BACKGROUND ON LTR

- LTR is a spinal reflex
- LTR potentials have been shown to be ablated with peripheral nerve sectioning but not by spinal cord lesioning cephalad to the segment where the LTR is produced. Hong CZ. Arch Phys Med Rehab 1994;75:12.
- Bilateral LTR's observed with unilateral needling of *active* TrP

HYPOTHESIS

- Is there a difference in the LTR response to needle stimulation in Active TrP's vs. Latent TrP's ?
- Null Hypothesis
  - LTR will have same pattern in both

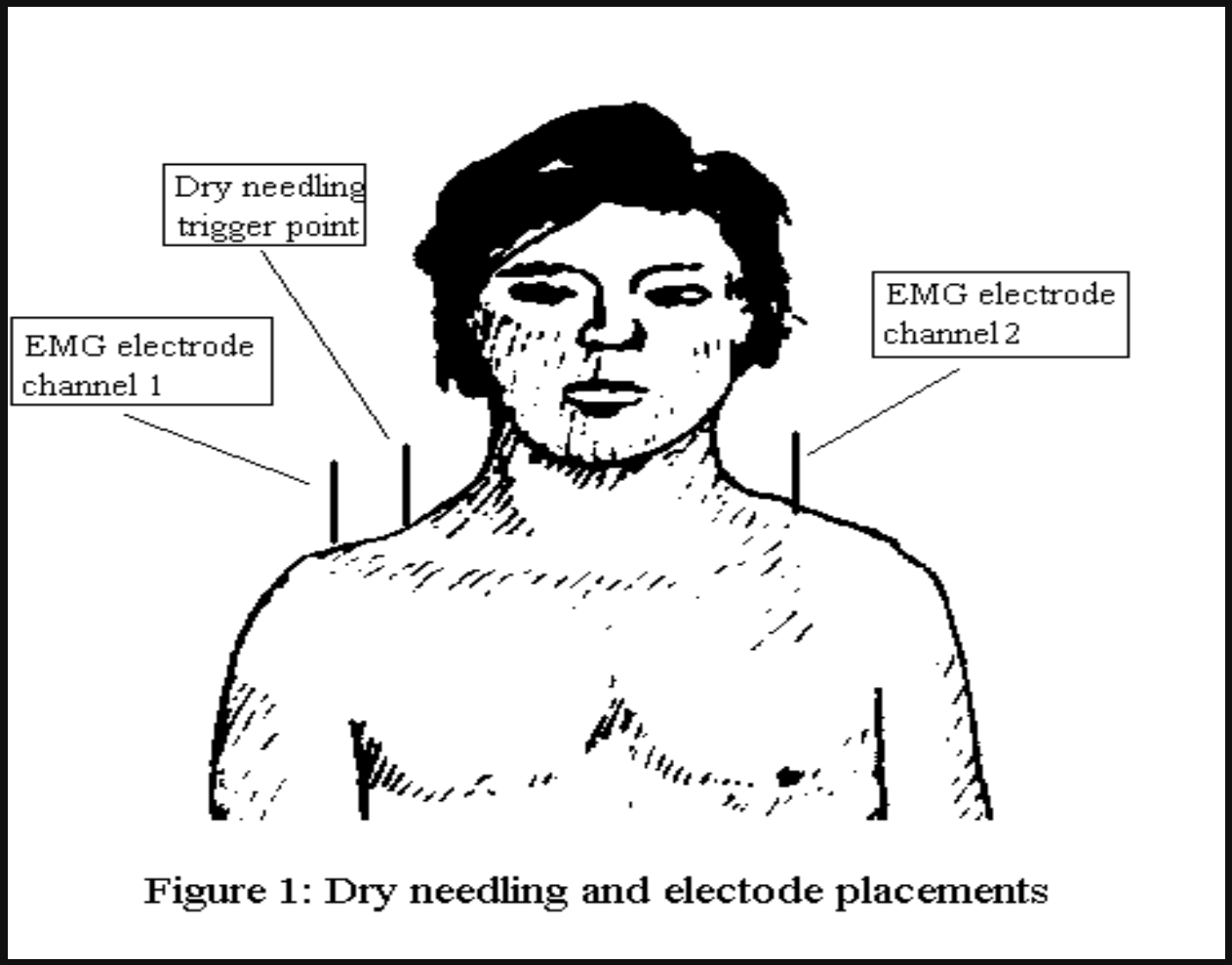
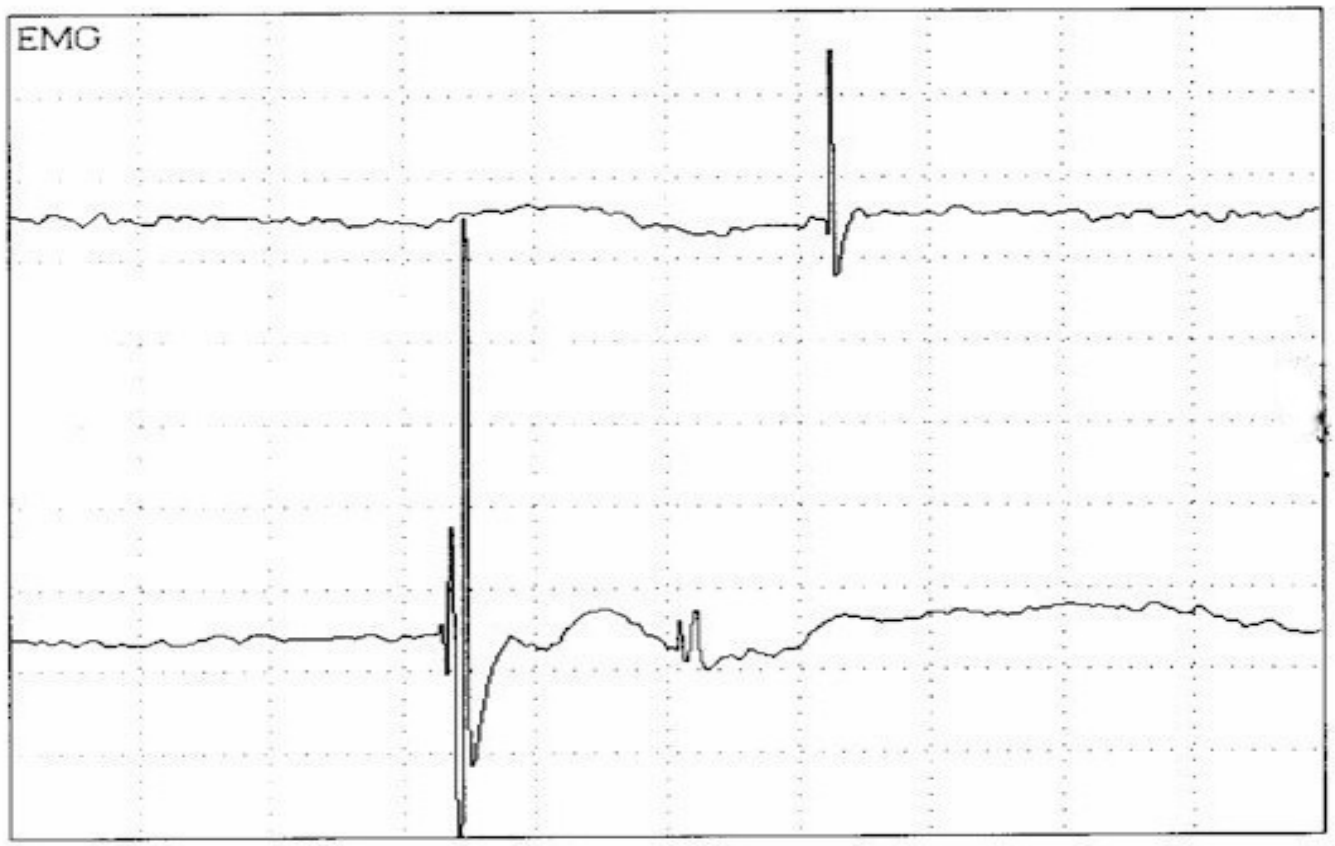


Figure 1: Dry needling and electode placements

Audette JF, Wang F Am J Phys Med Rehab 2004;83:368-374.



Ch	Hicut	Locut	Gain (μV/div)	Sweep (ms/div)
1	10000	10.00	200.0	20.0
2	10000	10.00	200.0	20.0

Ch	Hicut	Locut	Gain (μV/div)	Sweep (ms/div)
1	10000	10.00	200.0	20.0
2	10000	10.00	200.0	20.0

RESULTS

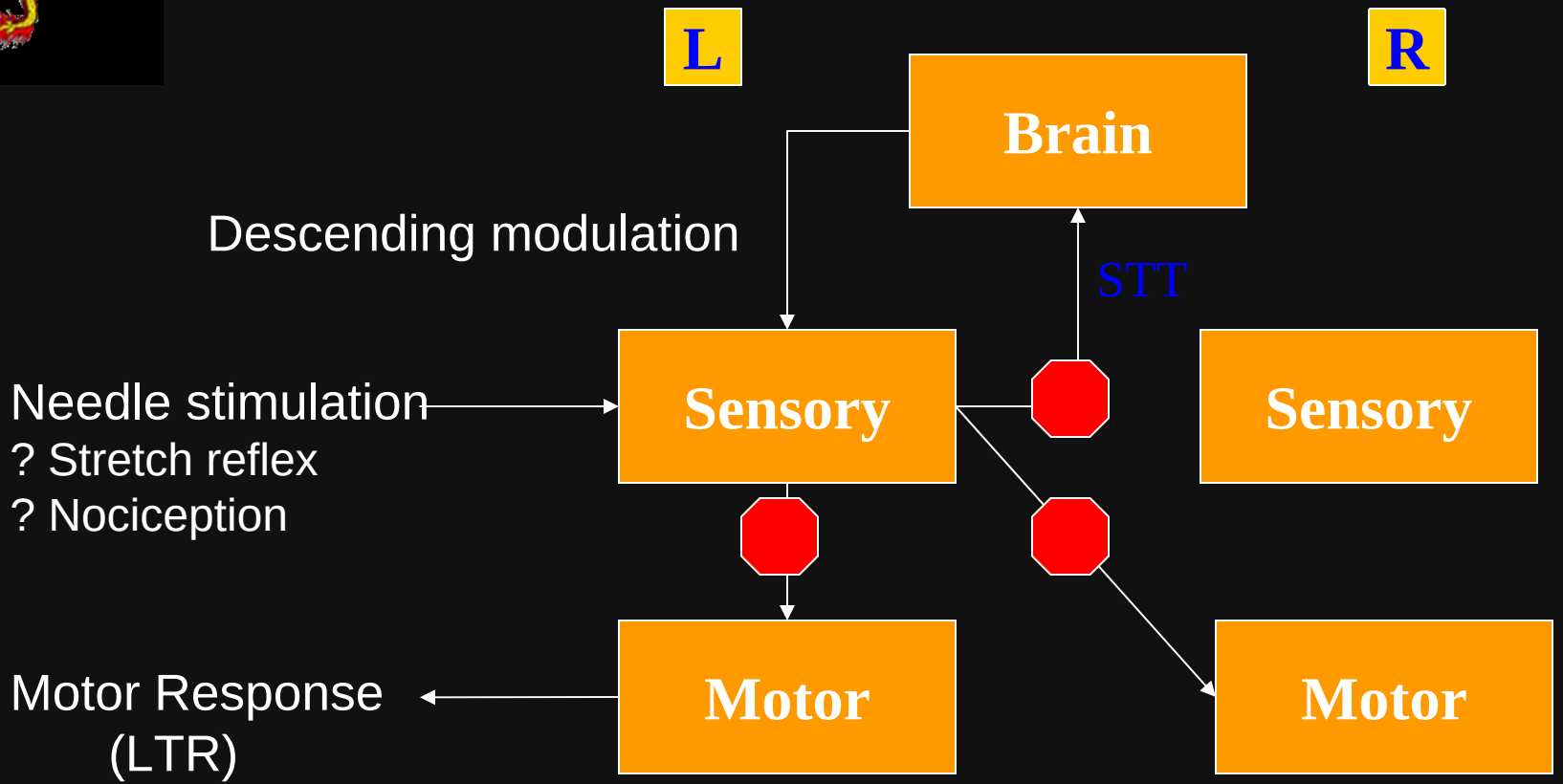
	Bilateral MUP	Ipsilateral MUP only	Total
Control (Latent MTrP) row %	**0**	**8** **100.00%**	**8** **100.00%**
Patients (Active MTrP) row %	**8** **61.54%**	**5** **38.46%**	**13** **100.00%**

61.5% of subjects with ***active*** MTrP had bilateral motor unit potentials while none in 8 control subjects with ***latent*** MTrP

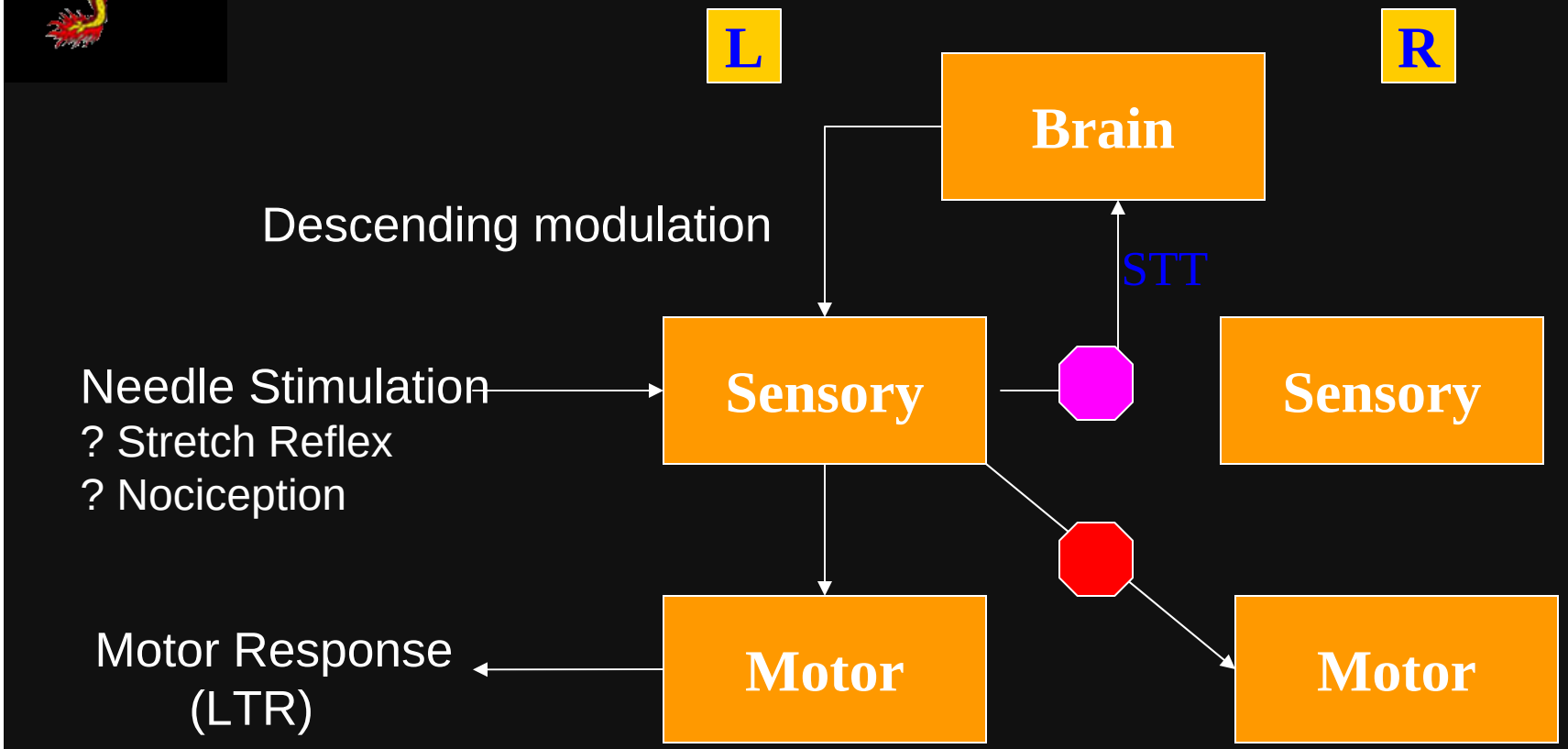
NEUROPLASTICITY and LTR

- Difference between Active vs Latent TrP due to maladaptive neuroplastic changes in CNS of both sensory and motor arms of system
- Mense has demonstrated such changes in experimental model of muscle pain (Pain 1994)

