pertovaara et al. Pain 1982
Moret et al. Pain 1991

Simmons & Oleson Anesth Prog 1993
Eriksson et al. Am J Chin Med 1991
Kitade Acupunct. Electrother. Res.1988

ENDOGENOUS OPIOIDS - FURTHER HINTS

- Acupuncture → endogenous Opioids in spinal fluid ↑

Clement Jones et al. Lancet 1980
Sjolund Acta Physiol. Scand 1977

- Dysfunctionl opioid receptors → Acupuncture analgesia ↓

Peets & Pomeranz, Nature 1978

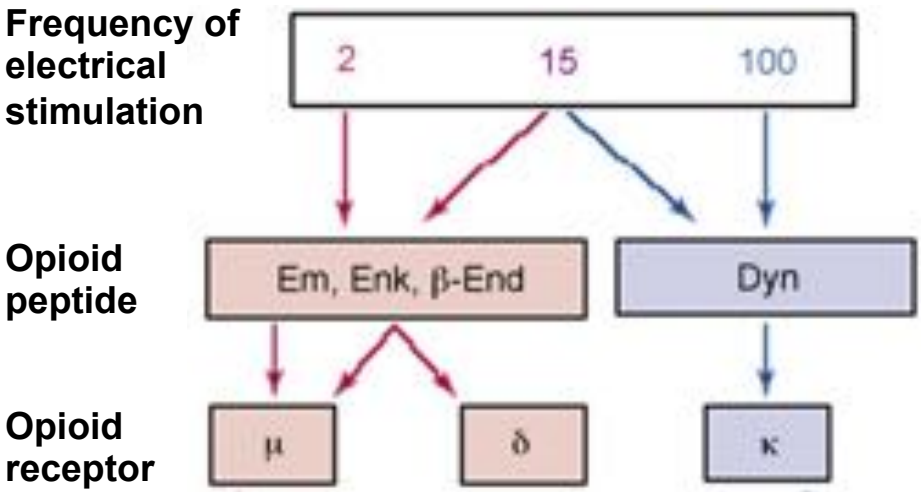
- Inhibition endogenous Opioid degradation → Acupuncture analgesia ↑

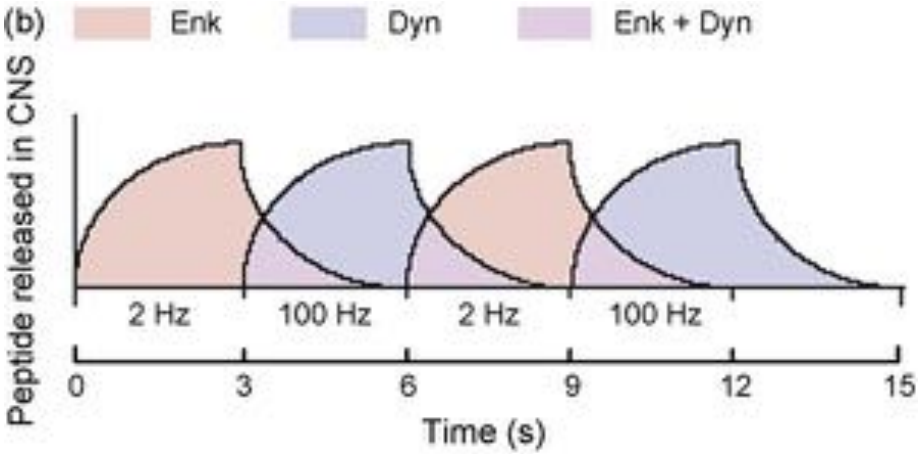
Chen & Pomeranz, Pain 1980
Kitade Acupunct. Electrother. Res.1988 / 1990

- Electroacupuncture → ß-Endorphin in Hypothalamus (PCOS) ↑

Stener-Viktorin et al. Biol Reprod 2004

ENDOGENOUS OPIOIDS - FREQUENCY OF EA

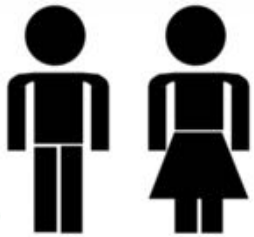




Han et al. Trends in Neuroscience 2003

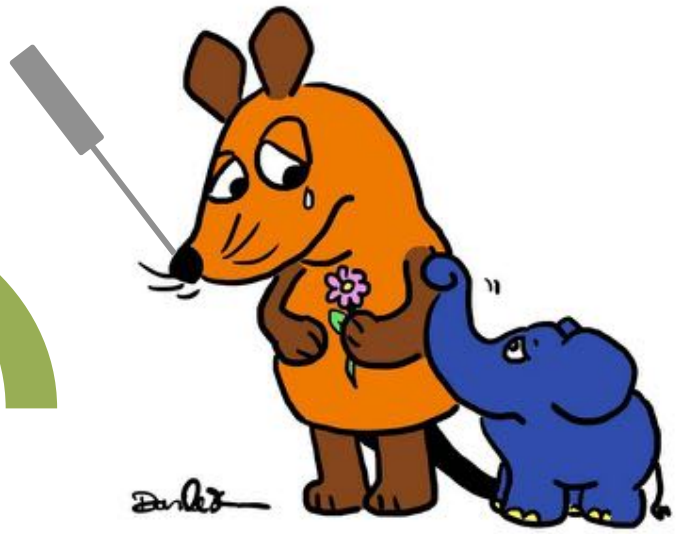
Also shown for TENS in humans

Han et al. Pain 1991
Hamza et al. Anaeshtesiology 1999



ENDOGENOUS OPIOIDS - RESPONDER

NON-RESPONDER



CCK-8
antisense RNA

CCK8 expression

Effect of CCK8 inhibitors

Tang et al. Pain 1997 Huang et al. Brain Res Bull 2007 Ko et al. Peptides 2007 Bilder: Armin Maiwald WDR

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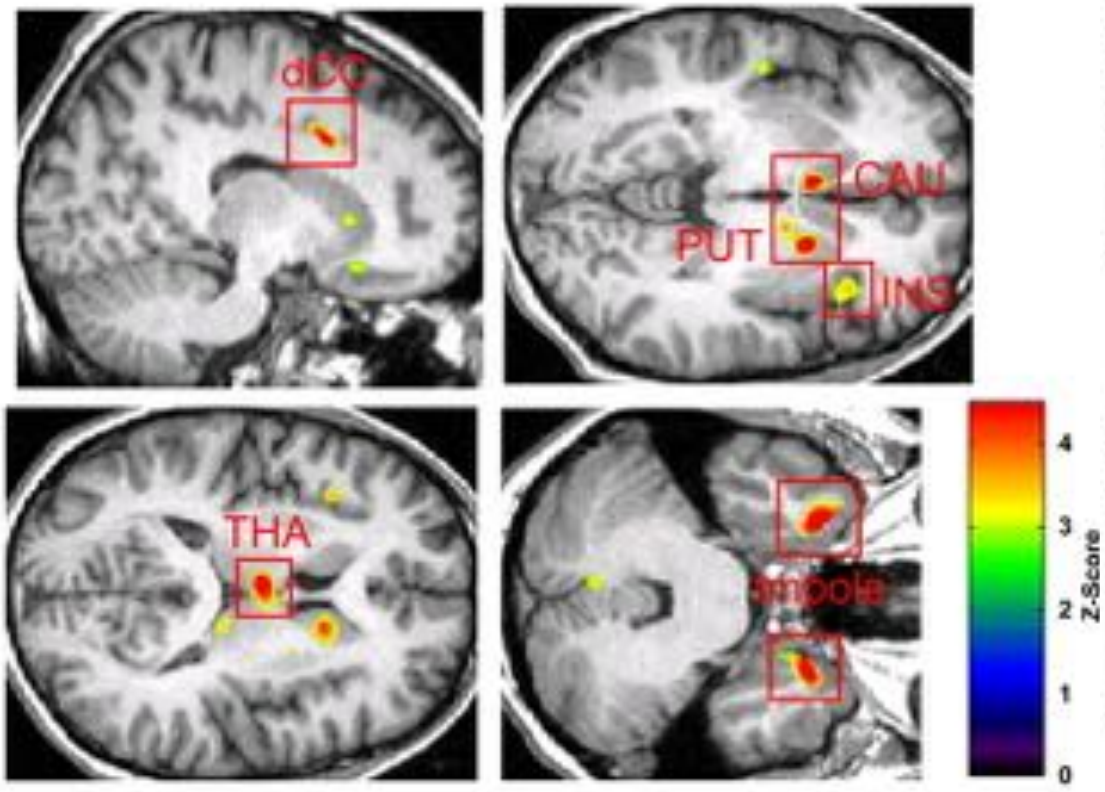
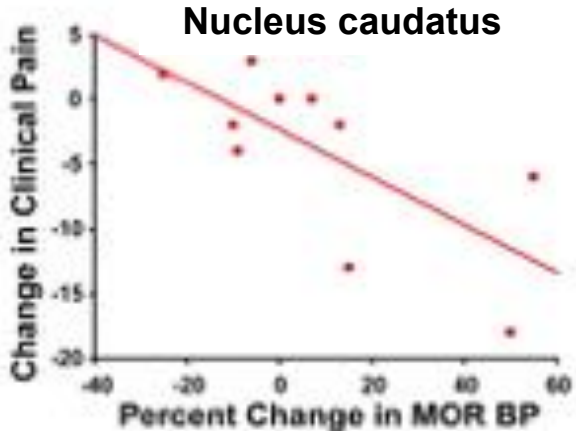
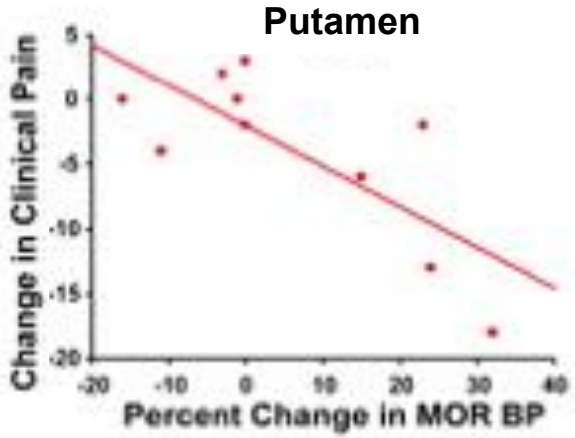
INCREASE IN μ-OPIOID-RECEPTOR BINDING POTENTIAL