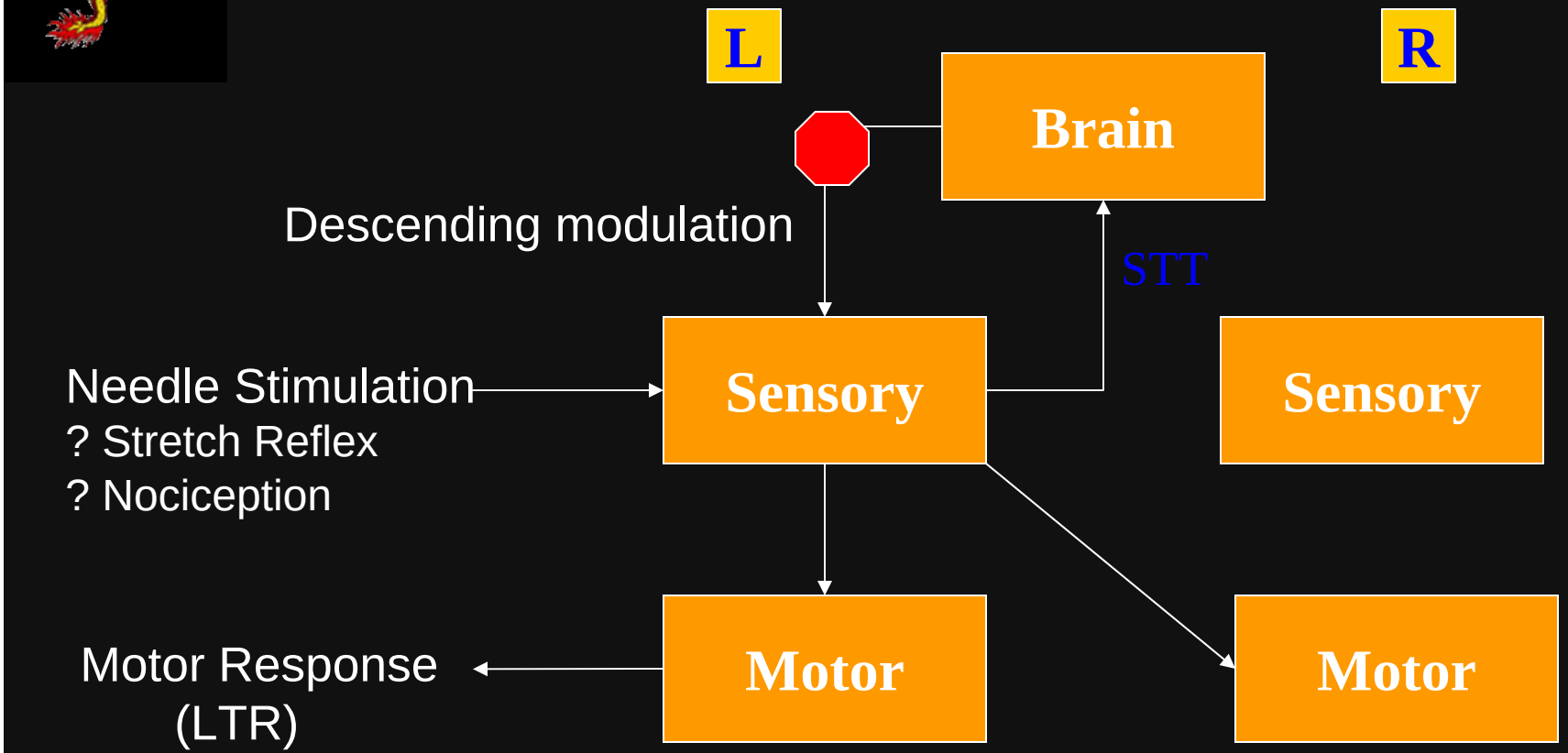
NORMAL


L
R
Brain
Descending modulation
STT
Needle stimulation
? Stretch reflex
? Nociception
Sensory
Sensory
Motor
Motor
Motor Response
(LTR)

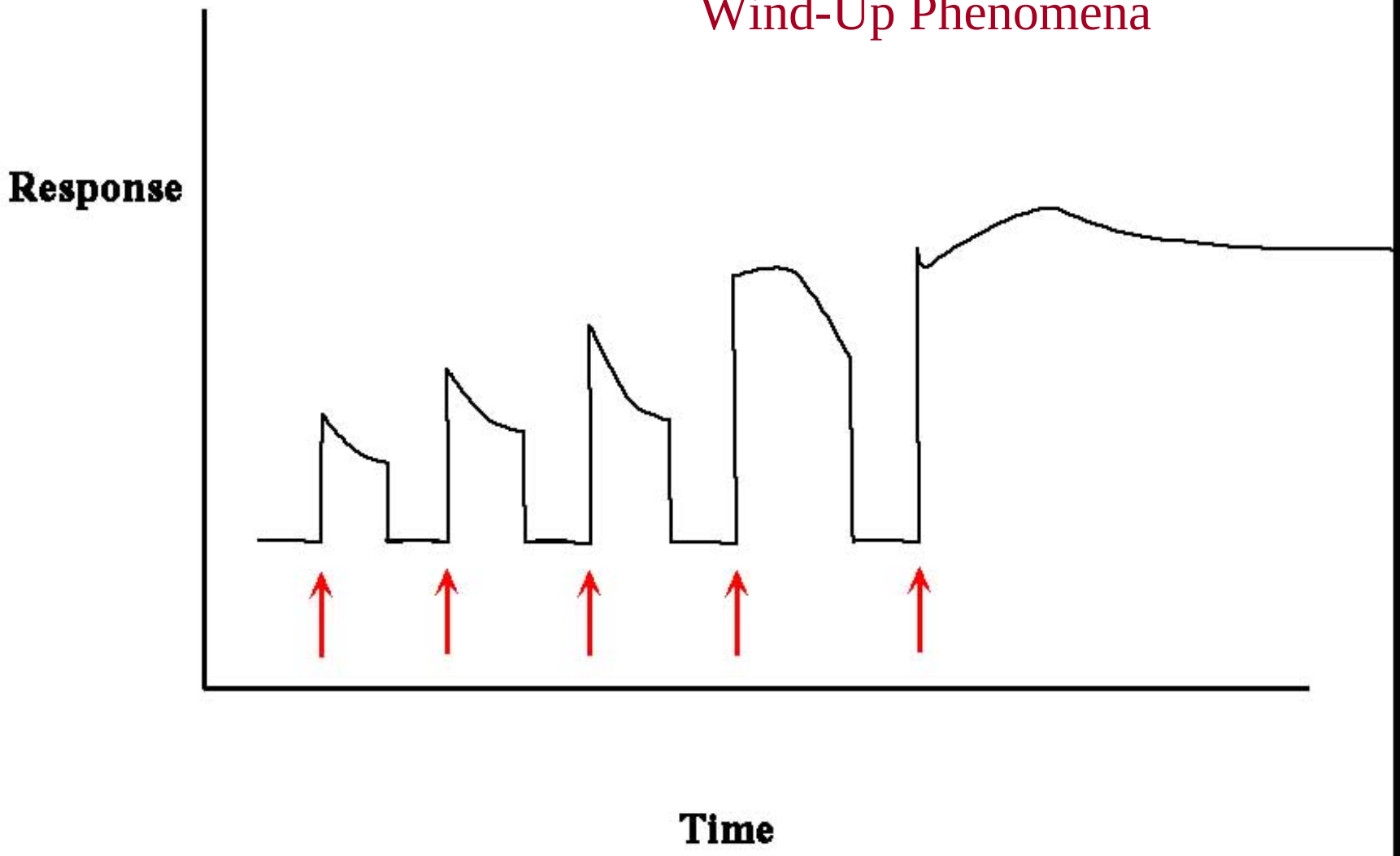
LATENT TrP


L
R
Brain
Descending modulation
STT
Needle Stimulation
? Stretch Reflex
? Nociception
Sensory
Sensory
Motor Response
(LTR)
Motor
Motor

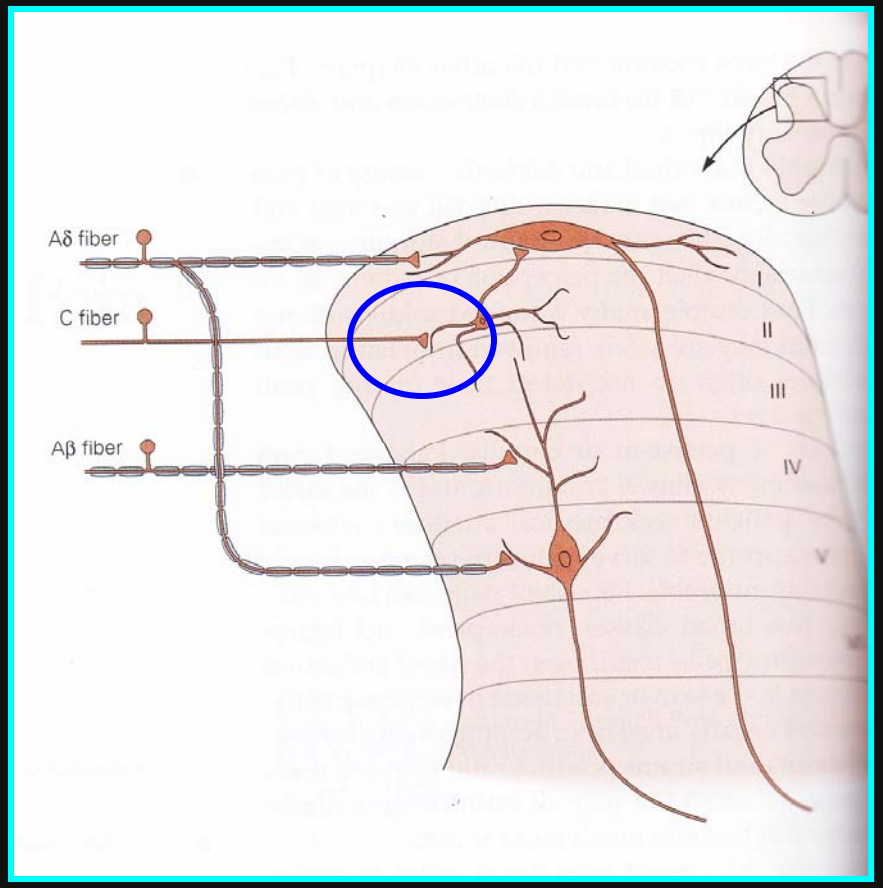
ACTIVE TrP

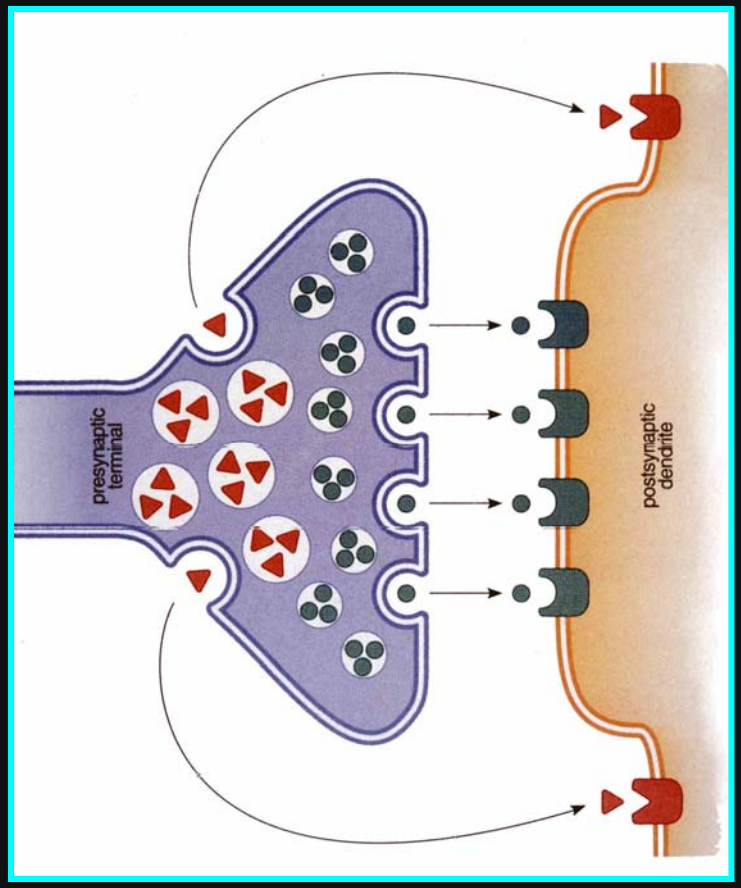

L
R
Brain
Descending modulation
STT
Needle Stimulation
? Stretch Reflex
? Nociception
Sensory
Sensory
Motor Response
(LTR)
Motor
Motor

Wind-Up Phenomena



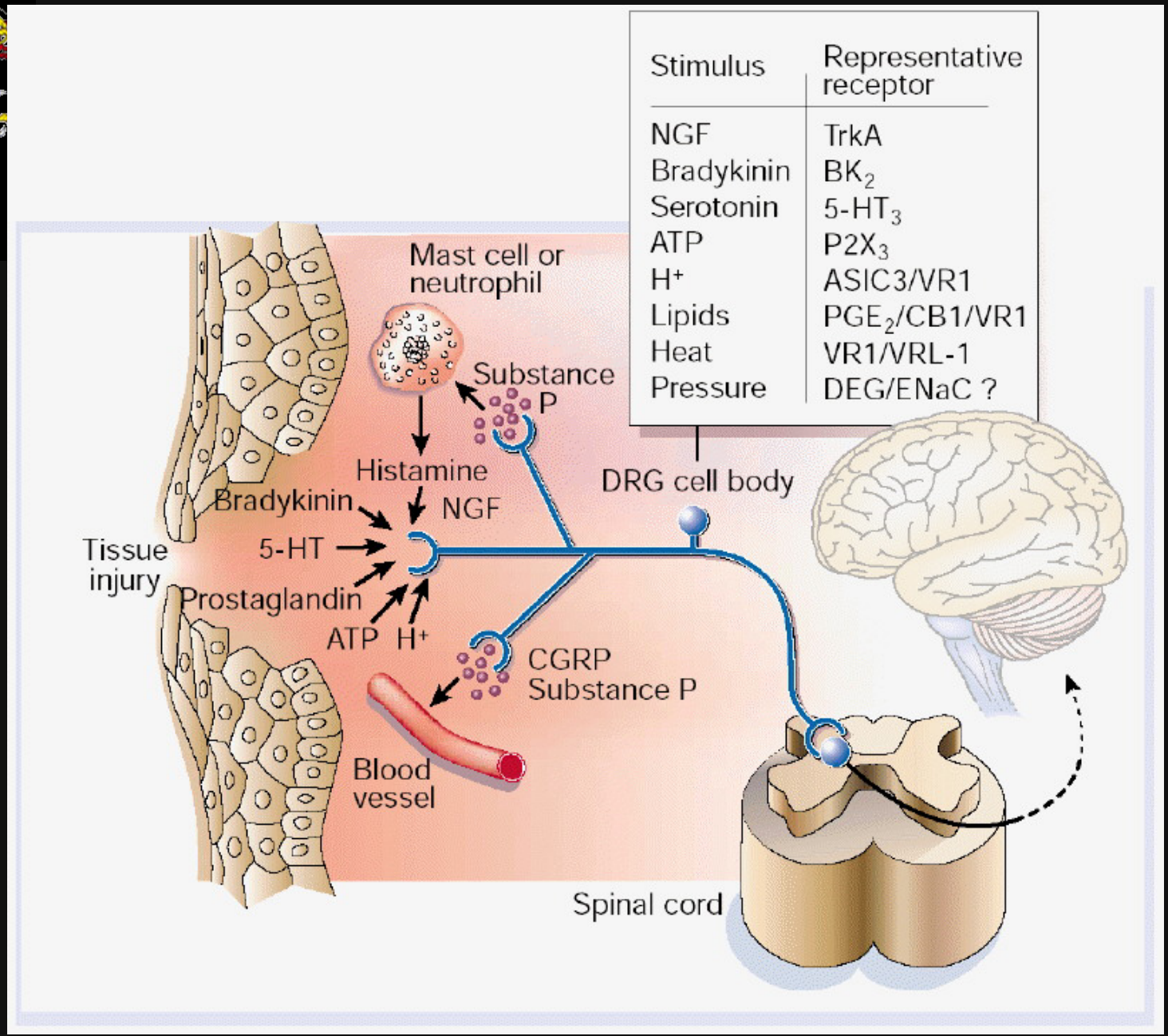
Dorsal Horn


Aδ fiber
C fiber
Aβ fiber
I
II
III
IV
V

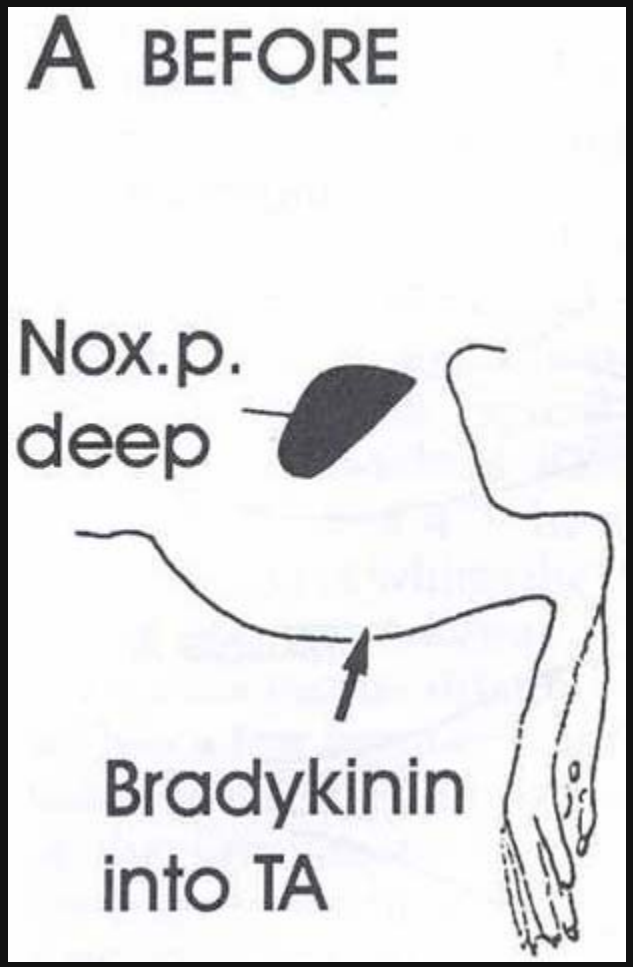

presynaptic terminal
postsynaptic dendrite

Neurogenic Inflammation

- Release of excitatory neuropeptides
  - SP, CGRP
- Histamine release from Mast Cells
- Bradykinin release from Endothelial Cells
- Activation of local Immune Cells
  - Release of cytokines and other activating substances
- Change in peripheral nerve sensitization


Stimulus
Representative receptor
NGF
TrkA
Bradykinin
BK_2
Serotonin
$5\text{-}HT_3$
ATP
$P2X_3$
H^+
ASIC3/VR1
Lipids
PGE_2/CB1/VR1
Heat
VR1/VRL-1
Pressure
DEG/ENaC ?
Mast cell or neutrophil
Substance P
Histamine
NGF
Bradykinin
5-HT
Tissue injury
Prostaglandin
ATP
H^+
CGRP
Substance P
Blood vessel
DRG cell body
Spinal cord

Expansion of Receptive Field

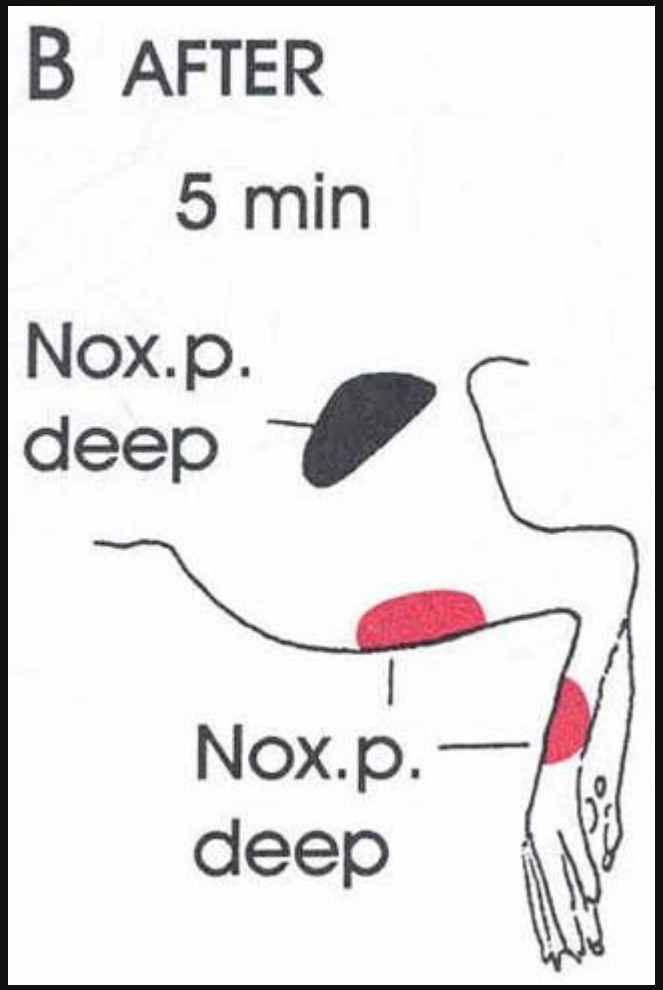


Selected neuron responds only to deep pressure in biceps femoris muscle

Hoheisel U, Mense S, Simons DG. Appearance of new receptive fields in rat dorsal horn neurons following noxious stimulation of skeletal muscle: a model for referral of muscle pain?