… correlates with pain reduction in fibromyalgia patients

after 8 acupuncture sessions

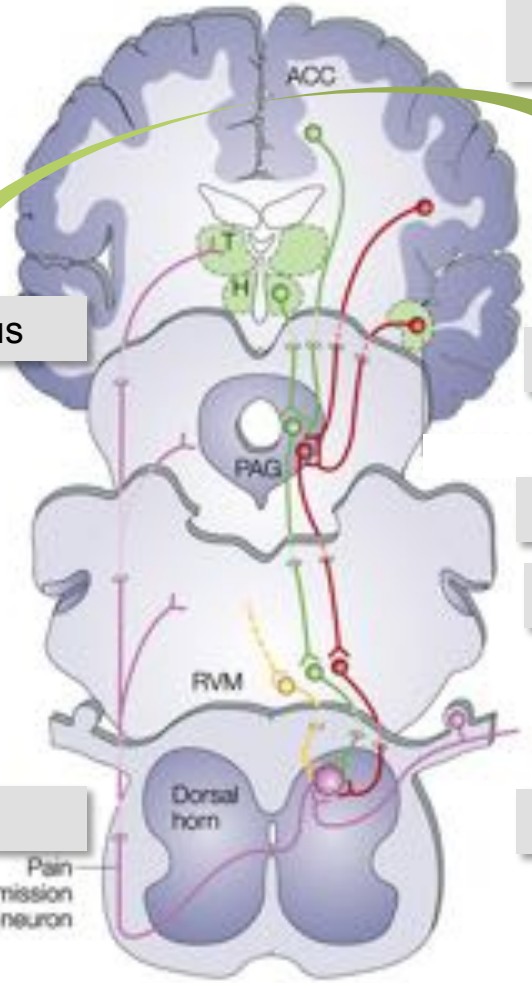






Harris et al. Neuroimage 2009

DESCENDING PAIN CONTROL



Prefrontal Cortex

Thalamus Hypothalamus

Insular Amygdala

Locu corulesus

Noradrenalin

Spinal Cord

GABA Enkephalin

Periaqueductal grey

ß-Endorphin

Enkephalin

RVM

Raphe Nuclei

Dynorphin

Serotonin

Spinal Cord

GABA Enkephalin

Fields 2004 Nature Reviews | Neuroscience

Summarized by:
Zhao, Prog Neruobiol, 2008
Zhang, Anaesthesiology 2014

ANTI-HYPERTENSIVE EFFECTS OF EA

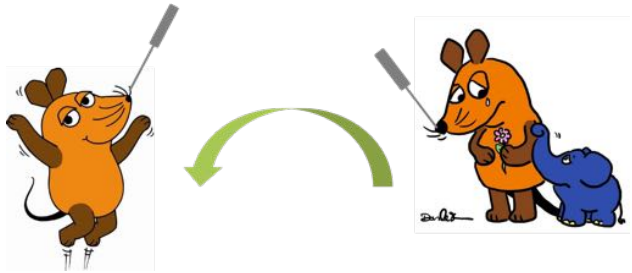
Acupuncture reduces cold induced hypertension

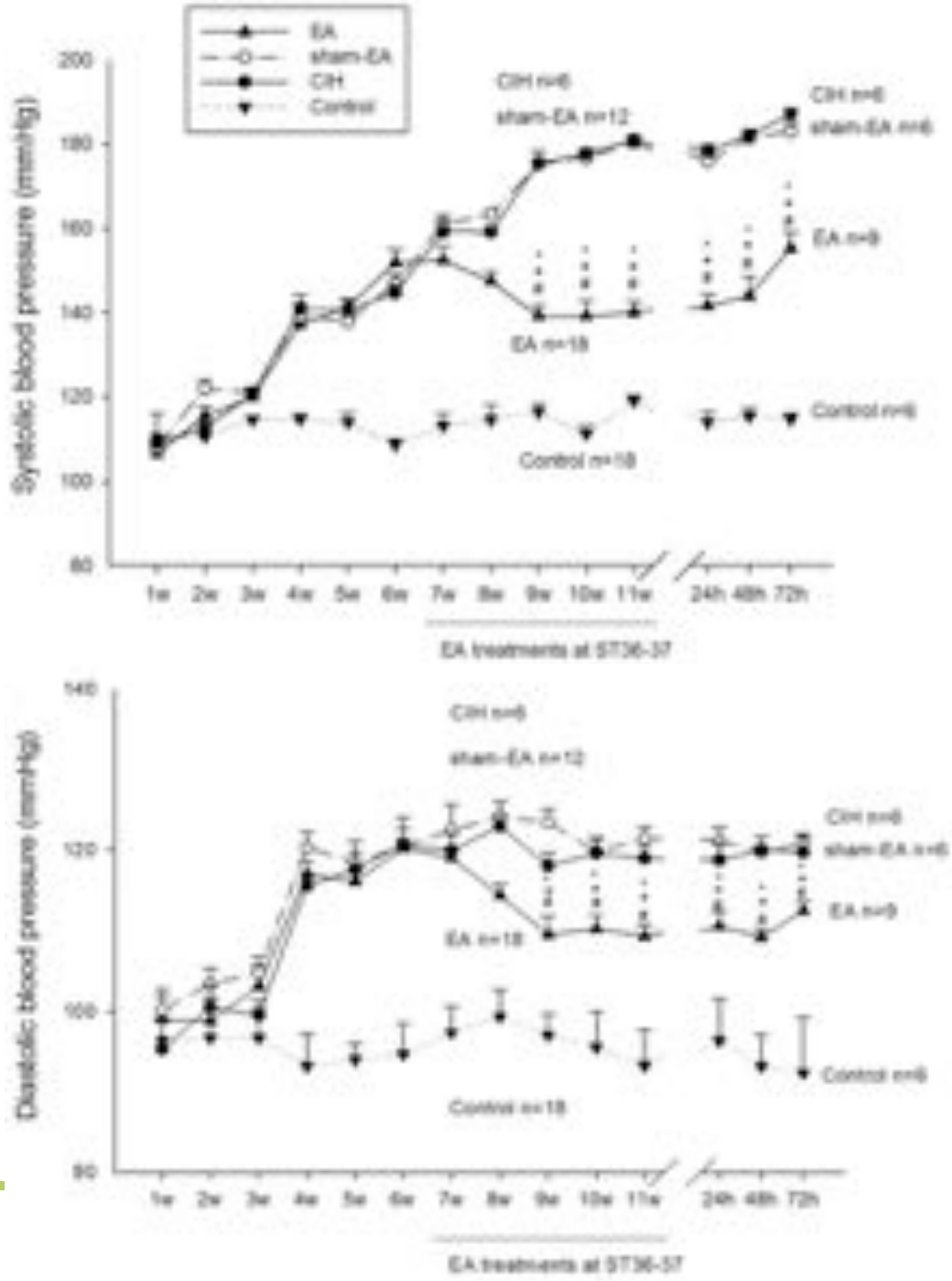
- Stable heart rate
- Crucial role of encephalin release