Neurosci lett 153:9-12, 1993

Expansion of Receptive Field

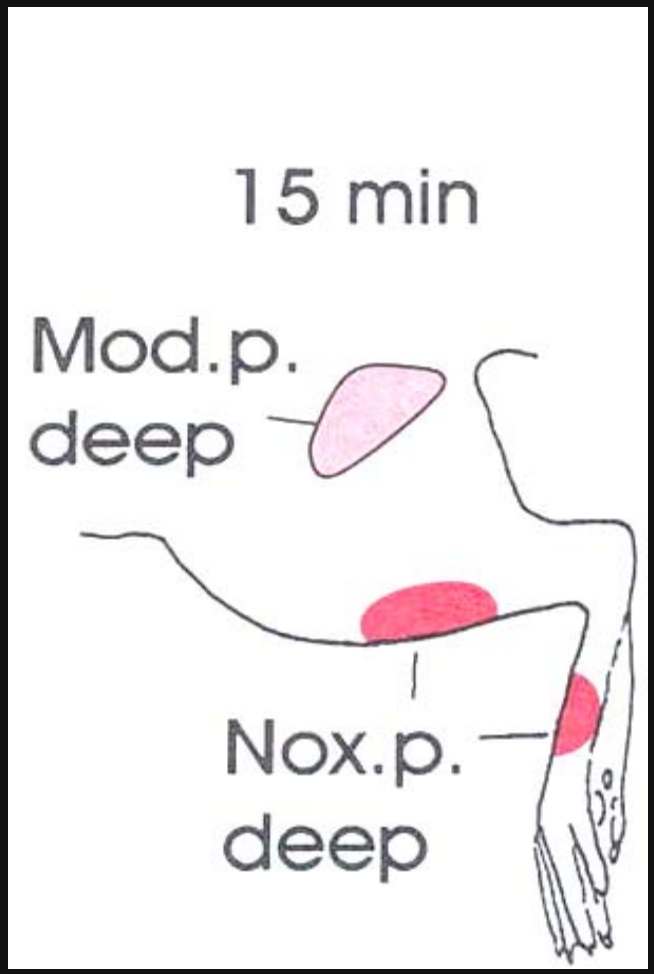


5 min after BK injection in TA, the neuron can be excited by additional RF's located in deep muscle and normally have high threshold

Hoheisel U, Mense S, Simons DG. Appearance of new receptive fields in rat dorsal horn neurons following noxious stimulation of skeletal muscle: a model for referral of muscle pain?

Neurosci lett 153:9-12, 1993

Expansion of Receptive Field

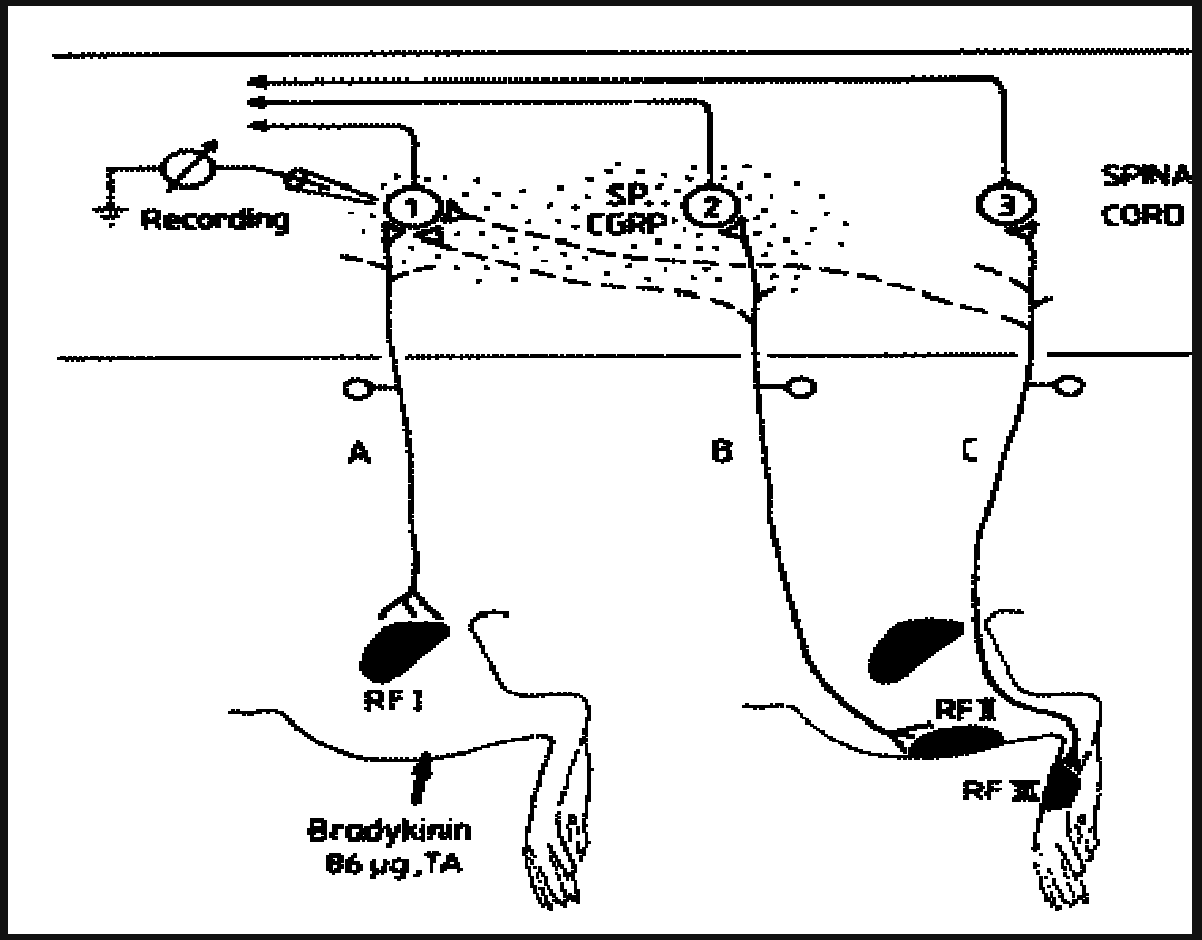


15 min after BK injection the neuron responds to moderate (*innocuous*) pressure in biceps femoris

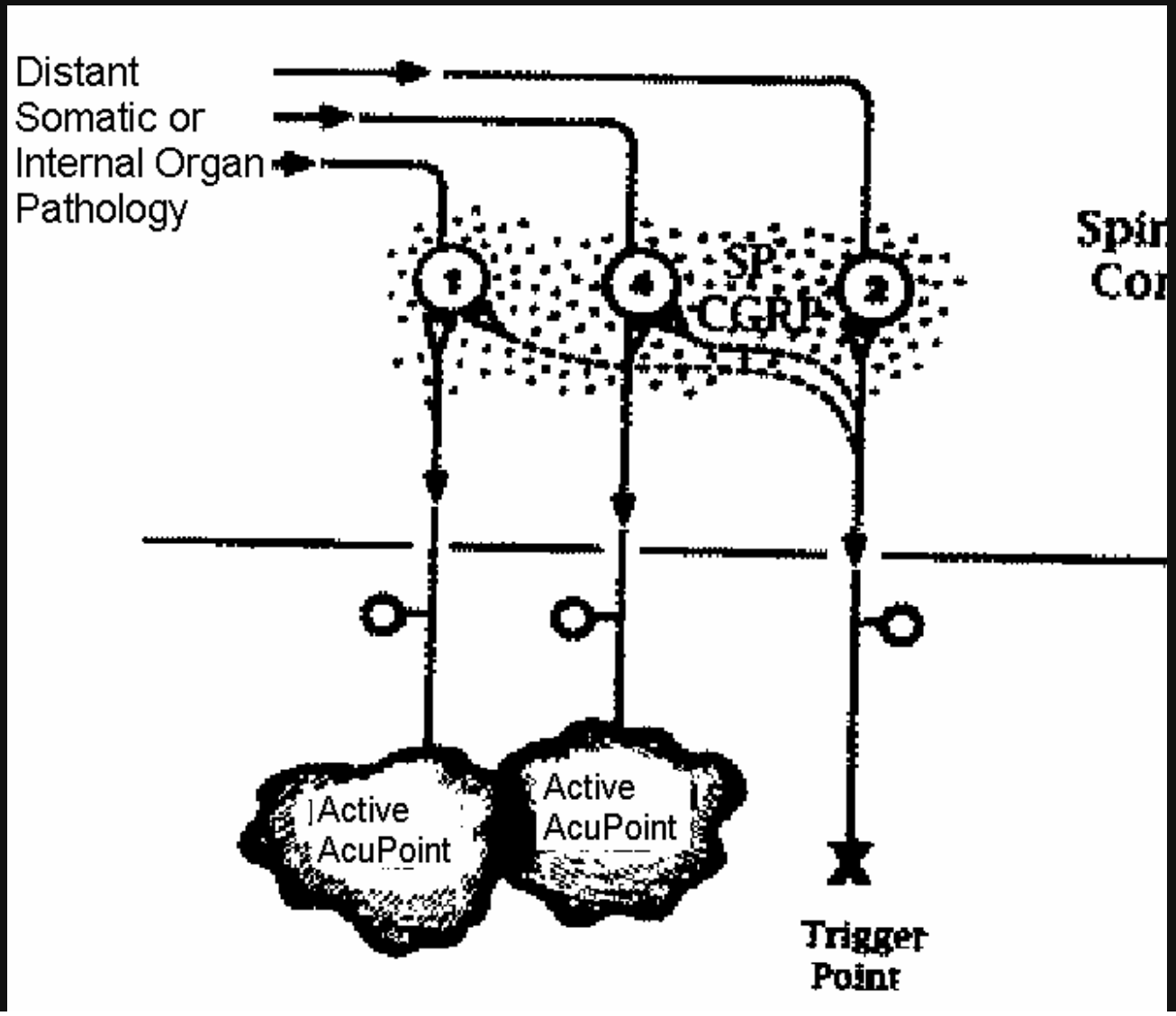
Hoheisel U, Mense S, Simons DG. Appearance of new receptive fields in rat dorsal horn neurons following noxious stimulation of skeletal muscle: a model for referral of muscle pain?

Neurosci lett 153:9-12, 1993

CHANGES IN RECEPTIVE FIELD

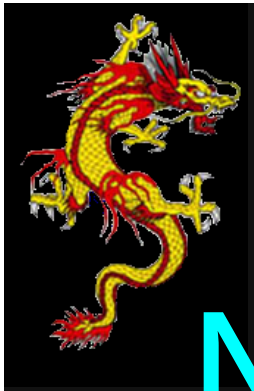


Dorsal Horn Reflex



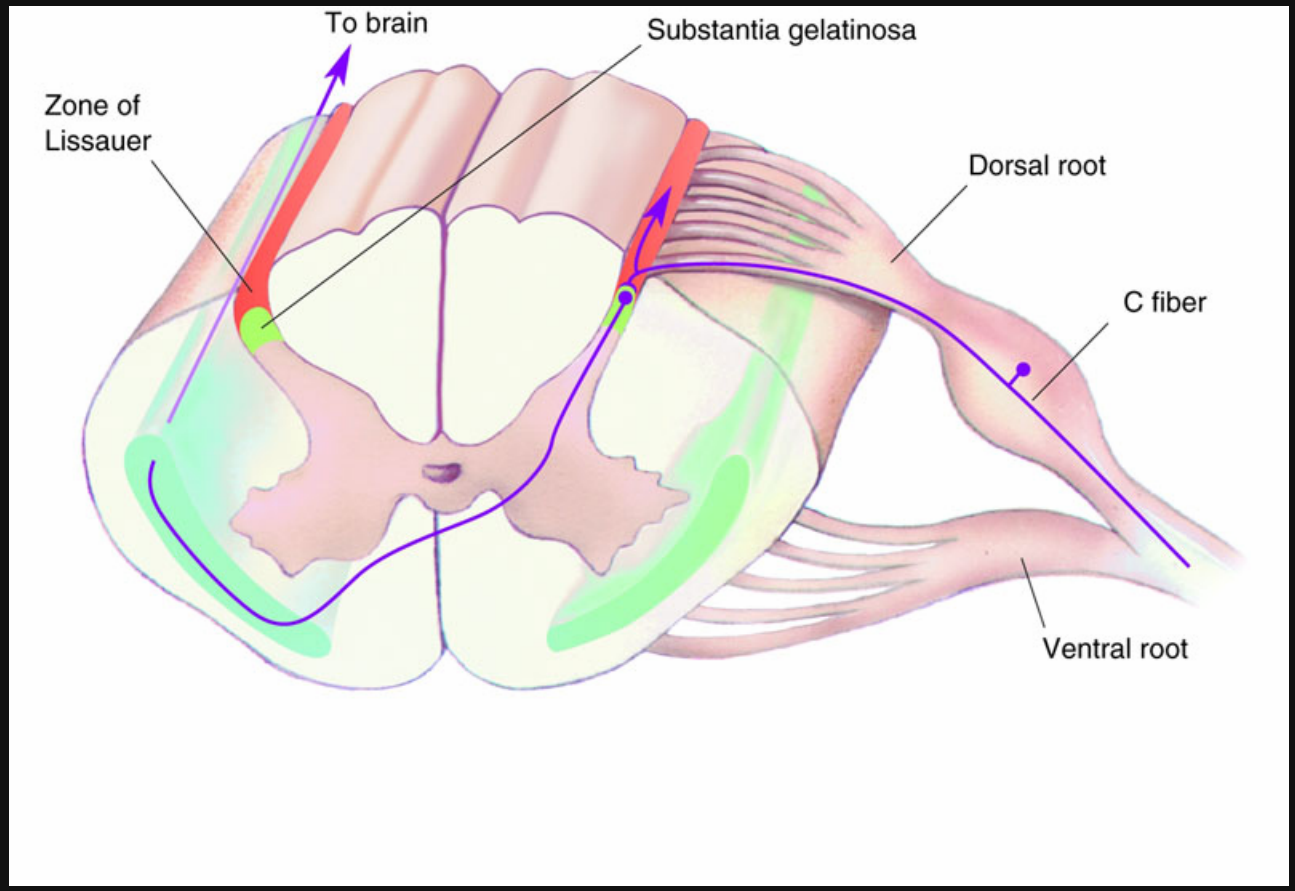
Spinal Memory System

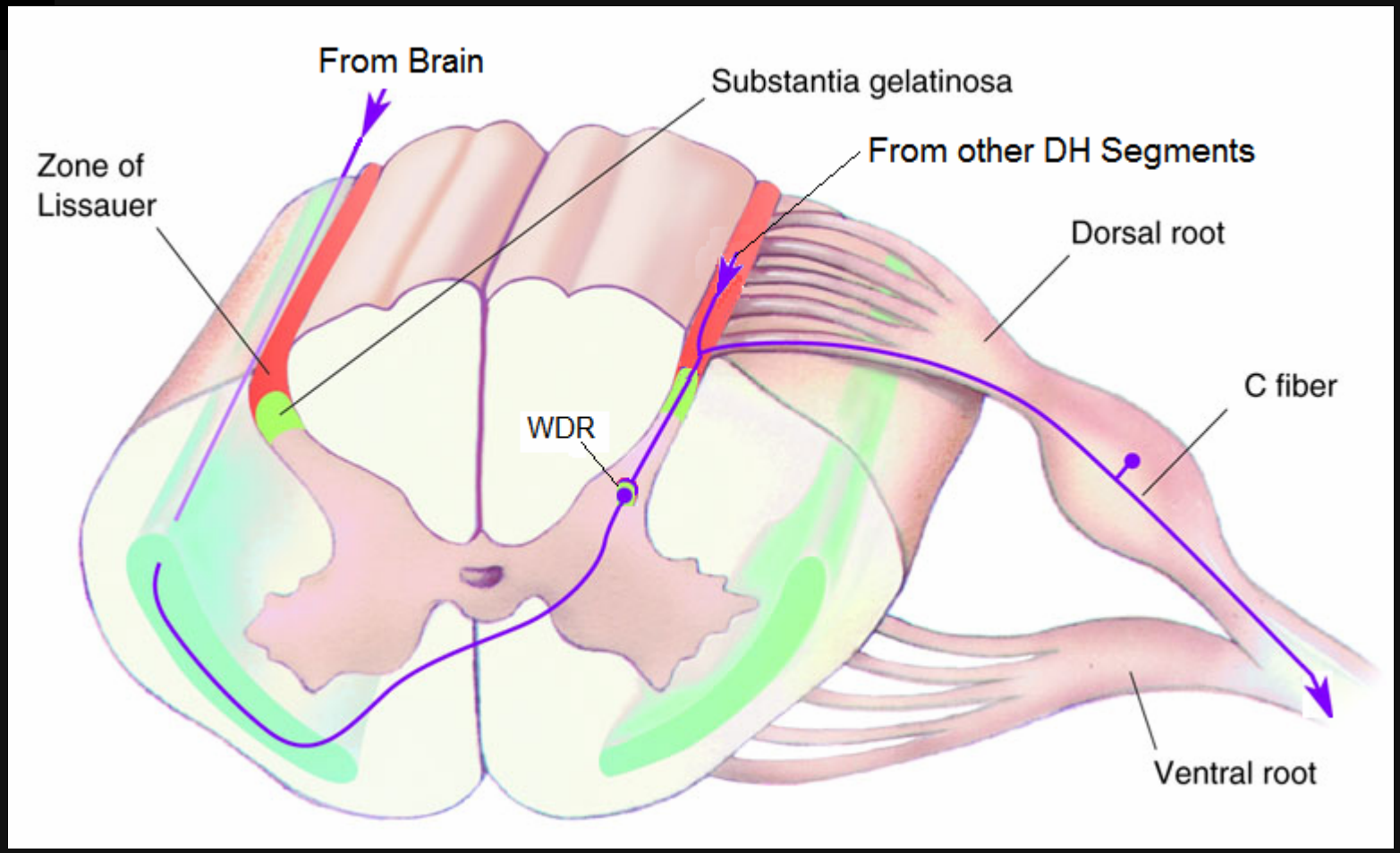
- Transcription-independent:
  - Wind-up
  - LTP
- Transcription-dependent
  - New receptors
  - Membrane response enhancers
- Structural Changes in the neural circuitry



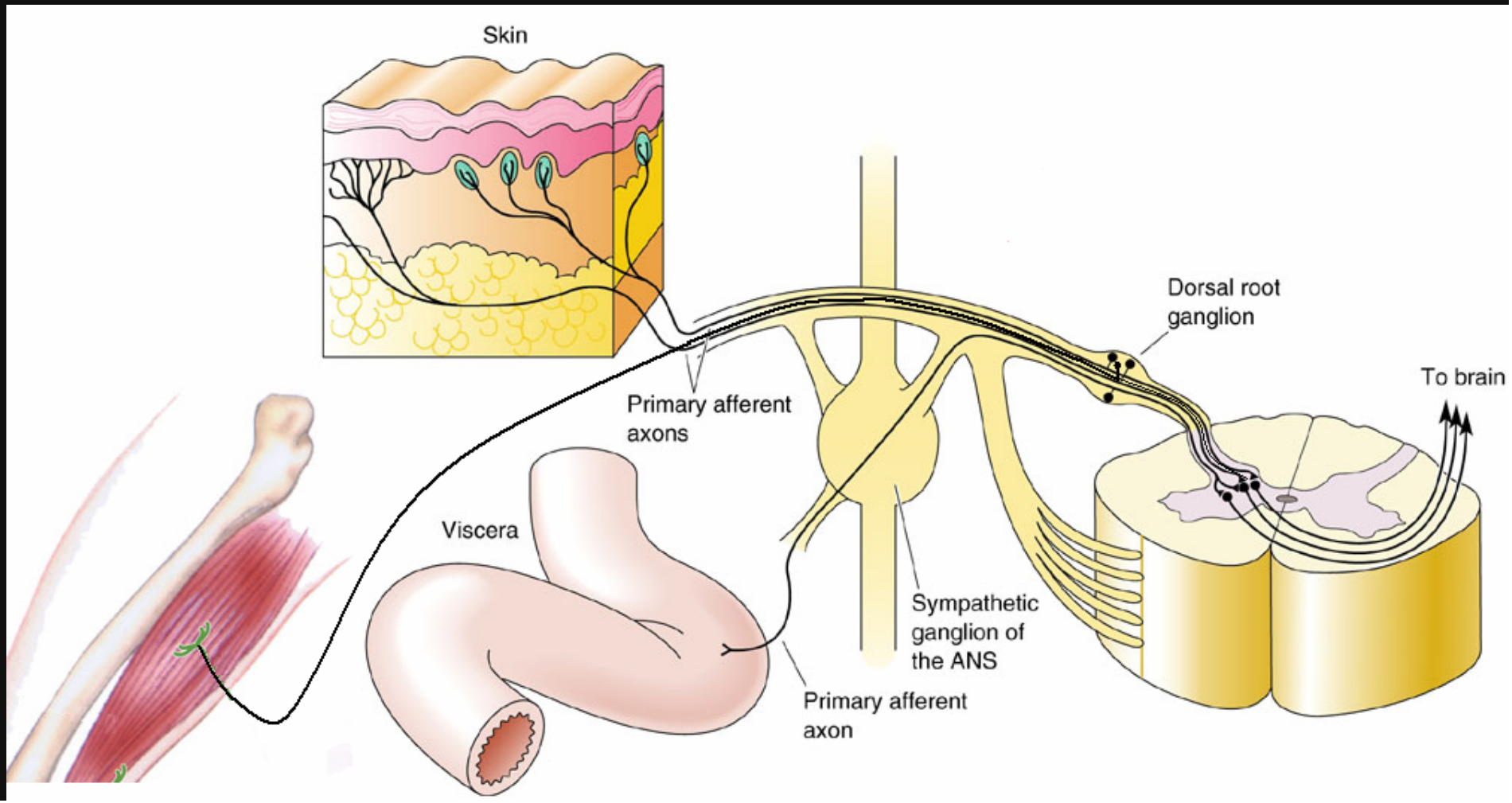
INTEGRATED NEUROMUSCULAR THEORY

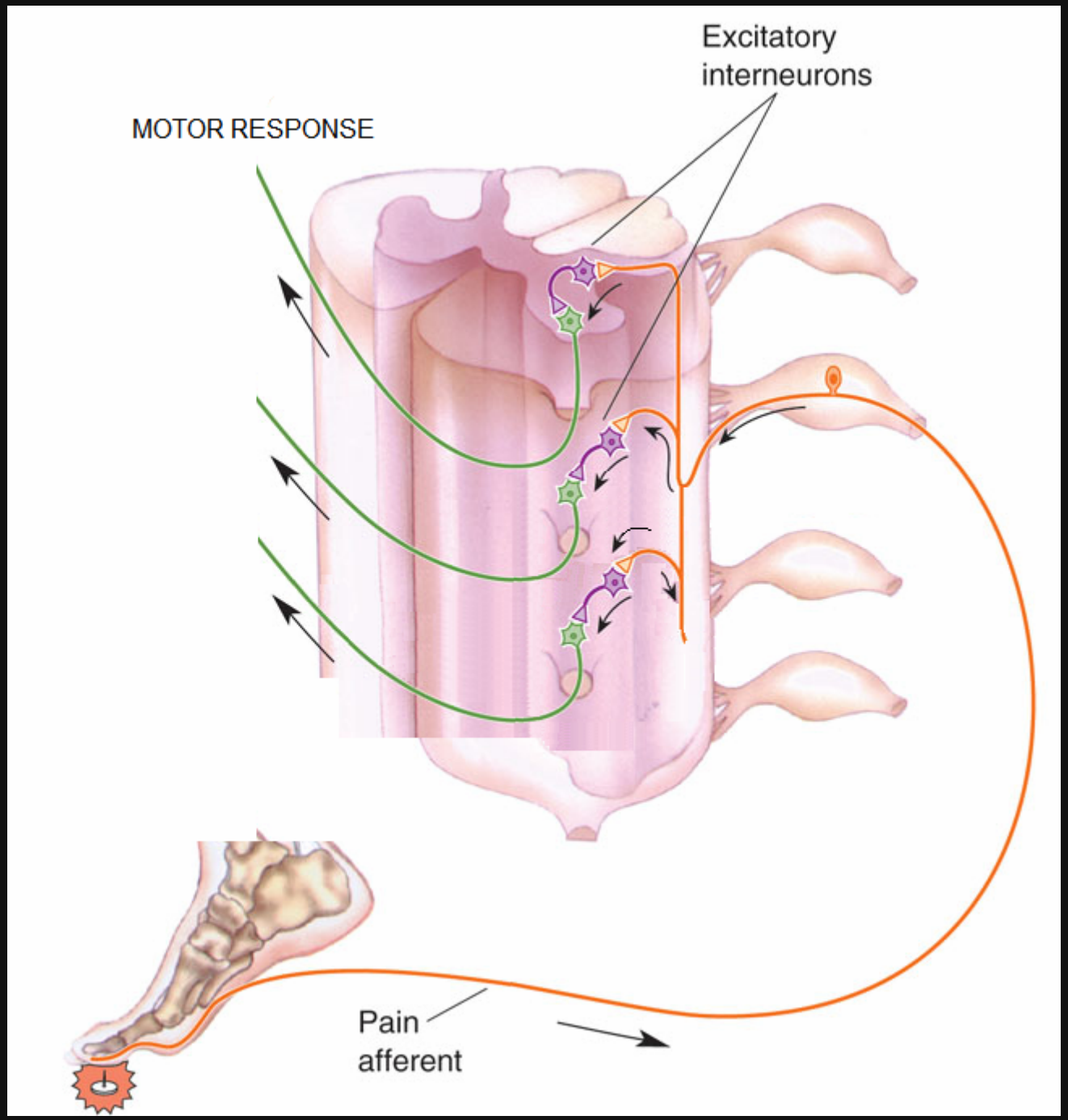
- Pain associated with *active* TrP depends on both peripheral muscle abnormalities and central changes in CNS
- Evidence pathology not solely peripheral
  - SEA and LTR present in *active* **(painful)** and *latent* **(nonpainful)** TrP's
- Pathology depends on central changes
  - Bilateral LTR obtained with unilateral needle stimulation in *active* but not *latent* TrP's

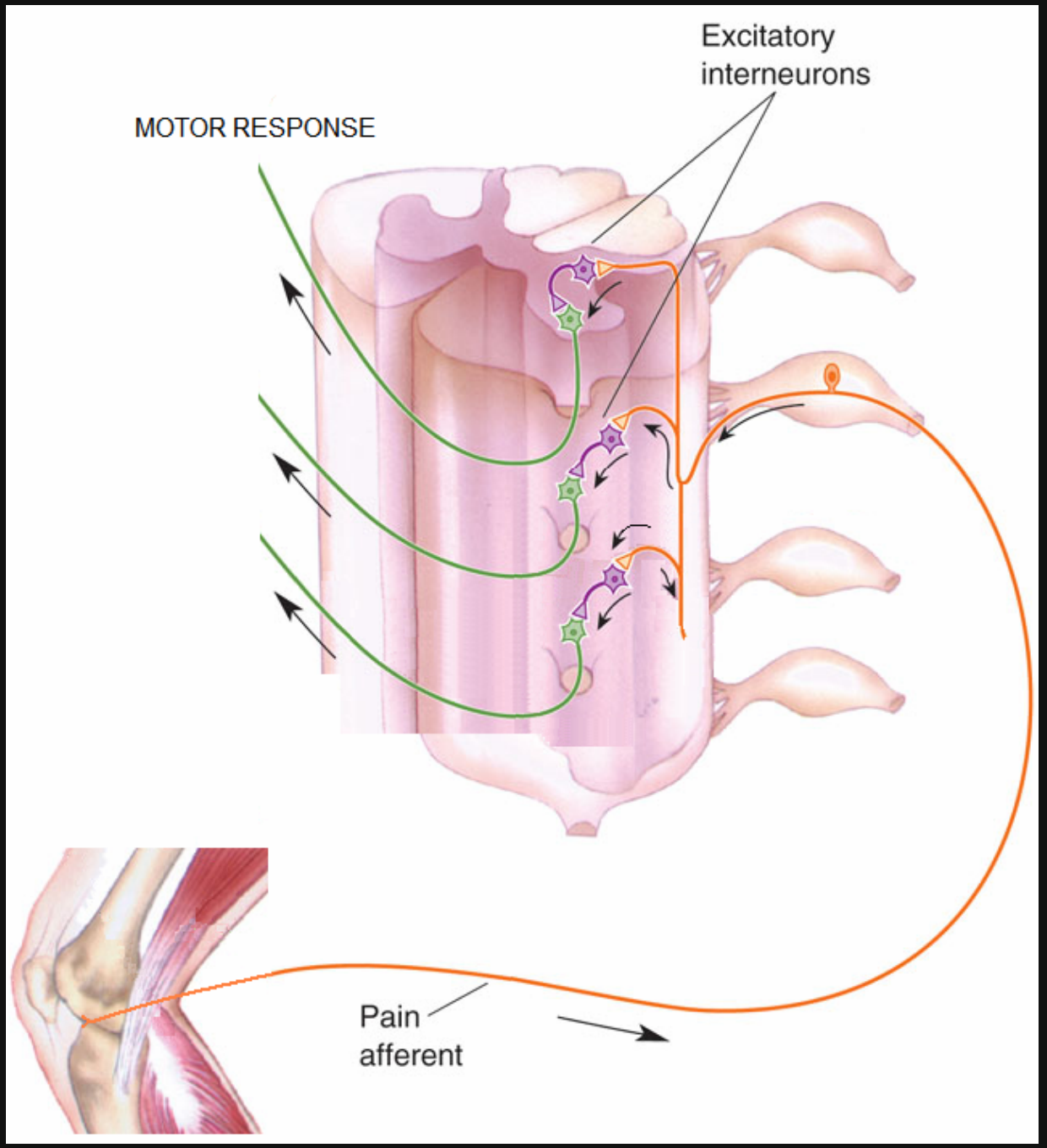

To brain
Substantia gelatinosa
Zone of
Lissauer
Dorsal root
C fiber
Ventral root

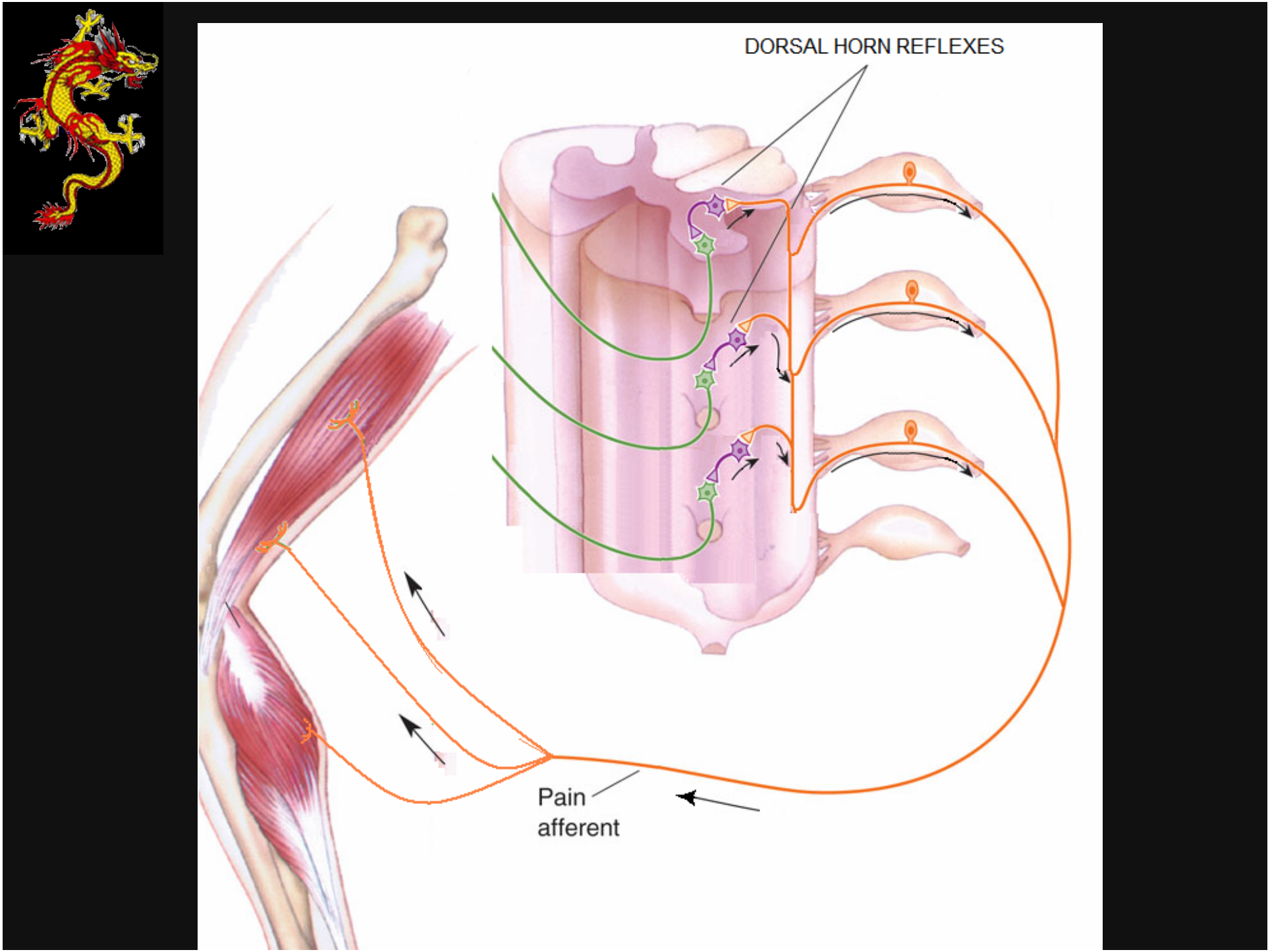

From Brain
Substantia gelatinosa
From other DH Segments
Zone of
Lissauer
Dorsal root
C fiber
WDR
Ventral root