Li et al. Science Reports 2016
Li et al. Chin Med 2015

CCK-8 antagonist again transforms non-responder to responder rats

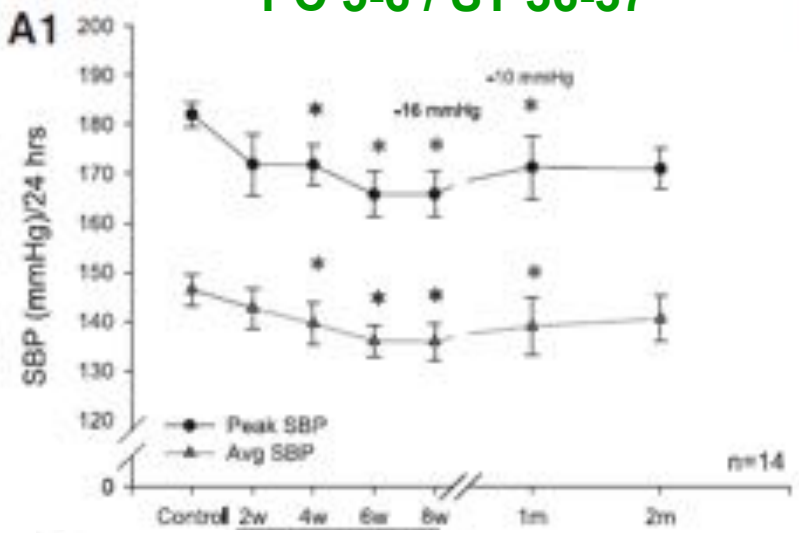
Li et al. Am J Physiol 2013

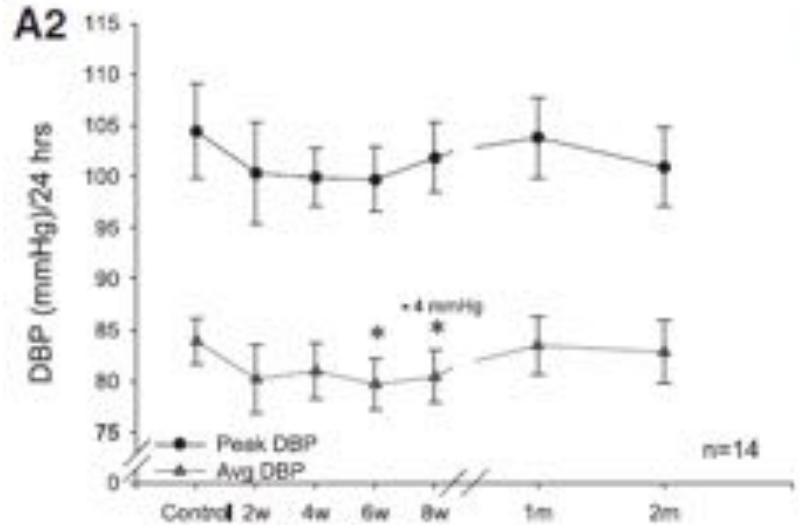




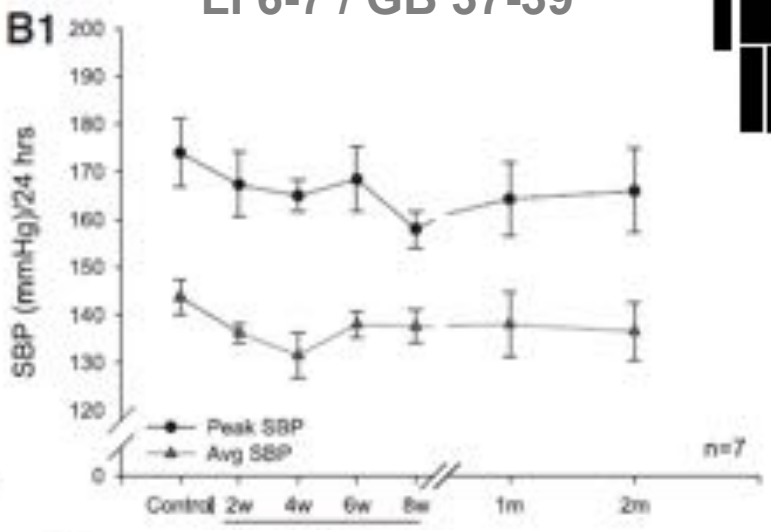
… ALSO IN HUMANS

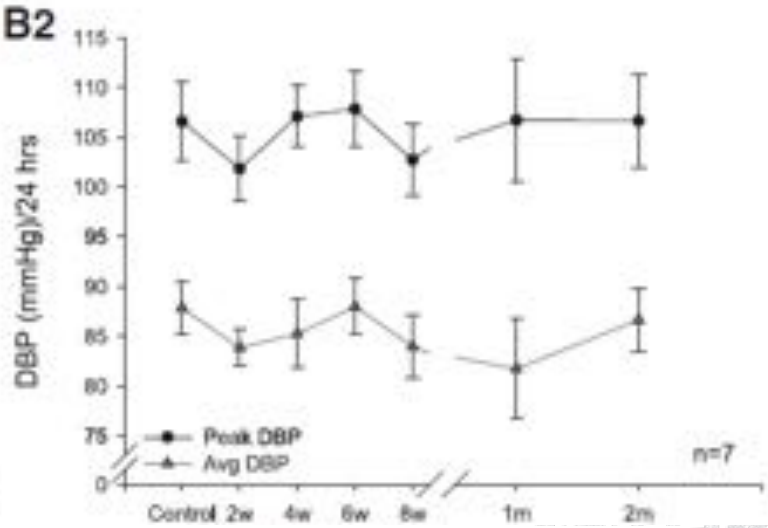
PC 5-6 / ST 36-37

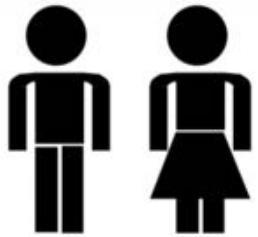




LI 6-7 / GB 37-39

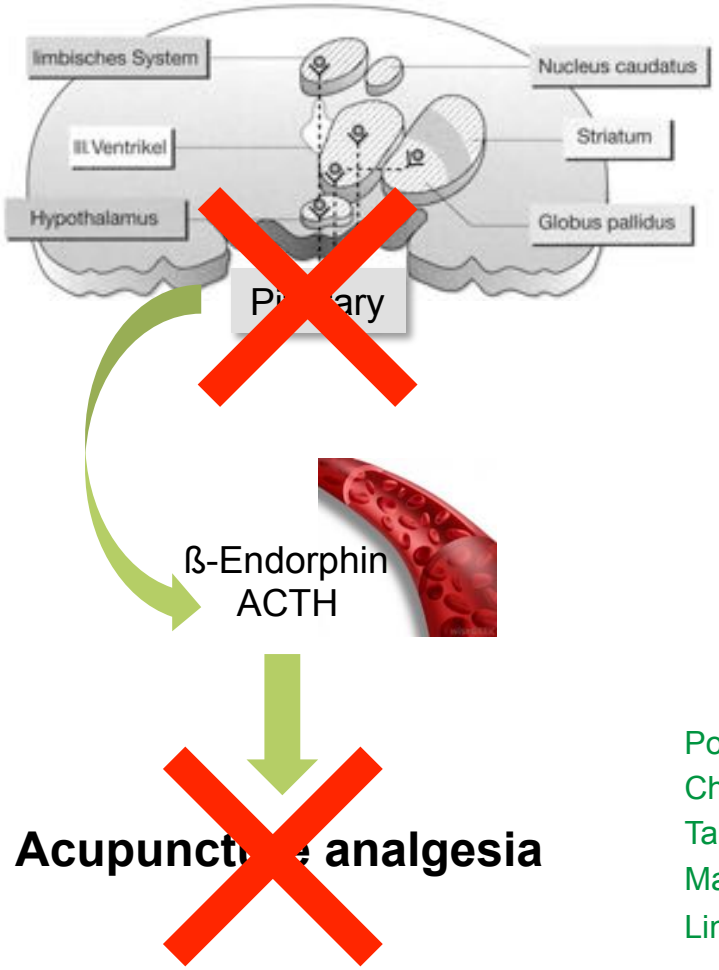






Li et al. Med Acup 2015

SYSTEMIC RELEASE OF ENDORPHINS AND ACTH



Pomeranz et al. Exp Neurol 1977
Cheng et al. Life Sci 1979
Takeshige et al. Brain Res Bull 1991/19929/1993
Masala et al. Acta Endocrinol (Copenh) 1977
Lin et al. Neurosci Lett 2002

ACUPUNCTURE REDUCES STRESS RESPONSE

Policystic ovaries

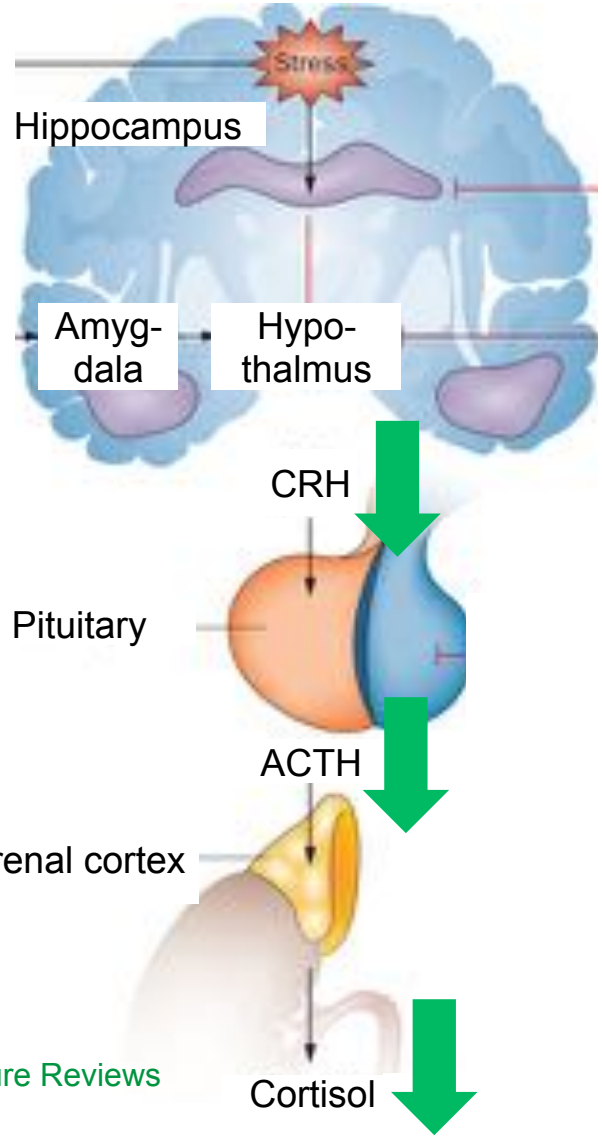
Stener-Victorin et al. Neuropeptides. 2001

Cold induced stress

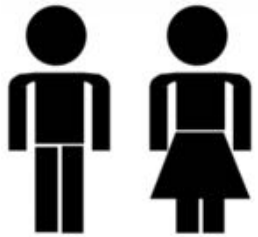
Eshkevari et al. J Endocrinolo 2013

Irritable bowel

Wu et al. Neurosci Lett 2009



Papadopoulos & Cleare Nature Reviews Endocrinology 2012



EA for depression

Le et al. Neursci Lett 2016

MA during heroin withdrawal

Wen et al. Bull Narc 1978

EA for osteoarthritis of the knee

Ahsin et al. PAIN 2009

MA in women before IVF

So et al. Hum Reprod. 2009

Perioperative EA prostatectomy

Ntritsou et al. Acu Med 2014

MA & EA for LBP

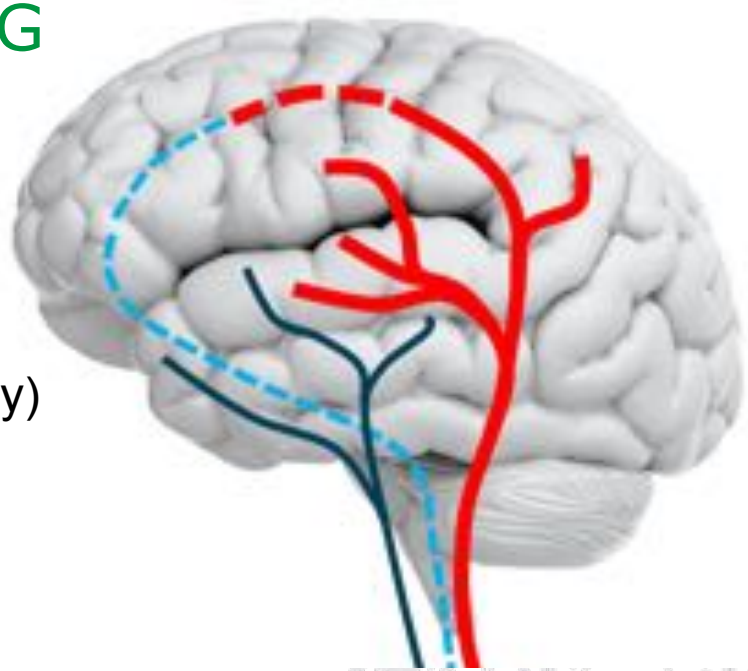
Harbach et al. Eur J Anesth 2007

CENTRAL MECHANISMS OF ACUPUNCTURE

… MUCH MORE THAN JUST ENDORPHINS

EVIDENCE FROM BRAIN IMAGING

- Reversal of pain related cortical restructuring
- Increase of white matter integrity (anisotropy)
- Regulation of connectivity between brain centers relevant to pain processing

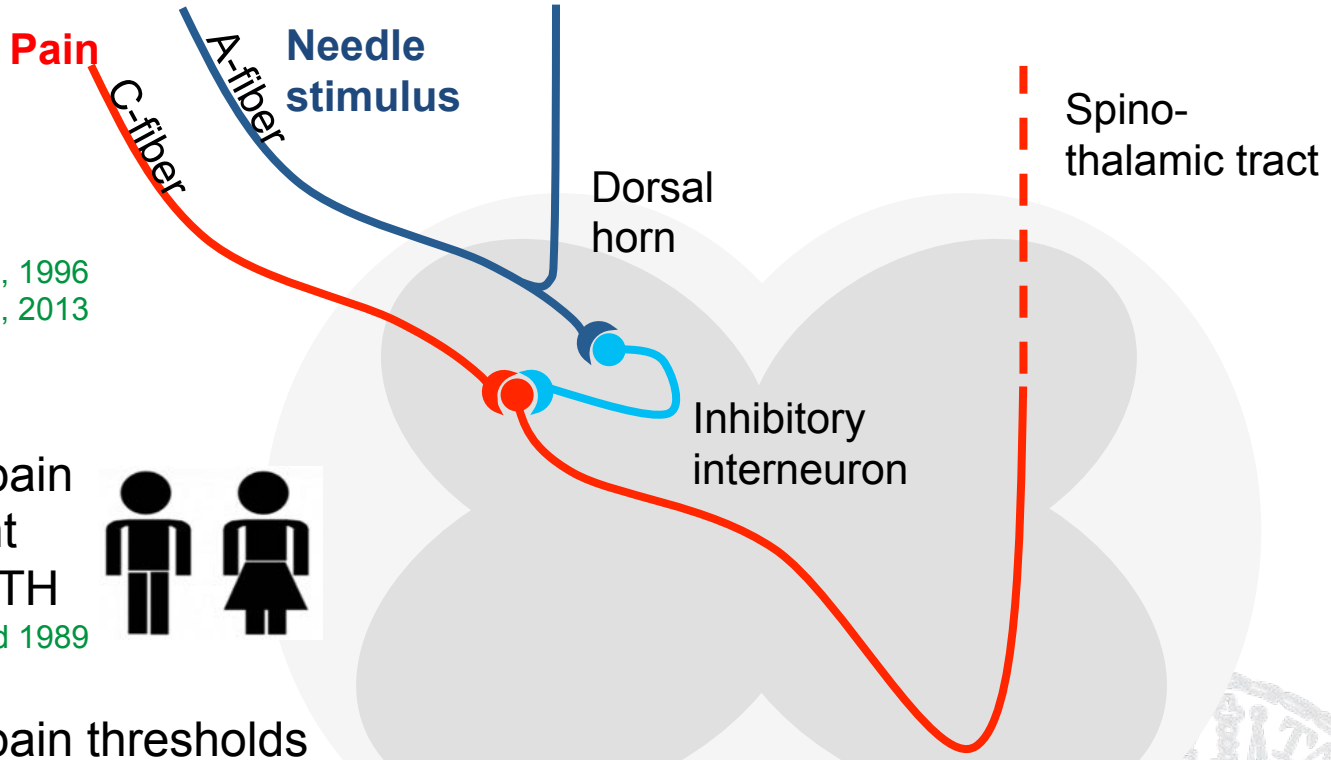


Napadow Hum Brain Map 2013
Maeda et al., BRAIN 2017
Napadow et al., NeuroImage 2007
Napadow et al., HBM 2006

SPINAL MECHANISMS - SEGMENTAL INHIBITION

- Evidence from animal experiments

  Sandkühler Prog Neurobiol, 1996
  Melin et al. Eur J Neurosci, 2013



- Segmental effects on pain thresholds independent from ß-Endorphin / ACTH

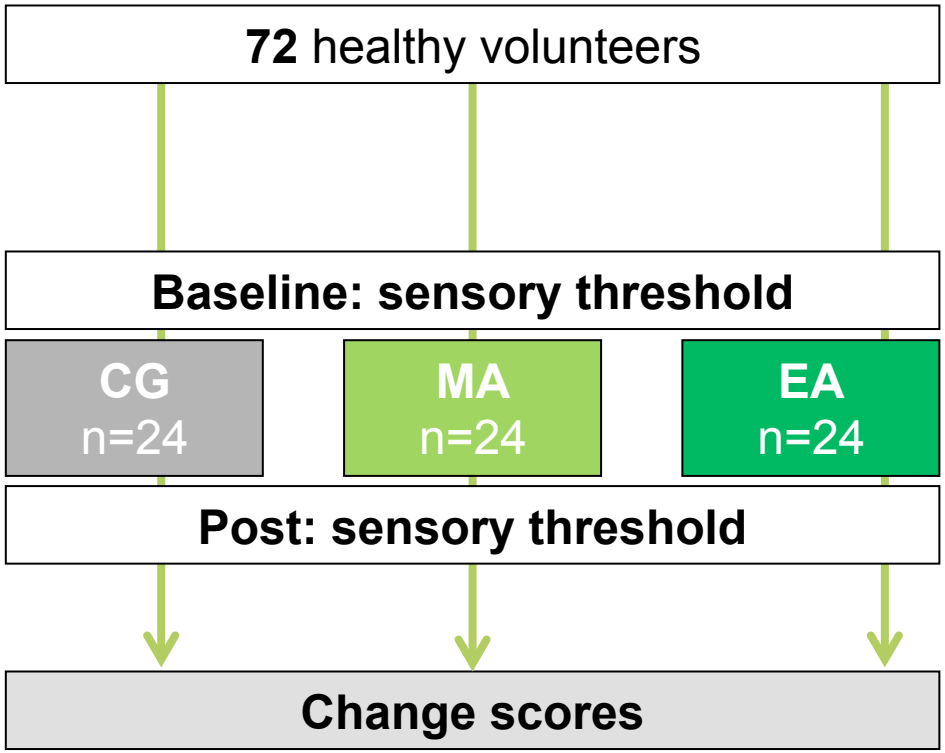
  Lundeberg et al. Am J Chin Med 1989

- Segmental effects on pain thresholds larger than heterosegmental or contralateral effects

  Barlas P et al. Pain 2006, Lang PM et al. Anest Analg 2010
  Leung A et al. J Alt and Compl Med 2005
  Leung AY et al. BMC Comp Alt Med 2008
  Bäumler et al. PAIN 2015