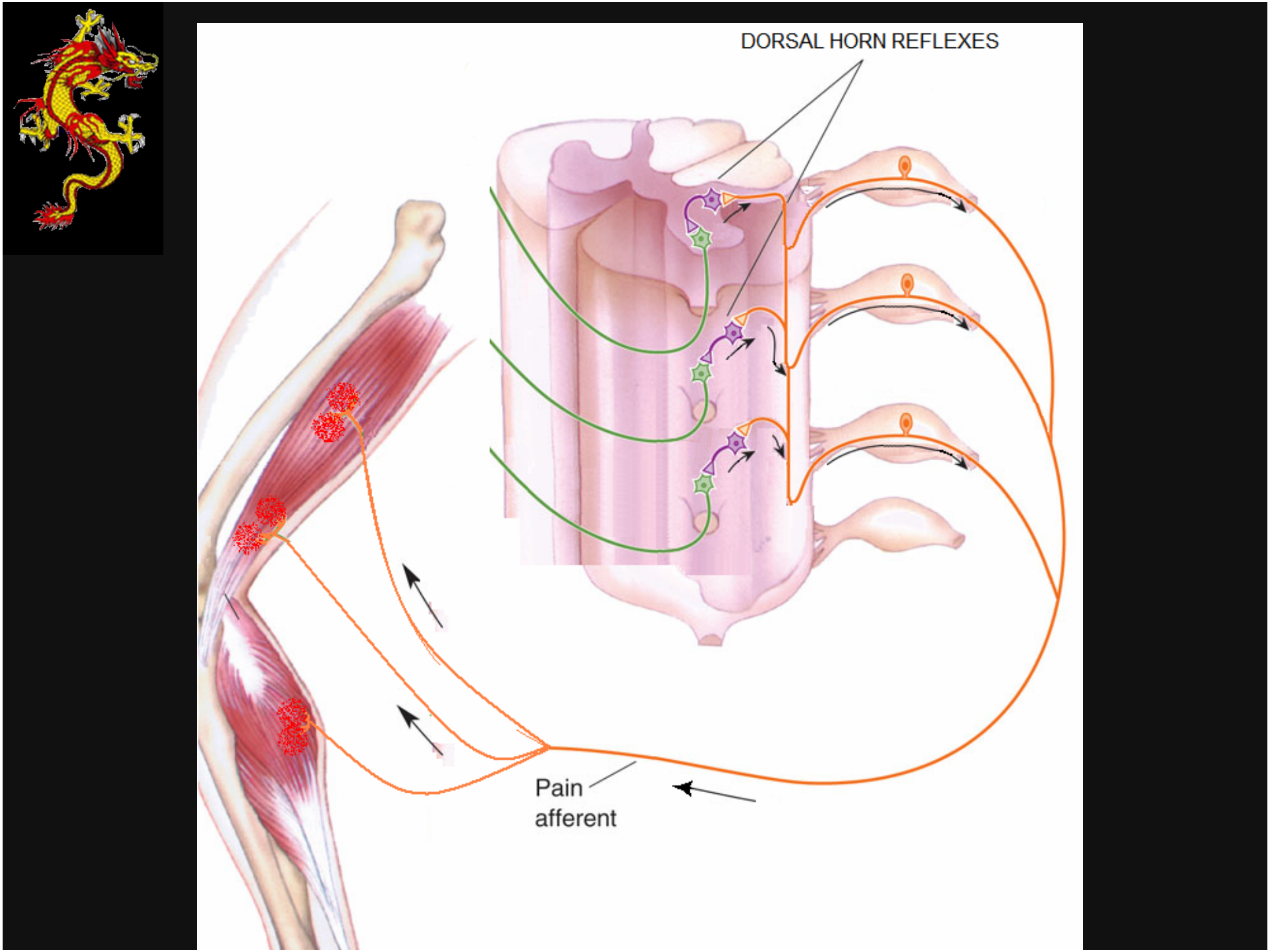
Convergence of Input to WDR Neuron

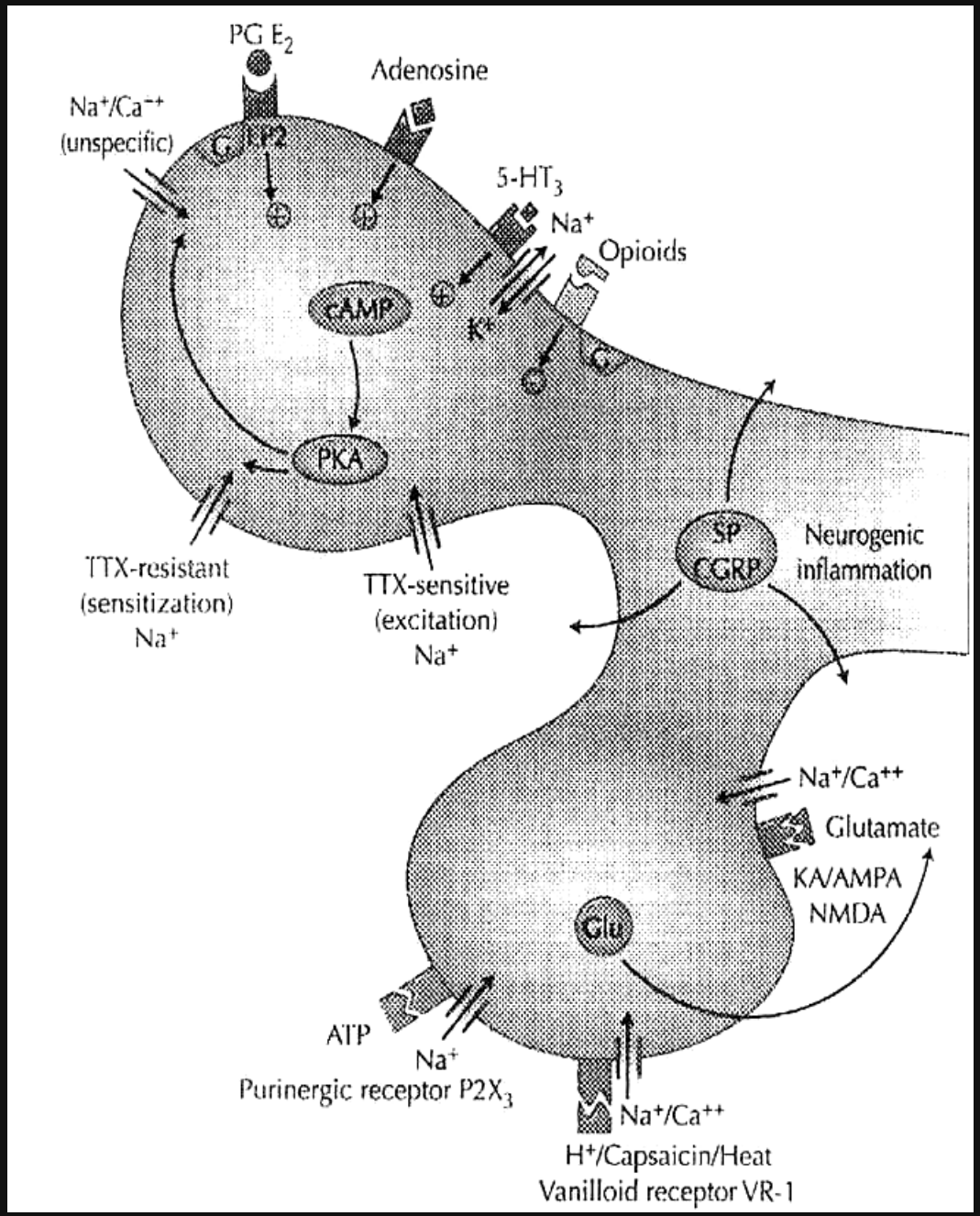


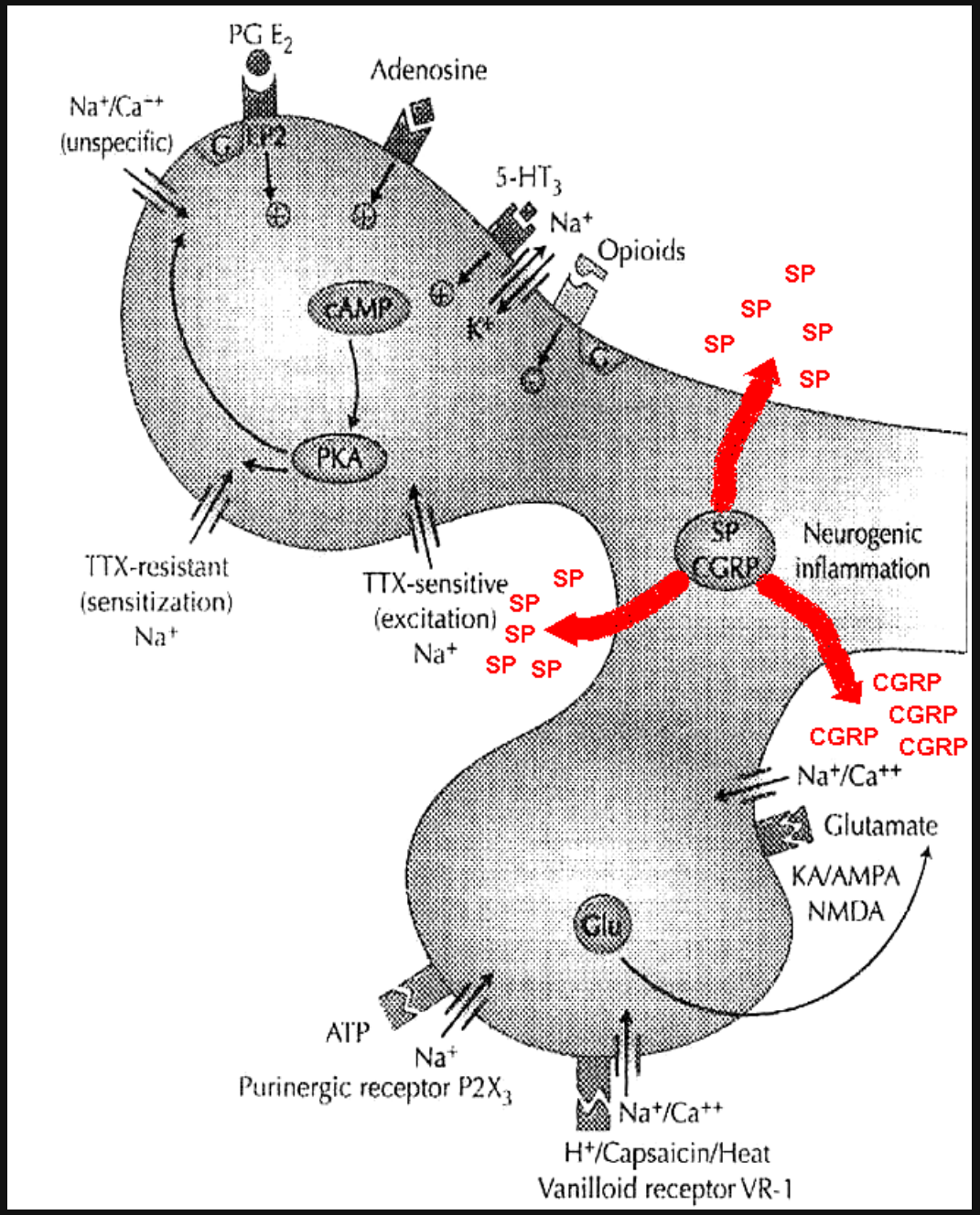

Excitatory
interneurons
MOTOR RESPONSE
Pain
afferent

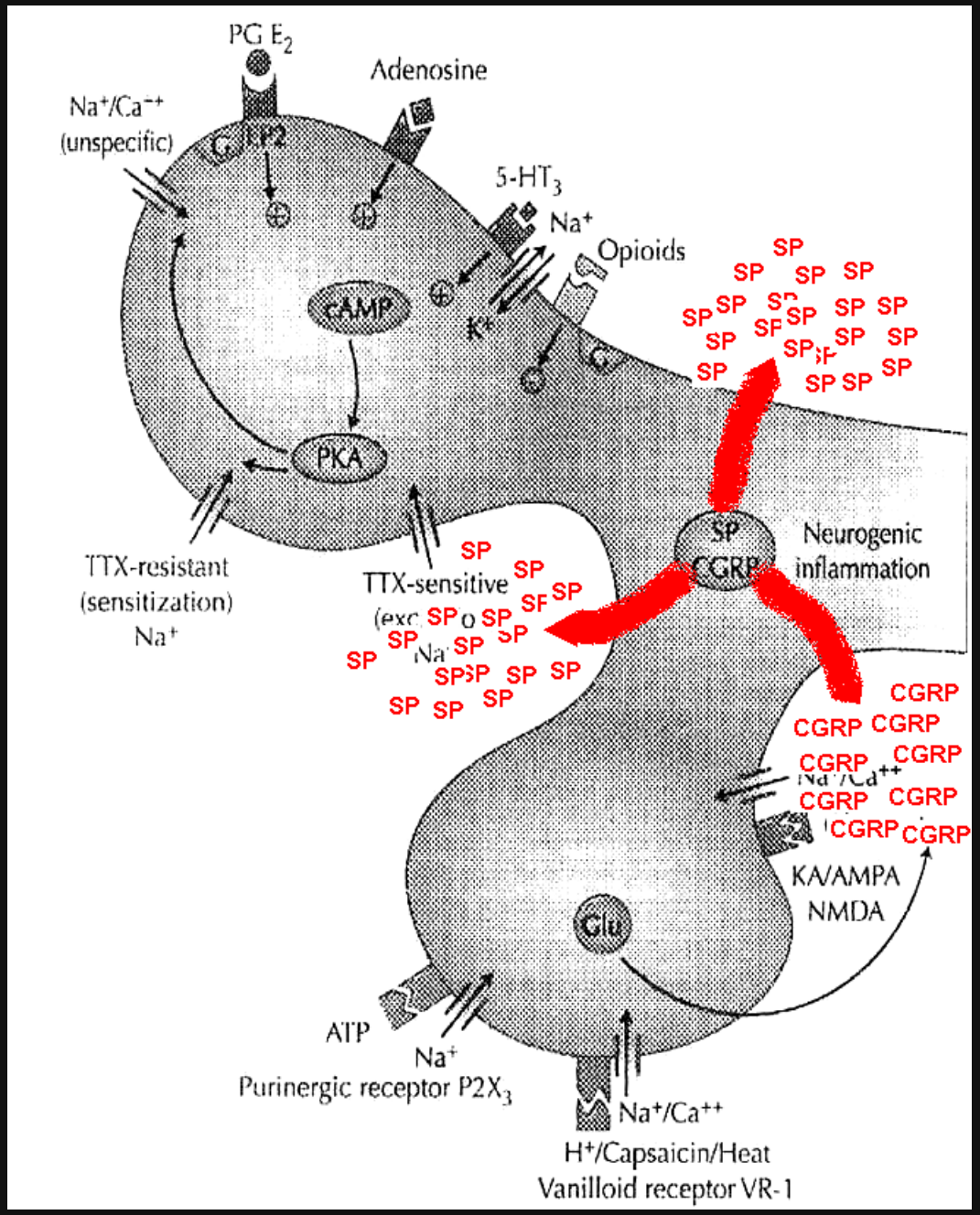

Excitatory
interneurons
MOTOR RESPONSE
Pain
afferent

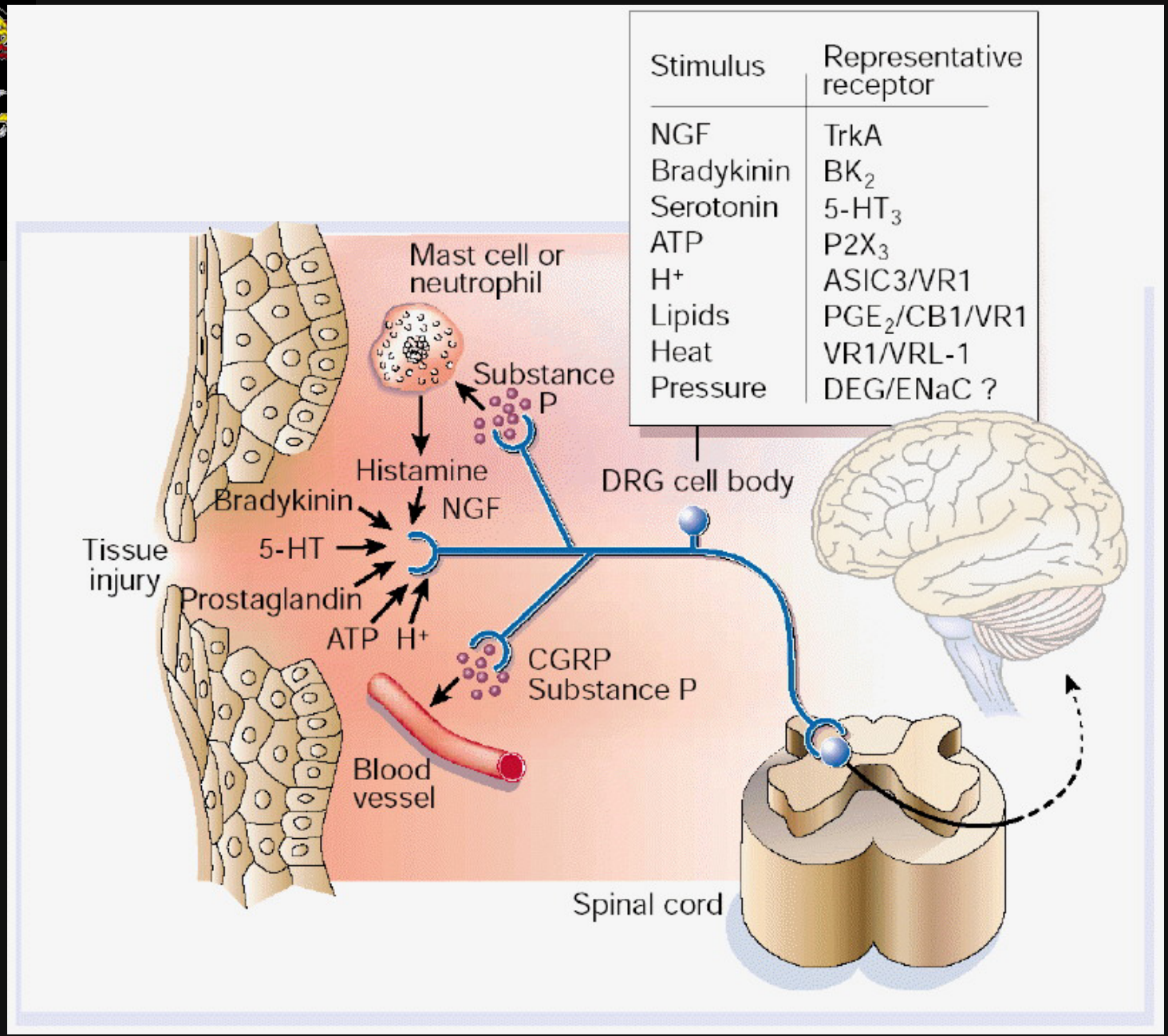

DORSAL HORN REFLEXES
Pain
afferent

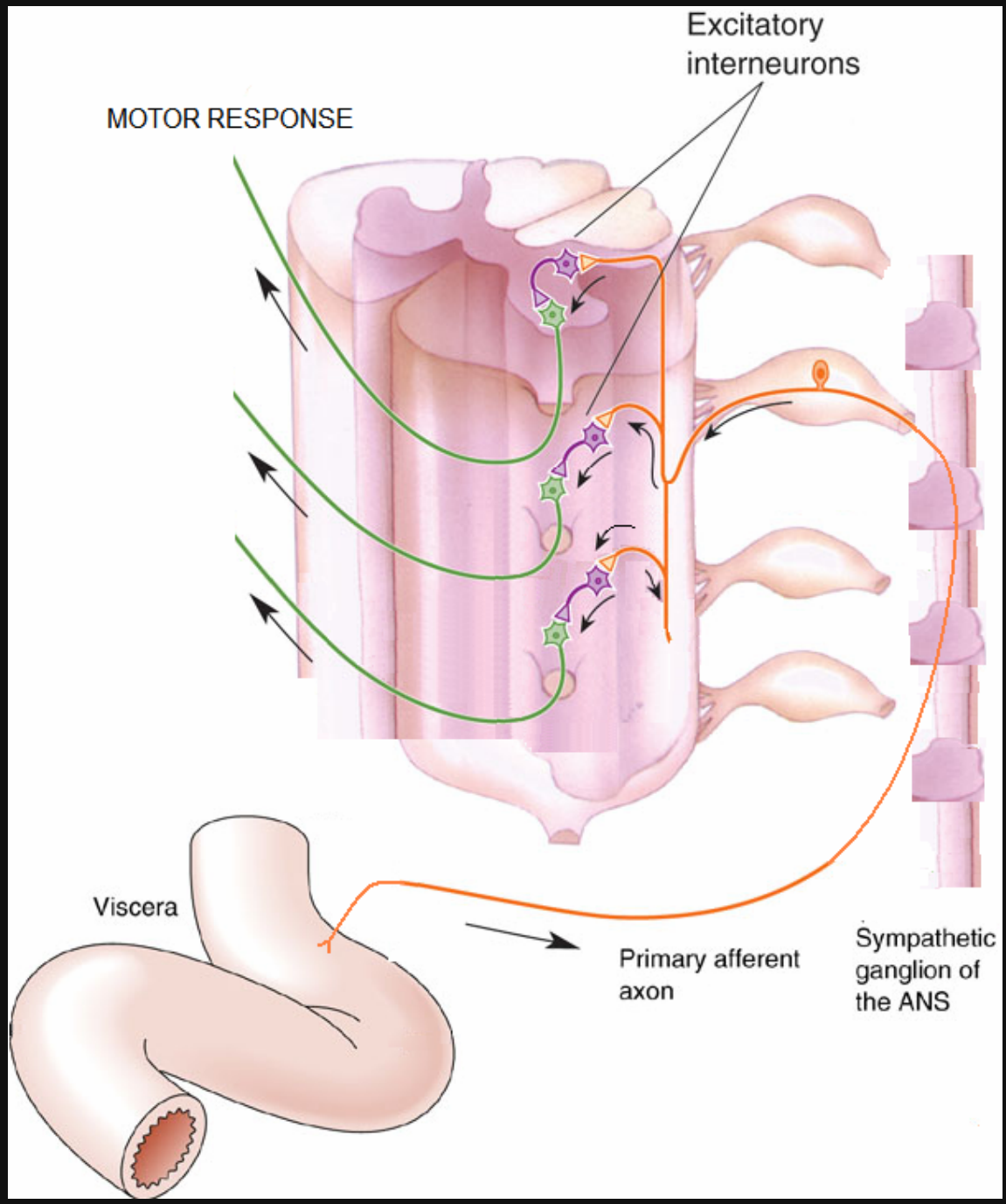

DORSAL HORN REFLEXES
Pain
afferent

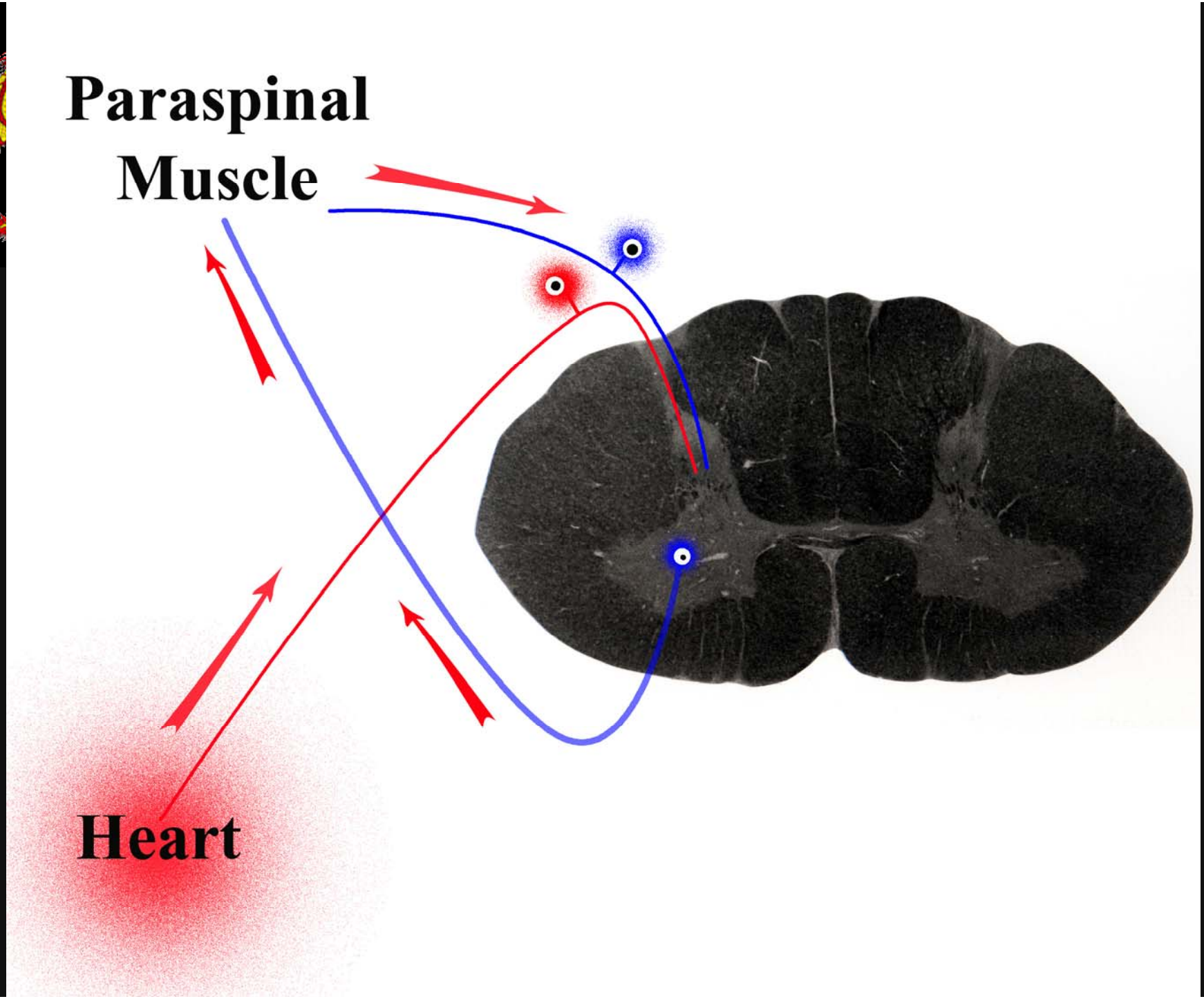

PG E_2
Adenosine
Na^+/Ca^{-+}
(unspecific)
P_2
5-HT_3
Na^+
Opioids
cAMP
K^+
PKA
TTX-resistant
(sensitization)
Na^+
TTX-sensitive
(excitation)
Na^+
SP
CGRP
Neurogenic
inflammation
Na^+/Ca^{++}
Glutamate
KA/AMPA
NMDA
Glu
ATP
Na^+
Purinergic receptor $P2X_3$
Na^+/Ca^{++}
H^+/Capsaicin/Heat
Vanilloid receptor VR-1


PG E_2
Adenosine
Na^+/Ca^{-+}
(unspecific)
5-HT_3
Na^+
Opioids
cAMP
K^+
PKA
SP
CGRP
Neurogenic
inflammation
TTX-resistant
(sensitization)
Na^+
TTX-sensitive
(excitation)
Na^+
CGRP
Na^+/Ca^{++}
Glutamate
KA/AMPA
NMDA
Glu
ATP
Na^+
Purinergic receptor $P2X_3$
Na^+/Ca^{++}
H^+/Capsaicin/Heat
Vanilloid receptor VR-1

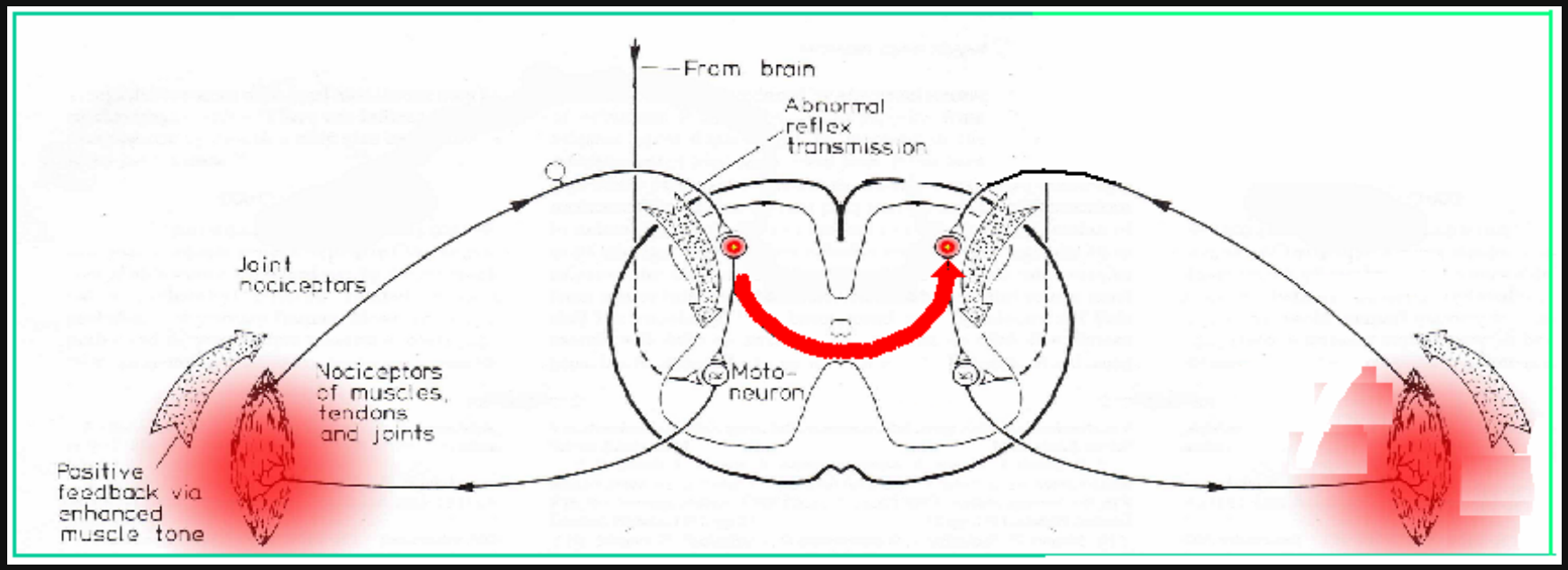

PG E_2
Adenosine
Na^+/Ca^{-+}
(unspecific)
P2
5-HT_3
Na^+
Opioids
SP
cAMP
K^+
PKA
TTX-resistant
(sensitization)
Na^+
TTX-sensitive
SP
CGRP
Neurogenic
inflammation
CGRP
Na^+/Ca^{++}
KA/AMPA
NMDA
Glu
ATP
Na^+
Purinergic receptor $P2X_3$
Na^+/Ca^{++}
H^+/Capsaicin/Heat
Vanilloid receptor VR-1

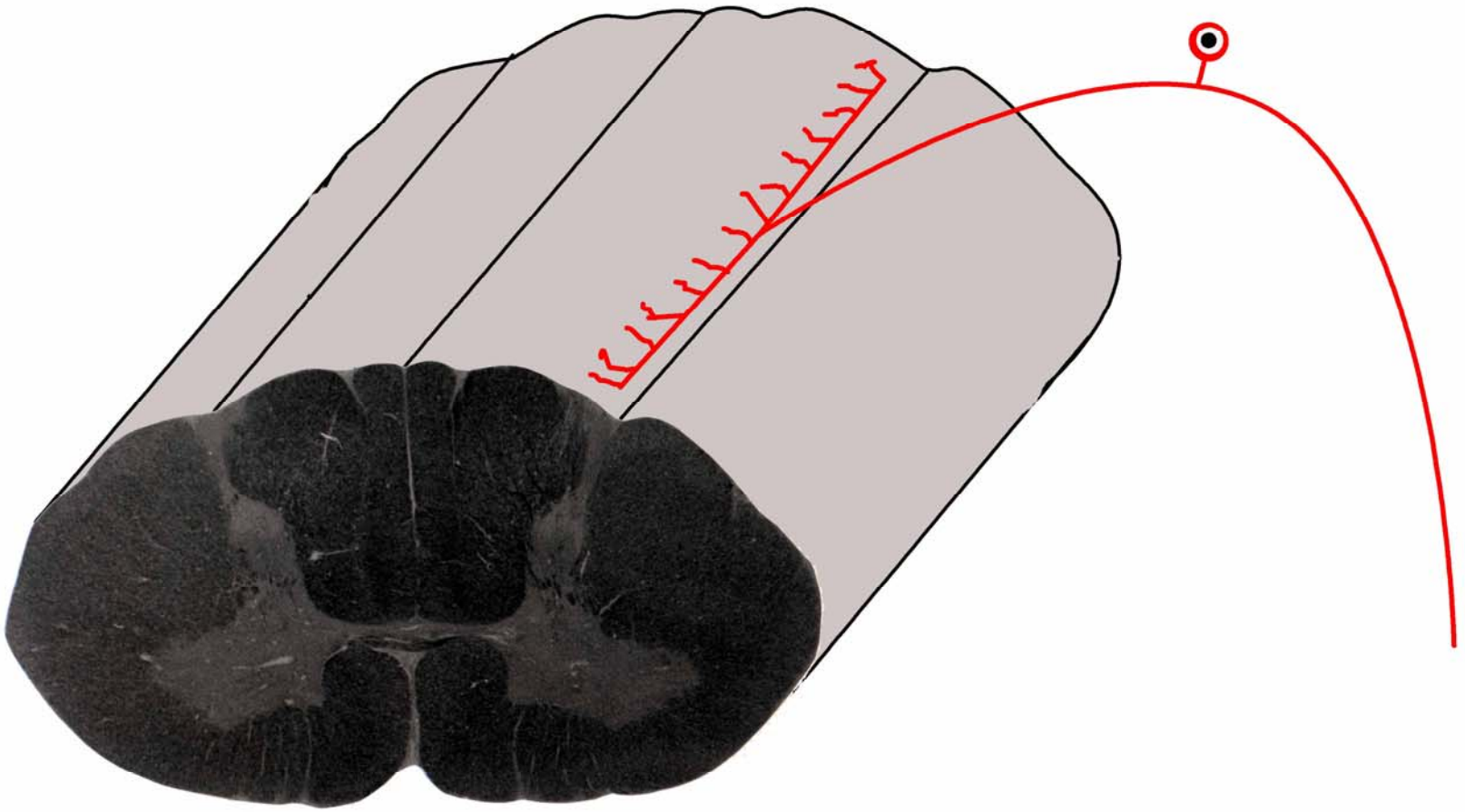

Stimulus
Representative receptor
NGF
TrkA
Bradykinin
BK_2
Serotonin
$5\text{-}HT_3$
ATP
$P2X_3$
H^+
ASIC3/VR1
Lipids
PGE_2/CB1/VR1
Heat
VR1/VRL-1
Pressure
DEG/ENaC ?
Mast cell or neutrophil
Substance P
Histamine
NGF
Bradykinin
5-HT
Tissue injury
Prostaglandin
ATP
H^+
CGRP
Substance P
Blood vessel
DRG cell body
Spinal cord

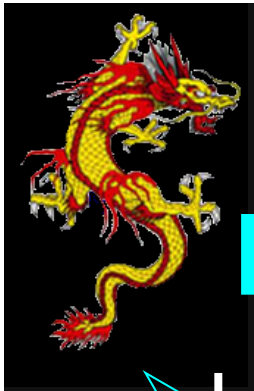

Excitatory
interneurons
MOTOR RESPONSE
Viscera
Primary afferent
axon
Sympathetic
ganglion of
the ANS