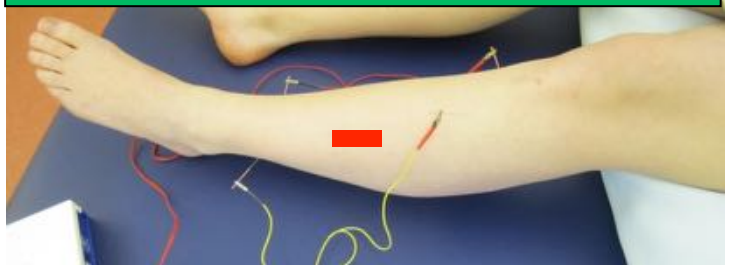
Picture Bäumler & Irnich DZA 2017

SEGMENTAL INHIBITION – RCT

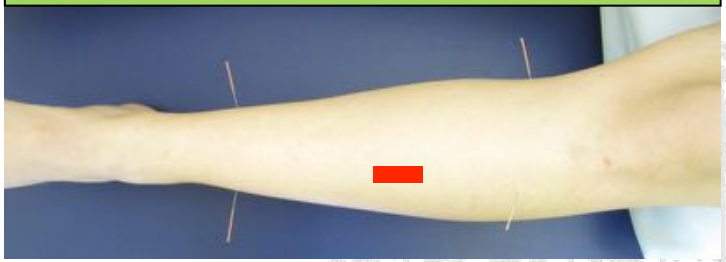


Control Group – CG
Rest 30 min

EA - Electroacupuncture
100 / 2 Hz alternating

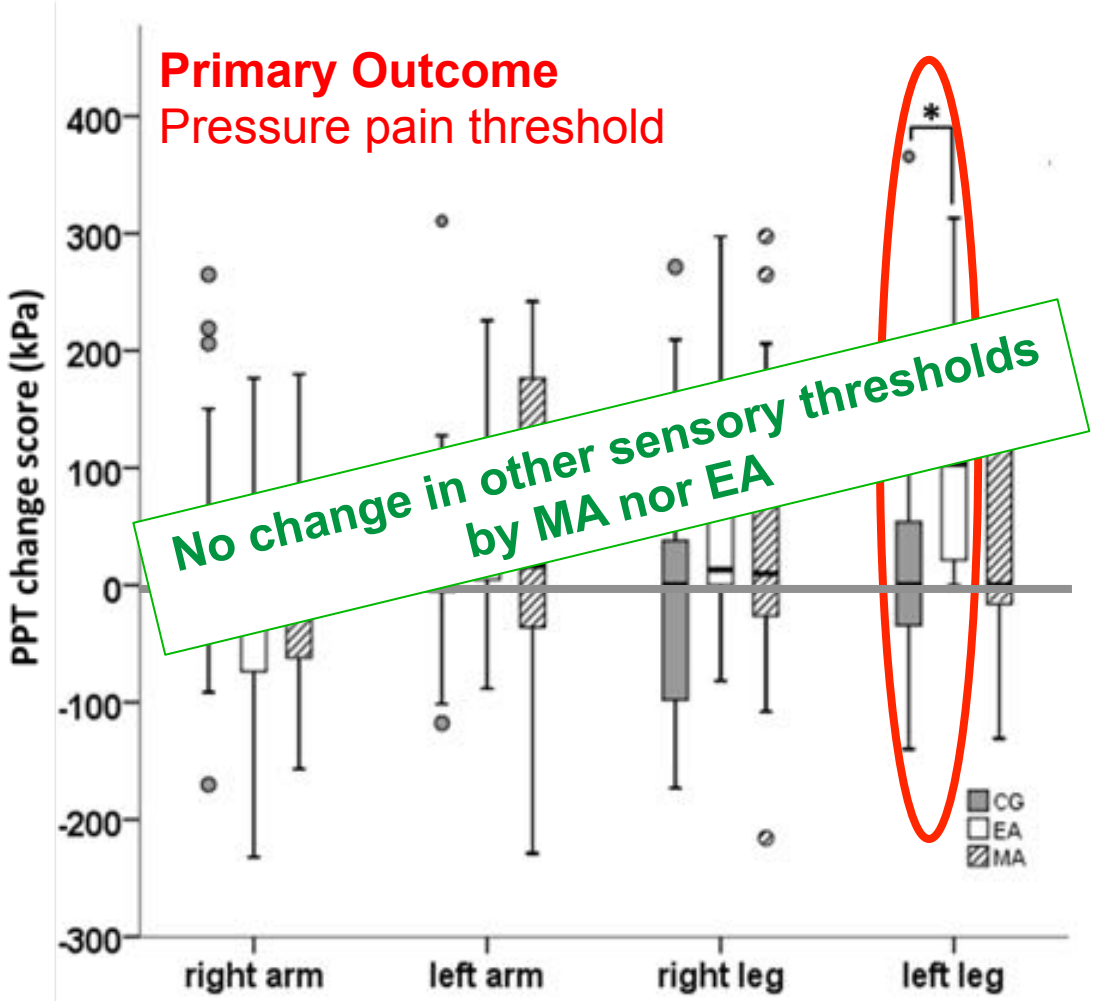


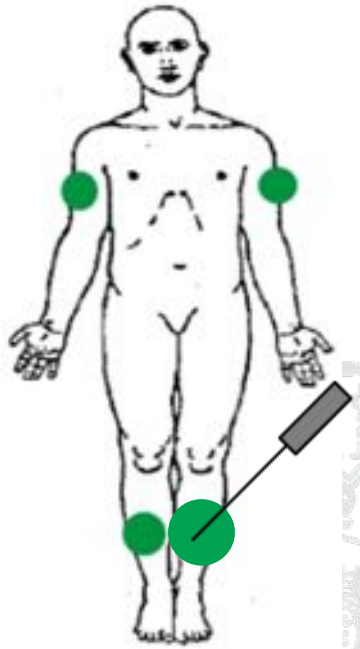
MA - Manual Acupuncture
rotation / up-down movement