Paraspinal
Muscle
Heart

Spread to Contralateral Side

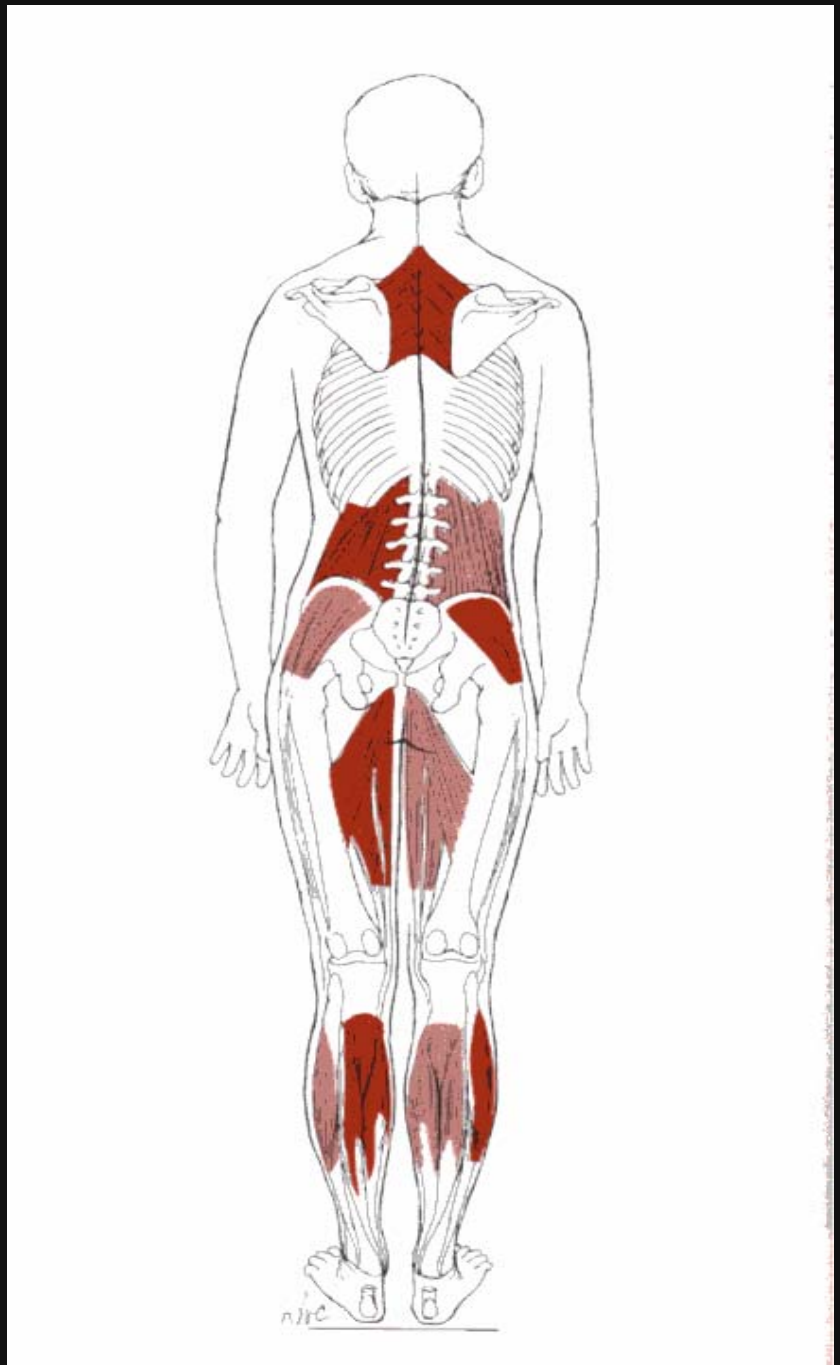


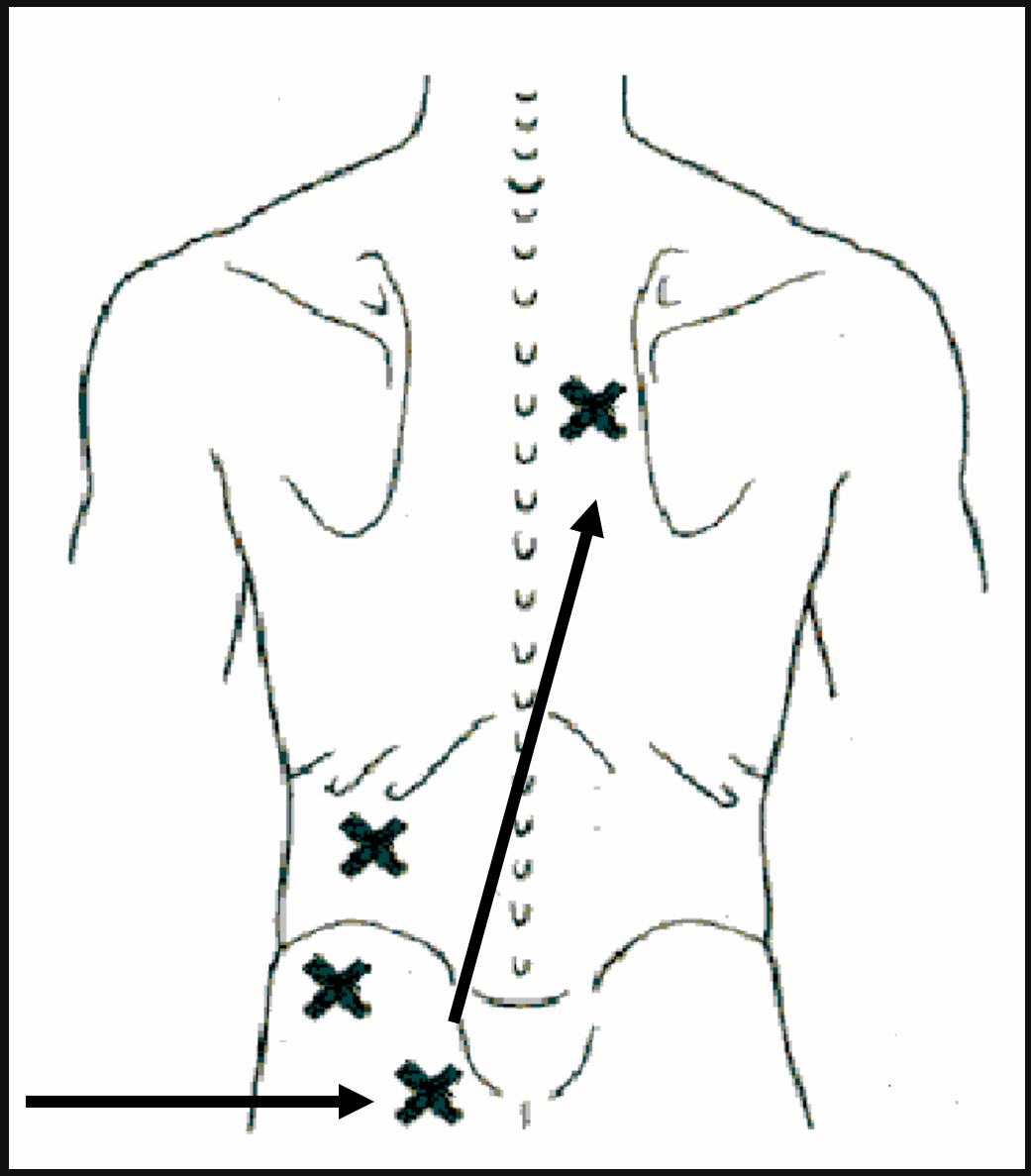




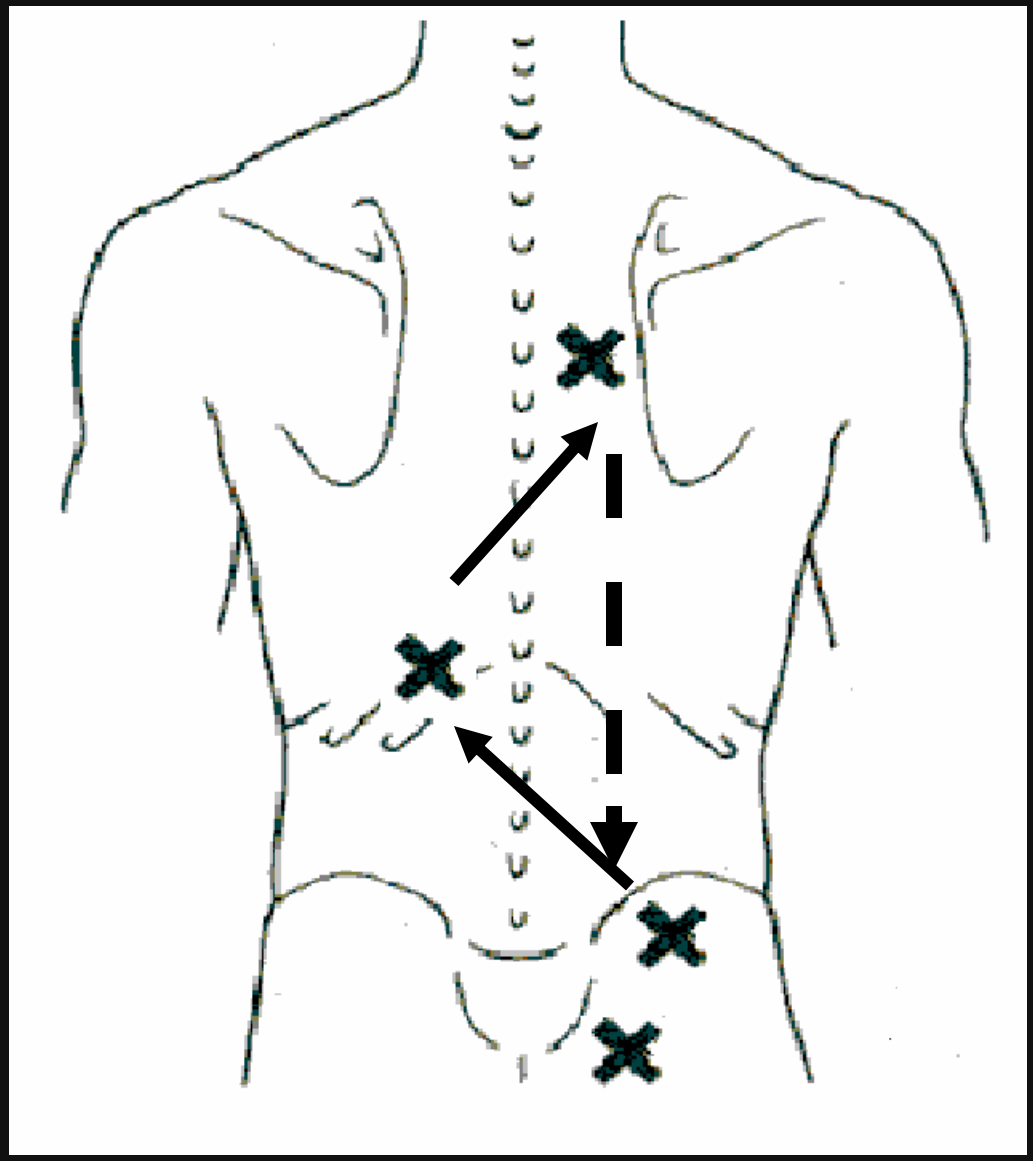
Local Distal Relationships

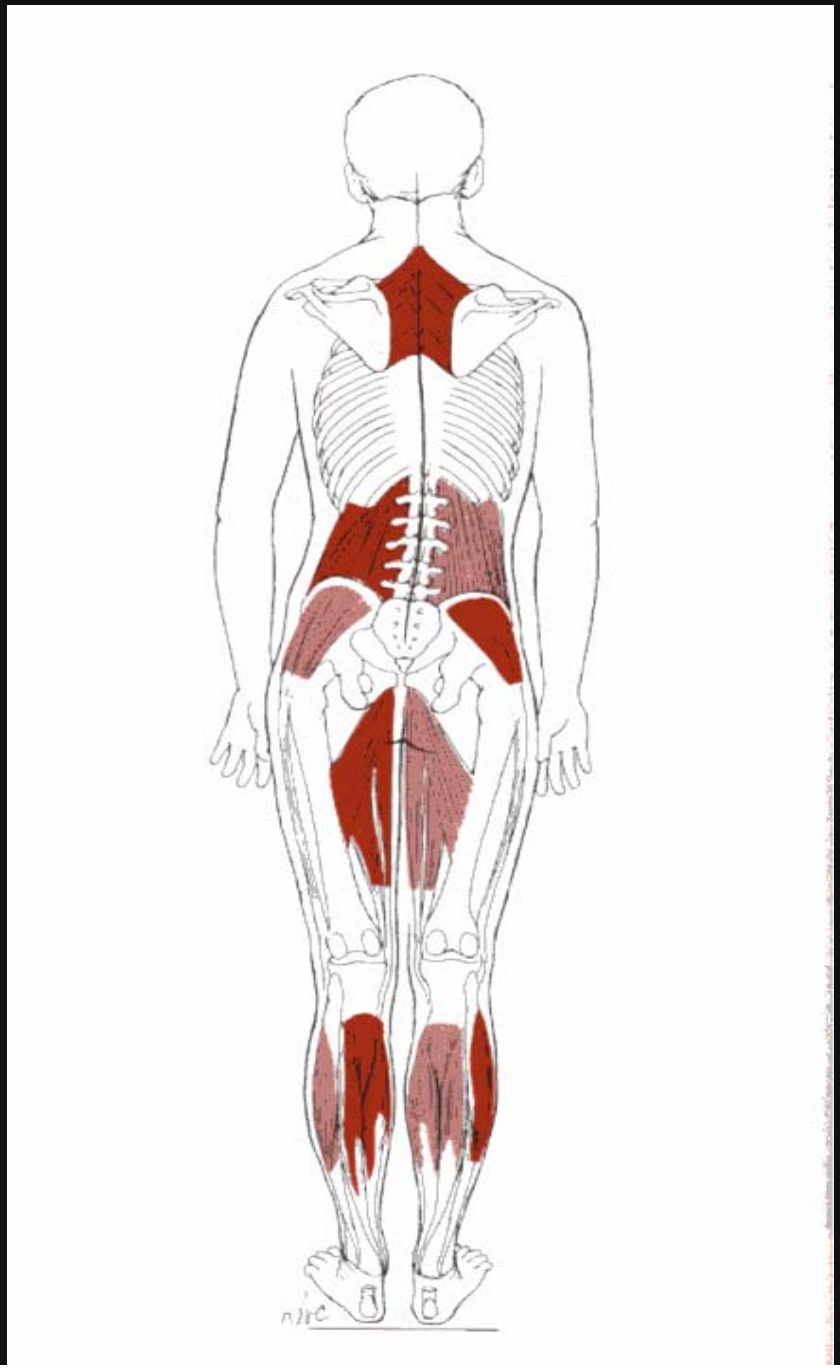
- Local muscle release with needle insertion in distal points in addition to direct treatment.
  - B60 to relieve suboccipital tension or B58 (Lateral Gastroc muscle) to release tension in T7 area of the back.
  - Kid 9 to relieve tenderness at Anterior Superior Iliac Spine
  - Lu5 to release Pects.
  - Sp9 to release tension in Upper Trap.