Bäumler et al. PAIN 2015

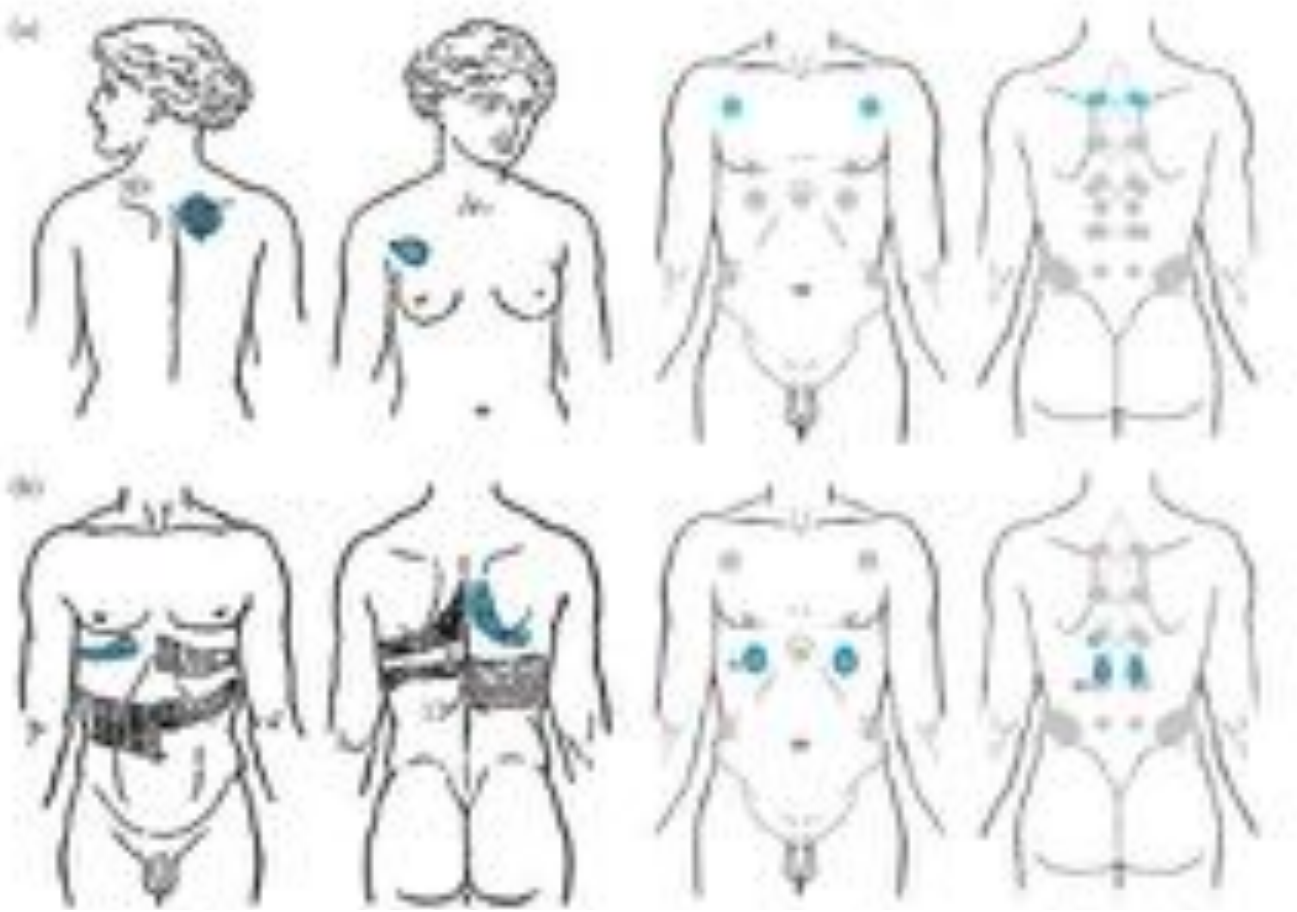
SEGMENTAL INHIBITION – RCT





Bäumler et al. PAIN 2015

HEAD ZONES - SHU / MU POINTS



Beissner et al. ECAM 2011

Acute Bronchitis

Lung zone

Biliary colic

Liver / gallbladder zones

SPINAL MECHANISMS – INHIBITION OF SYNAPTIC FACILITATION

Decrease of SP and its receptor NK1

EA in NGF induced pain model

Aloe et al. Neurosci Lett 2009

EA cancer pain model

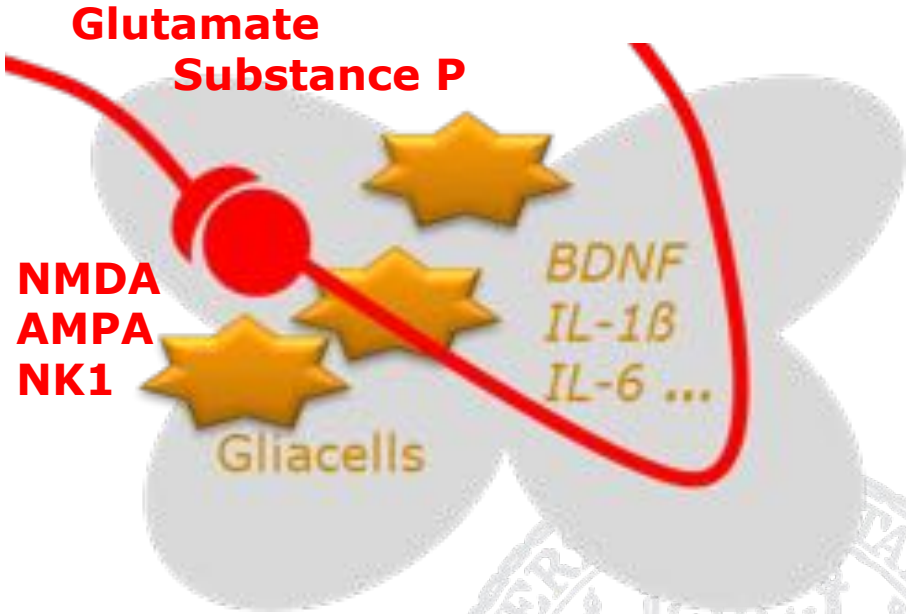
Lee et al. Acu & Electrother Res 2009

EA chronic inflammatory pain model

Zhang et al. Neurosci Lett 2005

Dry needling myofascial pain

Hsieh et al. BioMed Res Int 2014



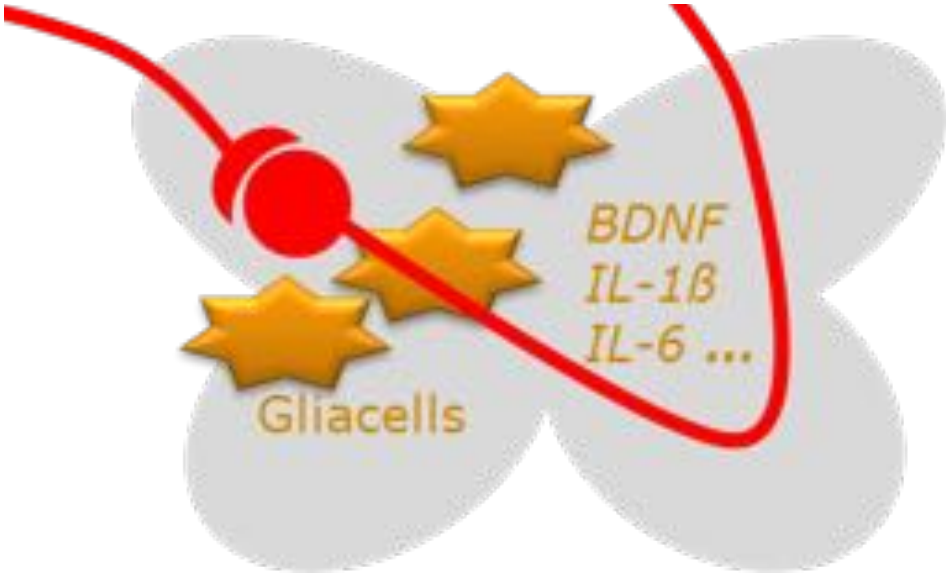
Inhibition of NMDA & AMPA upregulation

EA in chronic visceral hypersensitivity

Tian et al. Life sciences 2008

Liu et al. JPS 2016

SPINAL MECHANISMS – INHIBITION OF SYNAPTIC FACILITATION



Inhibition of gliacell activation

MA in chronic pain model (catchel-O-methyltransferase inhibitor induced)

Kim et al. J Pain 2018

EA neuropathic pain after spinal nerve ligation

Liang et al. Acu Med 2015

EA in monarthritis of the knee
Synergistic effect with minocycline (microglia inhibitor)

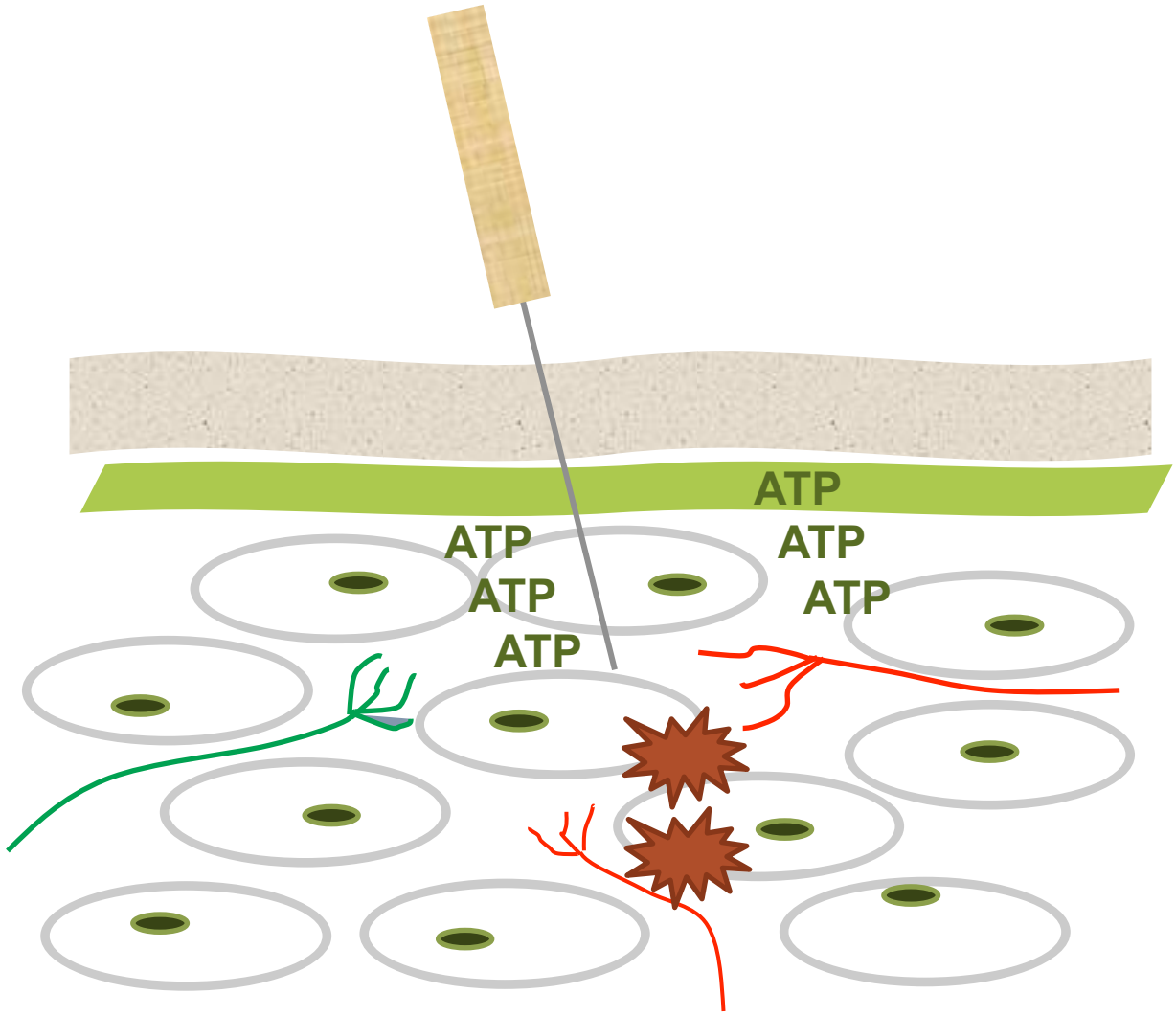
Shan et al. Neurobil Dis 2007

GFAP
glial fibrillary acidic protein
= astroglyosis marker

OX-42
microglia marker

p38
mitogen activated protein kinase

LOCAL MECHANISMS - ADENOSIN



Picture: Bäumler & Irnich DZA 2017

Tissue deformation

↓

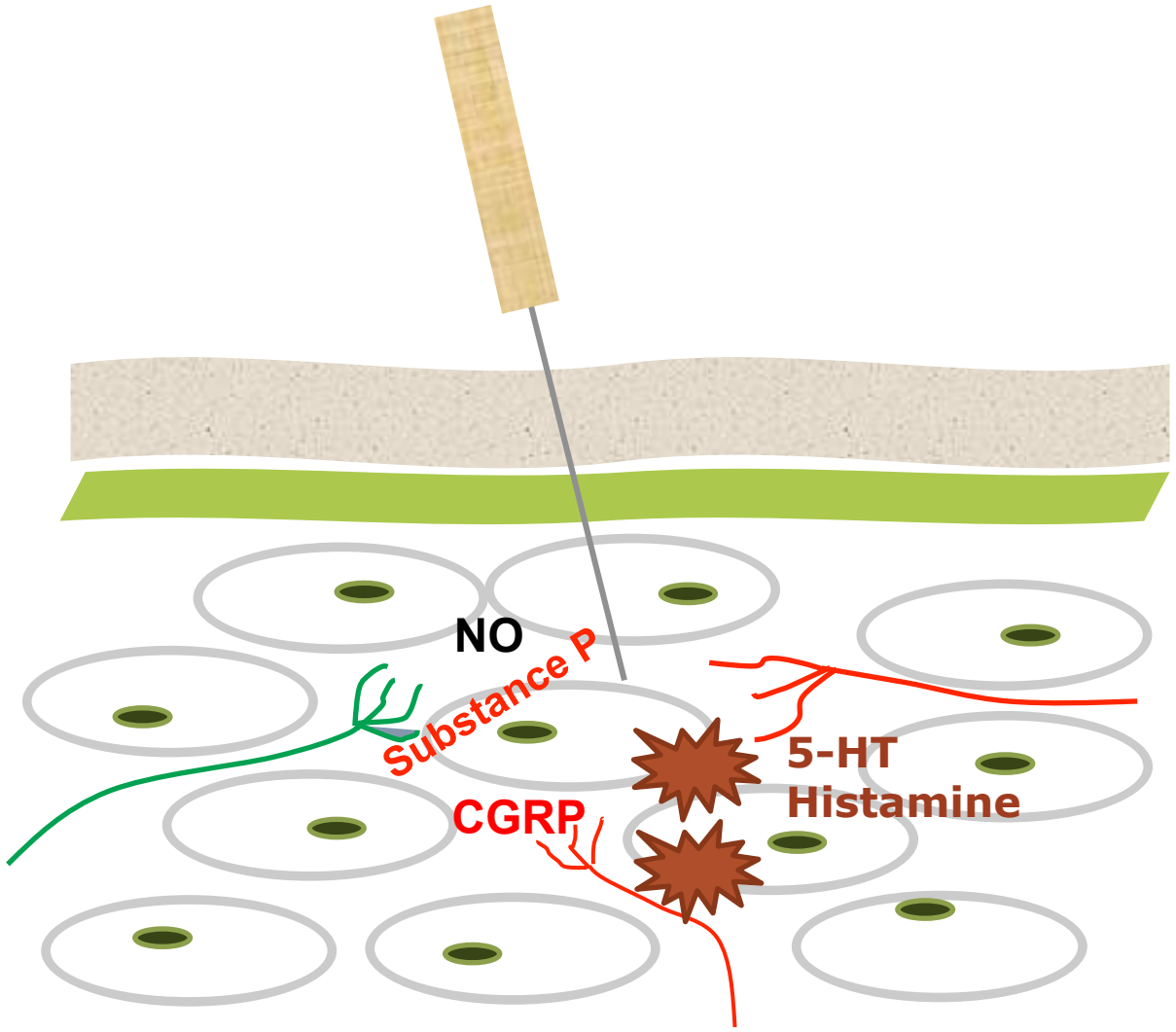
ATP release & degradation to **Adenosine**

↓

A1-receptor on peripheral nociceptors antinocieptive effect

Goldman et al., Nature Neuroscience 2010

LOCAL MECHANISMS – MASTCELL ACTIVATION



Picture: Bäumler & Irnich DZA 2017

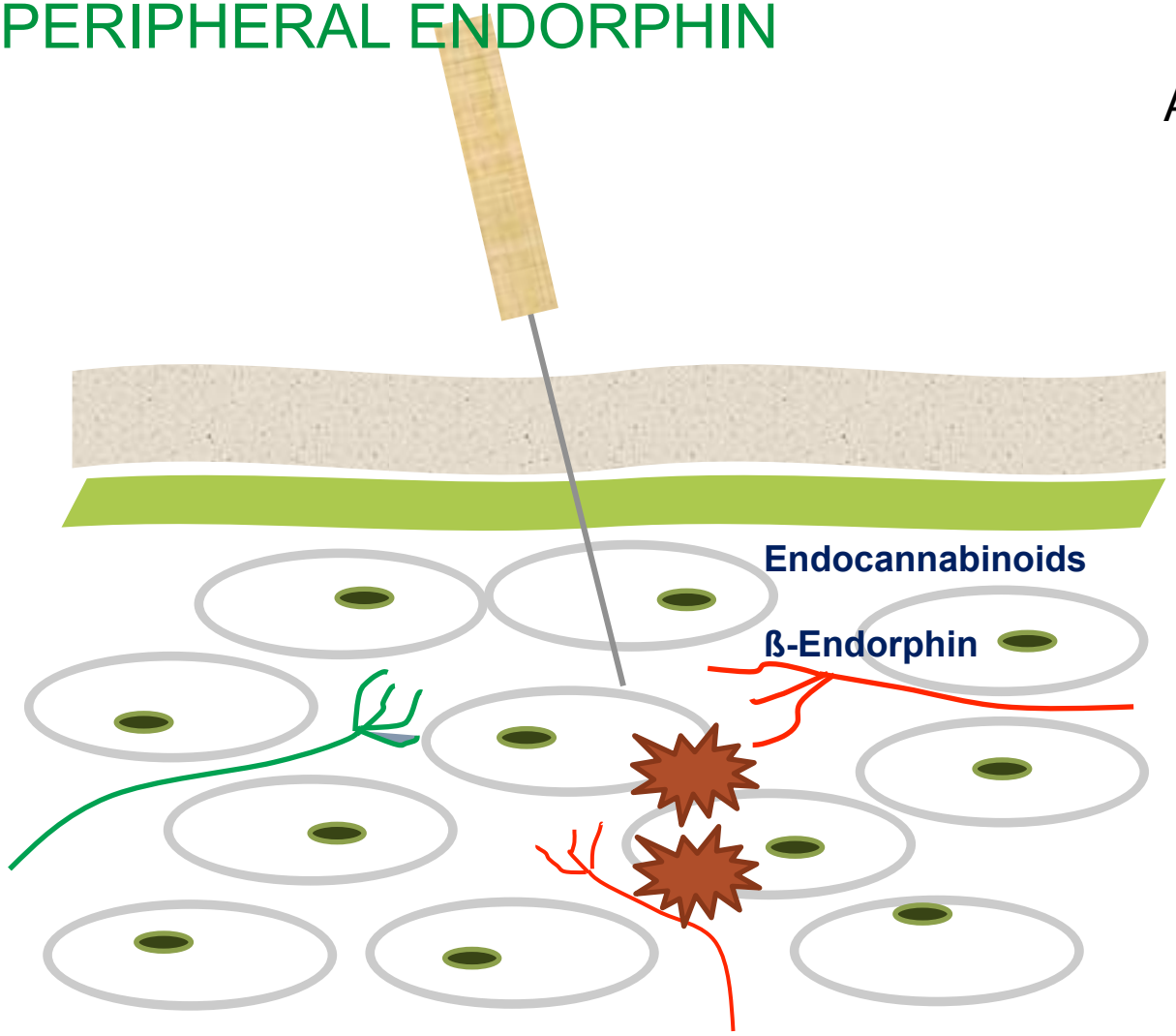
CGRP &Substance P released from primary afferents

Kashiba and Y. Ueda
Am J Chin Med 1991
Sato et al. Neurosci Lett 2000

Mastcell invasion and activation **histamine & serotonin** release

Karatay et al. Pain Med 2018
Chen et al. Sci Rep 2018 (TENS)
Ding et al. PLOSOne 2018

LOCAL MECHANISMS – ENDOCANNABINOIDS PERIPHERAL ENDORPHIN



Picture: Bäumler & Irnich DZA 2017

Aktivation of CB2 receptors
on macrophages
T-lymphocytes
skin cells

↓

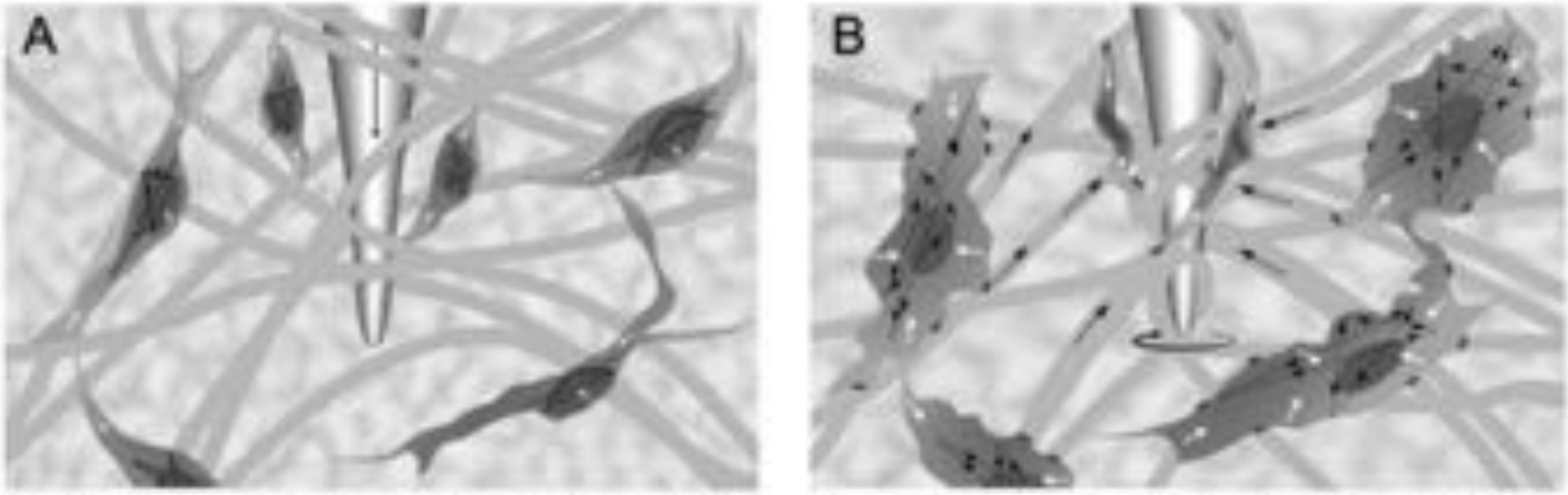
Release of
ß-endorophin

↓

Modulation of peripheral
nociceptor activity

Chen et al. J Pain 2009
Zhang et al. J Pain 2010
Martins et al. Pain Med 2012
Su et al. Molecular Pain 2011
Wang et al. Eur J Pain 2013

LOCAL MECHANISMS – MECHANOTRANSDUCTION



- Needle rotation stretches connective tissue by pulling collagen fibers
- Fibroblasts react by expanding cross-sectional area

Langevin et al. J Cell Physiol 2006
Langevin et al. FASEB 2001

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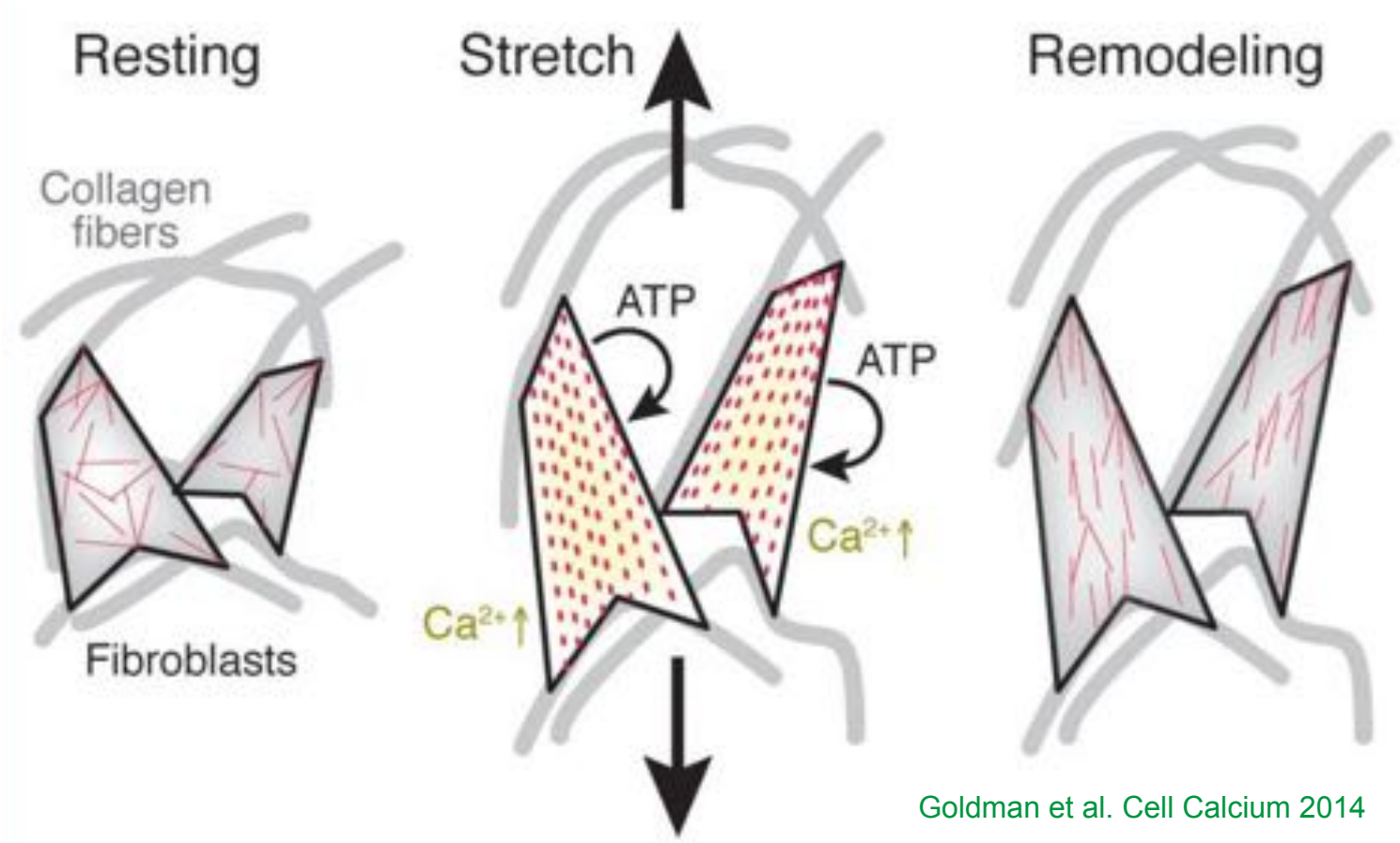
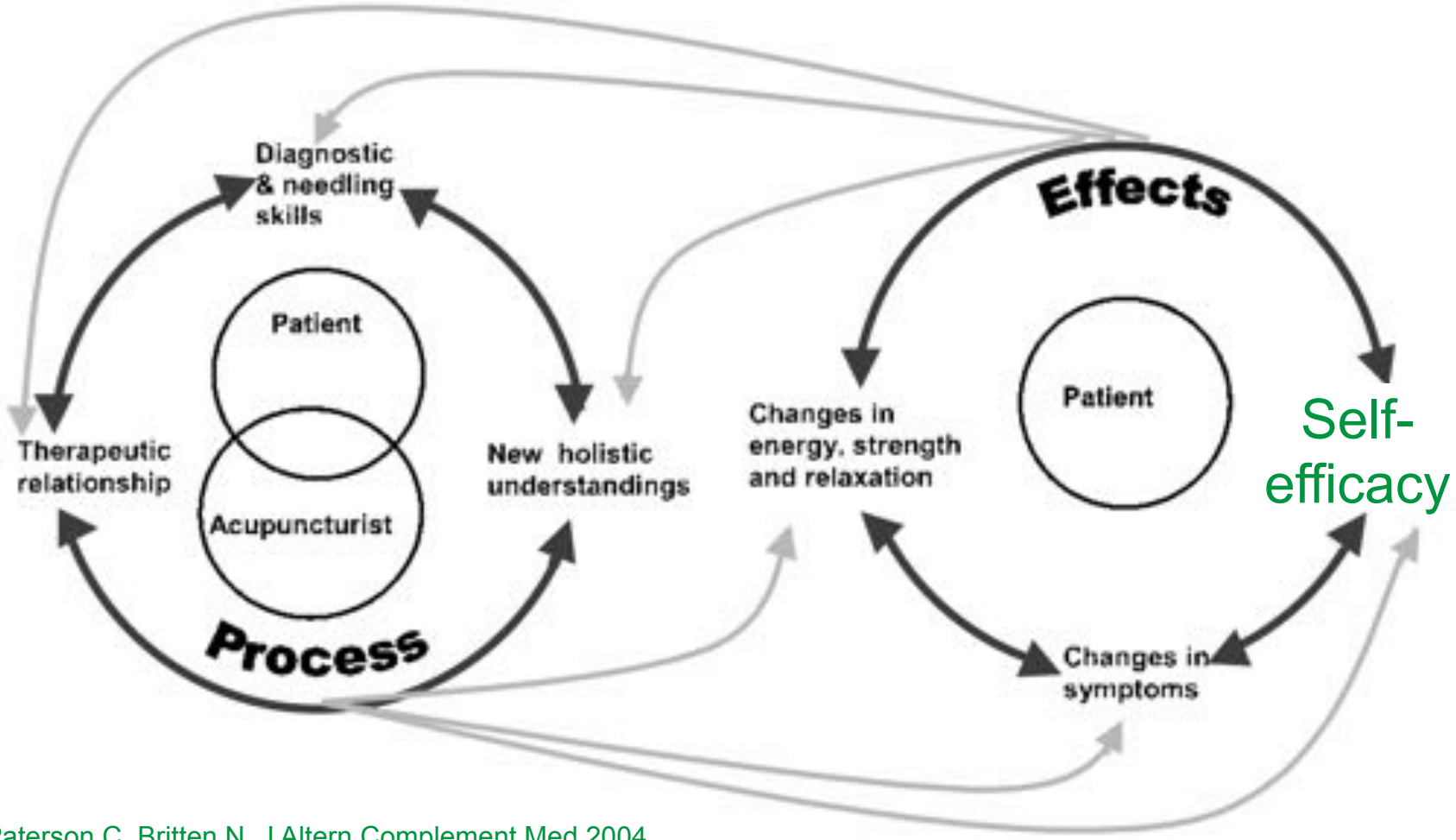
LOCAL MECHANISMS – MECHANOTRANSDUCTION

Formation change in fibroblasts mediated by ATP release



Goldman et al. Cell Calcium 2014

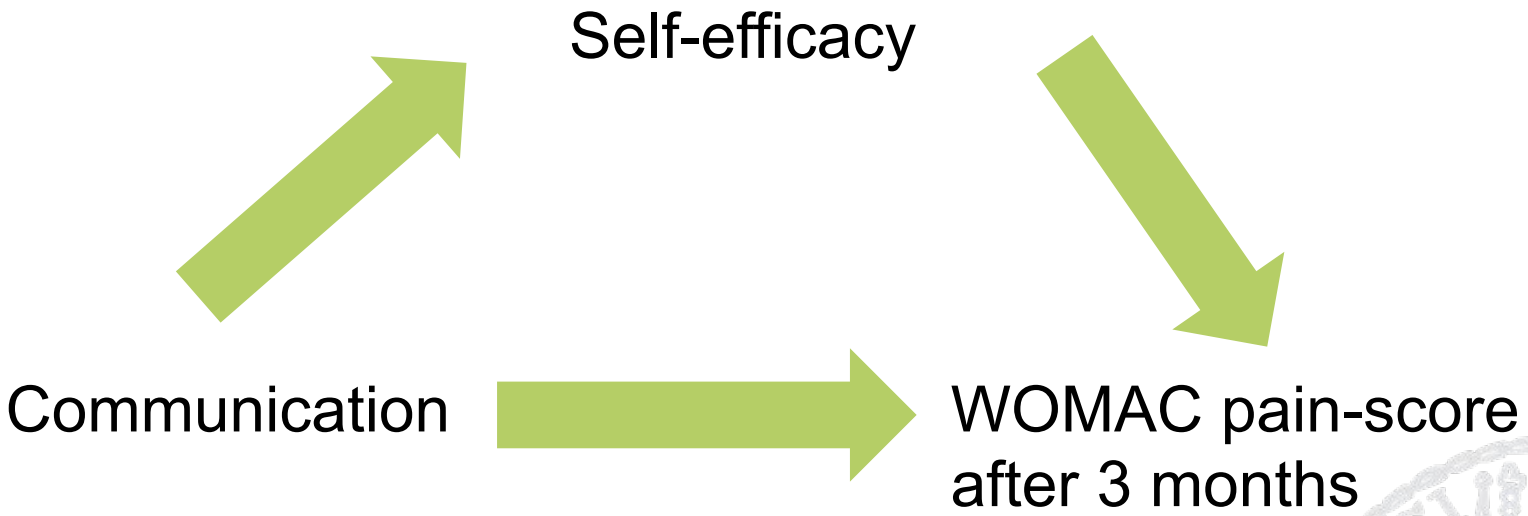
THE THERAPEUTIC PROCESS



Paterson C, Britten N. J Altern Complement Med 2004

PROMOTION OF SELF-EFFICACY

Secondary analyis of a 3-arm RCT on acupuncture for osteoarthritis of the knee



Lo et al. Arthr Care Res_2015

SUMMARY – ACUPUNCTURE MECHANISMS

- ✓ Central : release of endogenous opioid
  activation of descending pain control
  reversal of pain related cortical restructuring / anisotropy / connectivity

- ✓ Spinal: segmental inhibition
  reduction of synaptic facilitation

- ✓ Local: release of ATP / CGRP / substance P / endocannabinoids / endorphins /
  histamine / serotonin (interaction with immune cells9
  activation of fibroblast – mechanotransduction

- ✓ Acupuncture setting: holistic care - promotion of self-efficacy