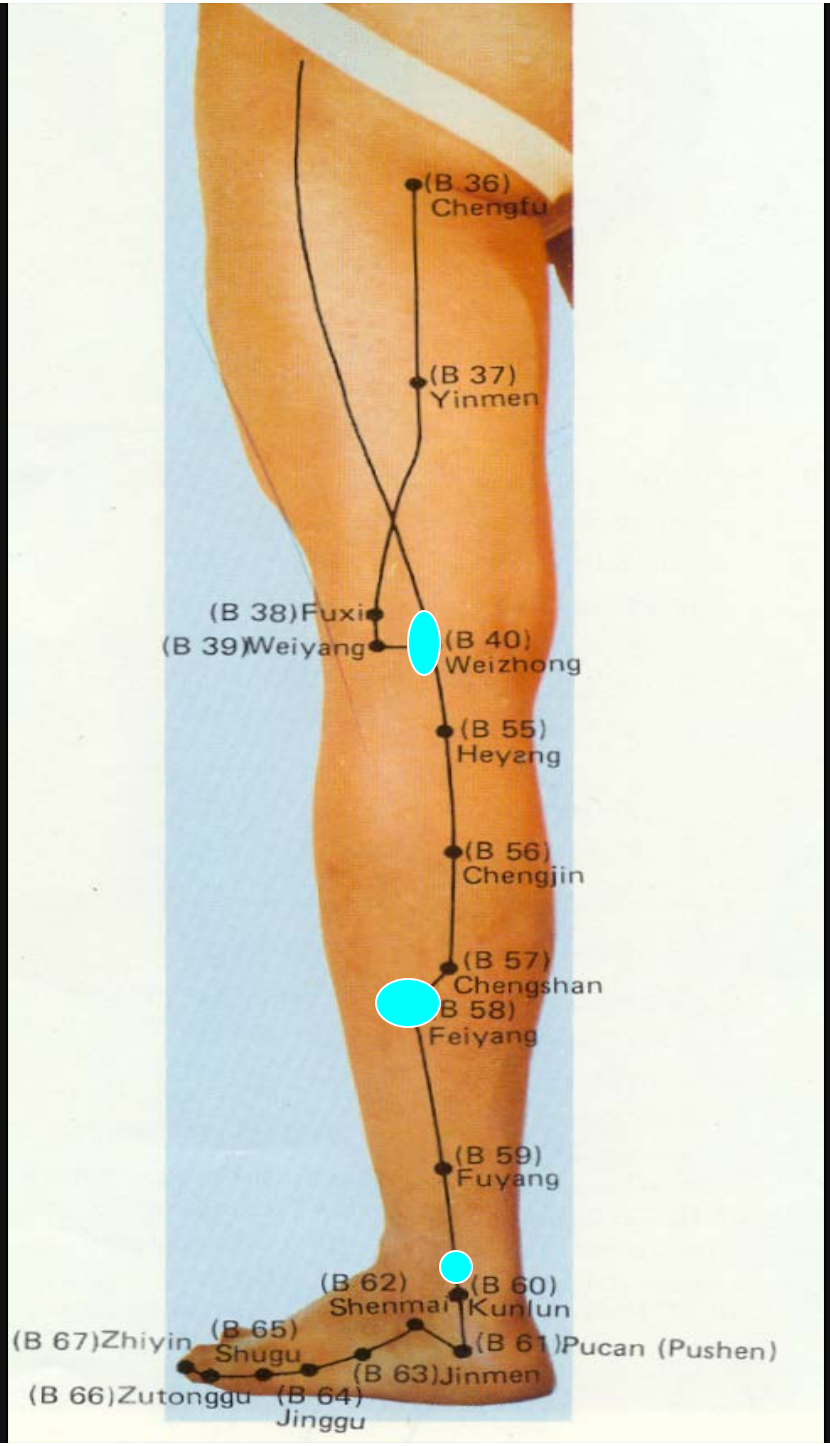


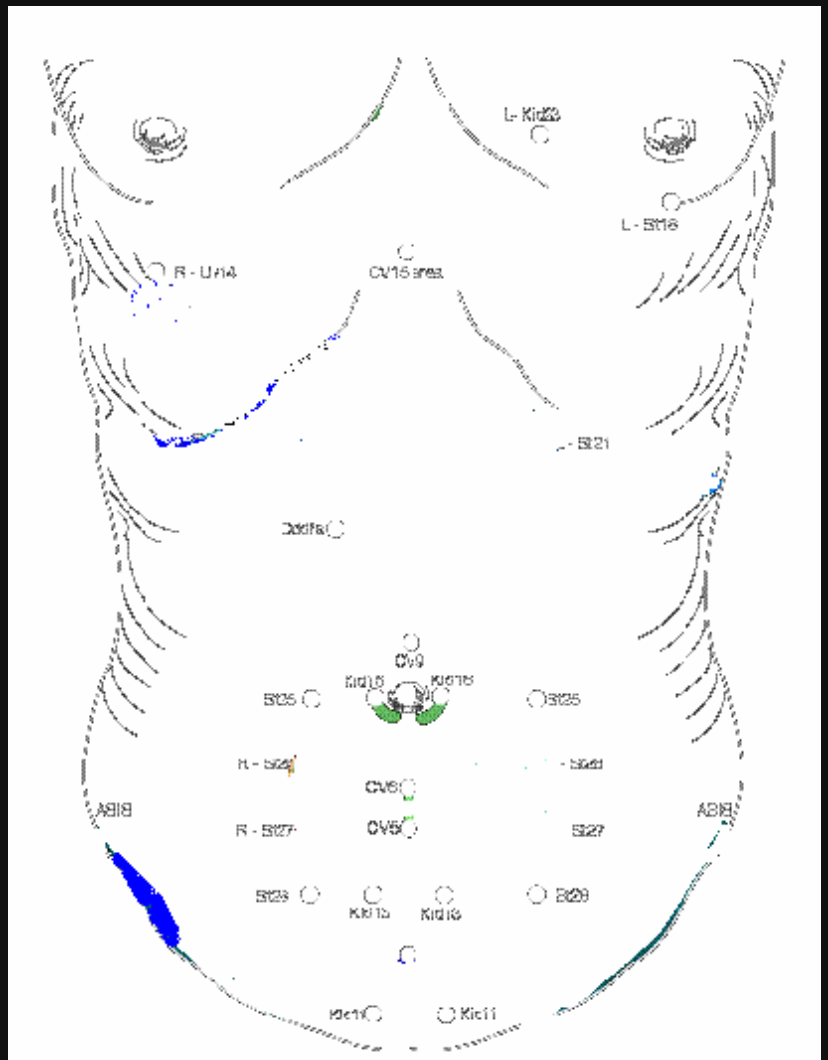


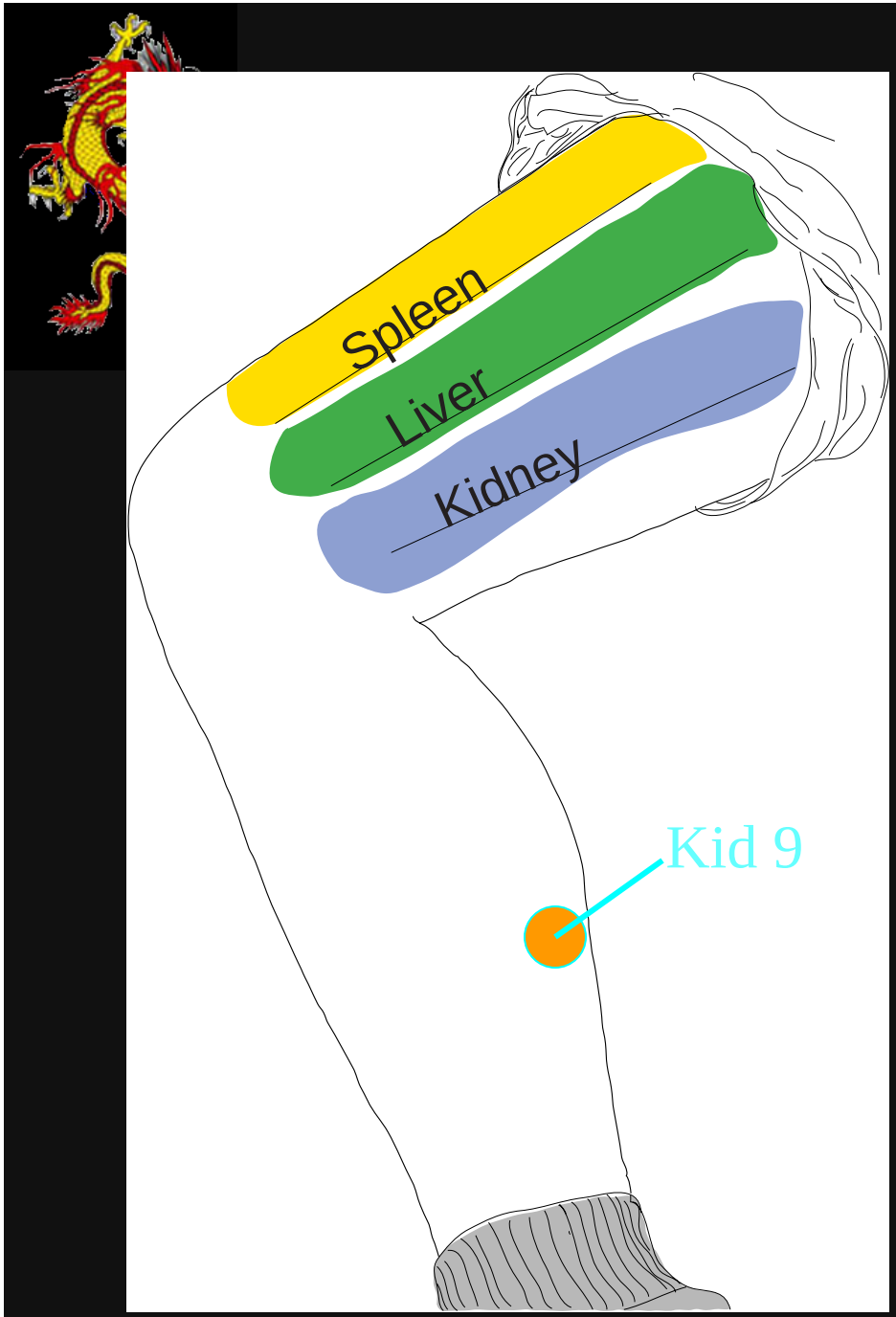
BL 35

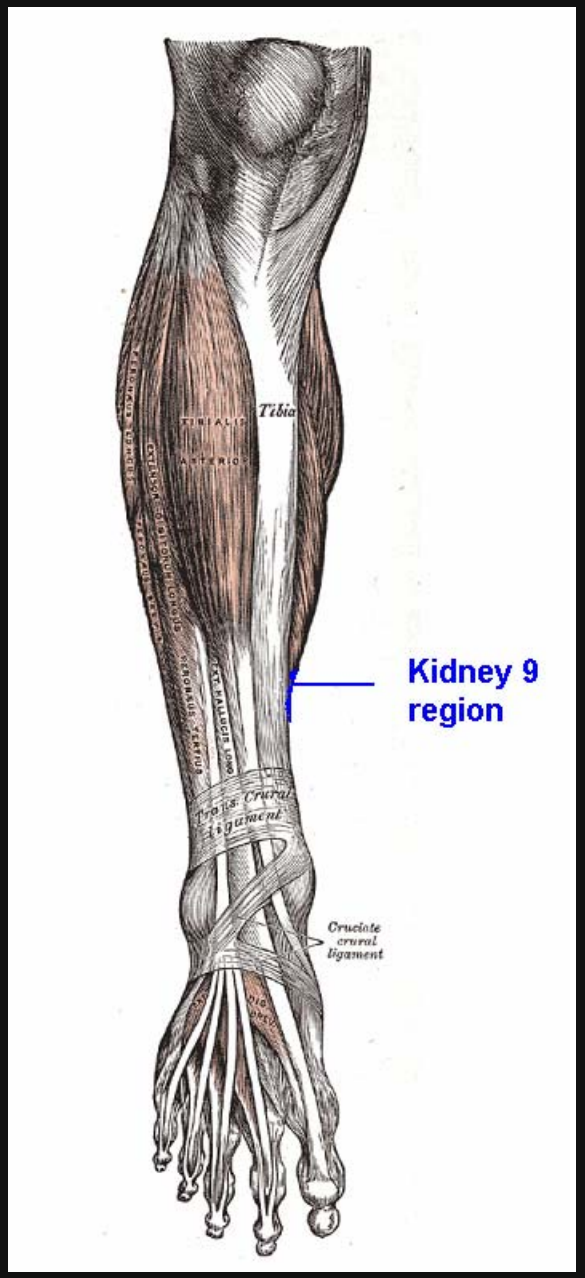


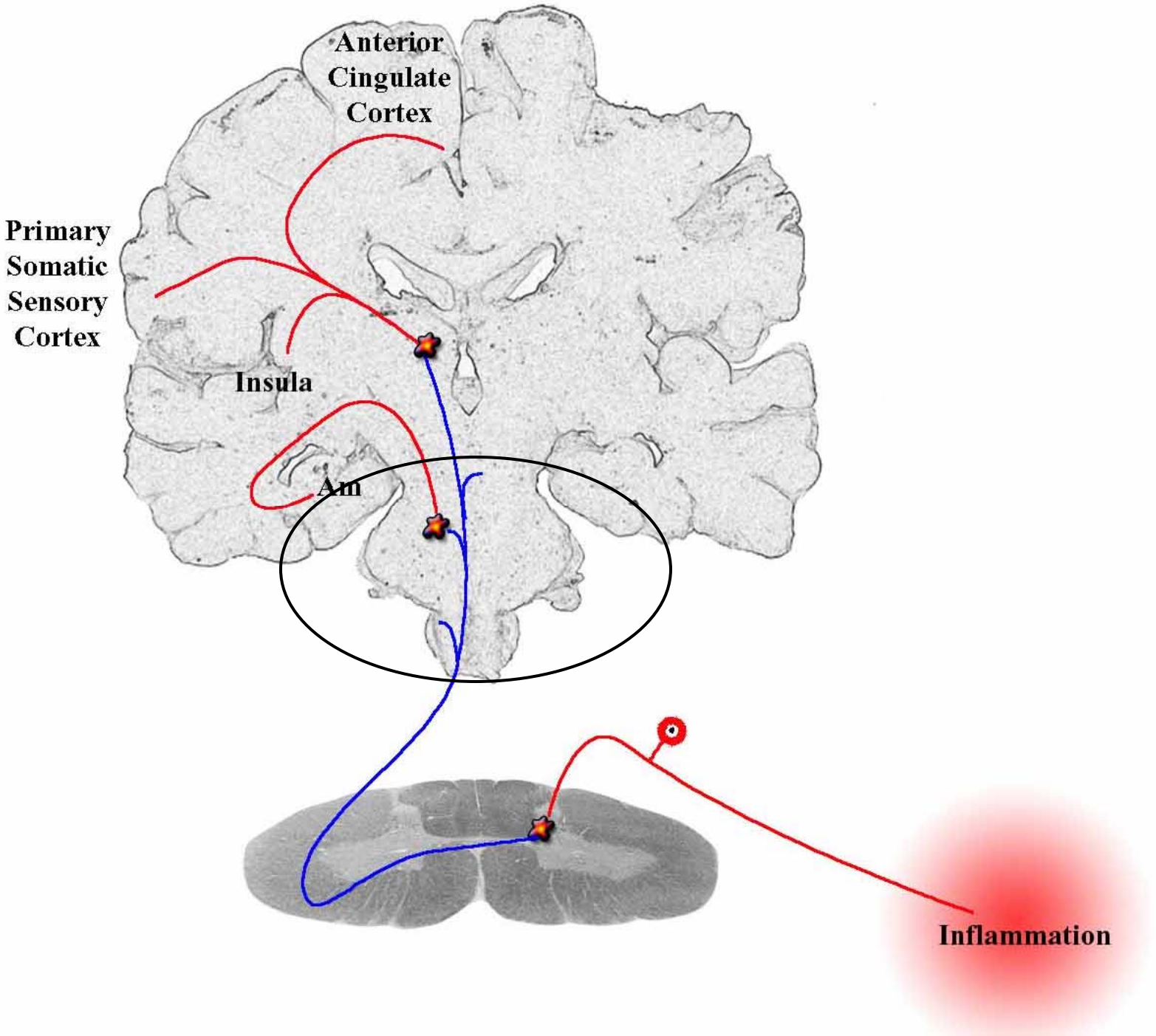



(B 36)
Chengfu
(B 37)
Yinmen
(B 38)Fuxi
(B 39)Weiyang
(B 40)
Weizhong
(B 55)
Heyang
(B 56)
Chengjin
(B 57)
Chengshan
(B 58)
Feiyang
(B 59)
Fuyang
(B 62)
Shenmai
(B 60)
Kunlun
(B 67)Zhiyin
(B 65)
Shugu
(B 61)Pucan (Pushen)
(B 63)Jinmen
(B 66)Zutonggu
(B 64)
Jinggu


L- Kid23
L - St16
R - Ut14
CV15 area
- St21
Dddfa
CV9
Kid16
Kid15
St25
St25
R - St24
- St24
CV6
ASIS
ASIS
R - St27
CV5
St27
St29
St29
Kid13
Kid19
Kid1
Kid1

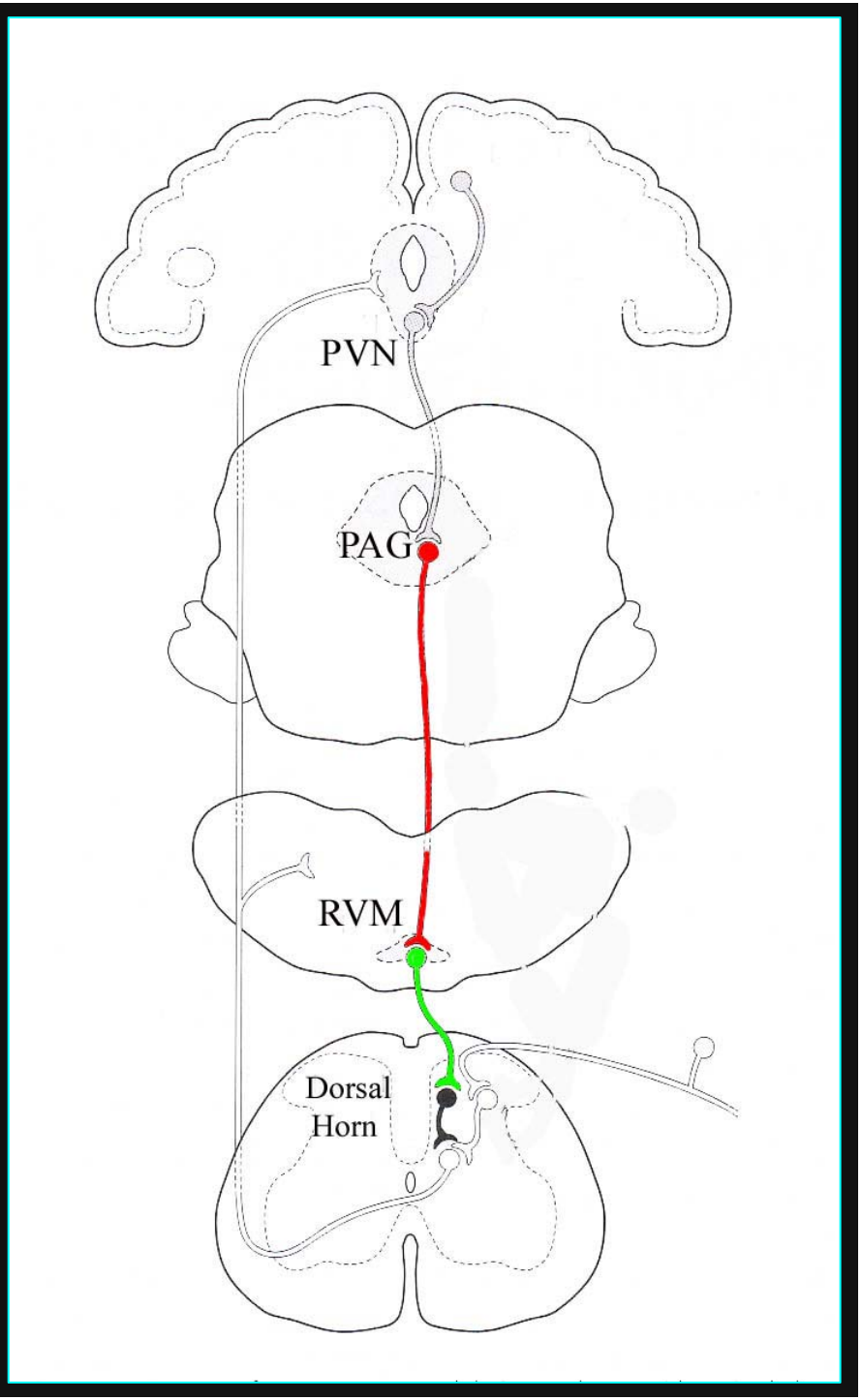

Spleen
Liver
Kidney
Kid 9

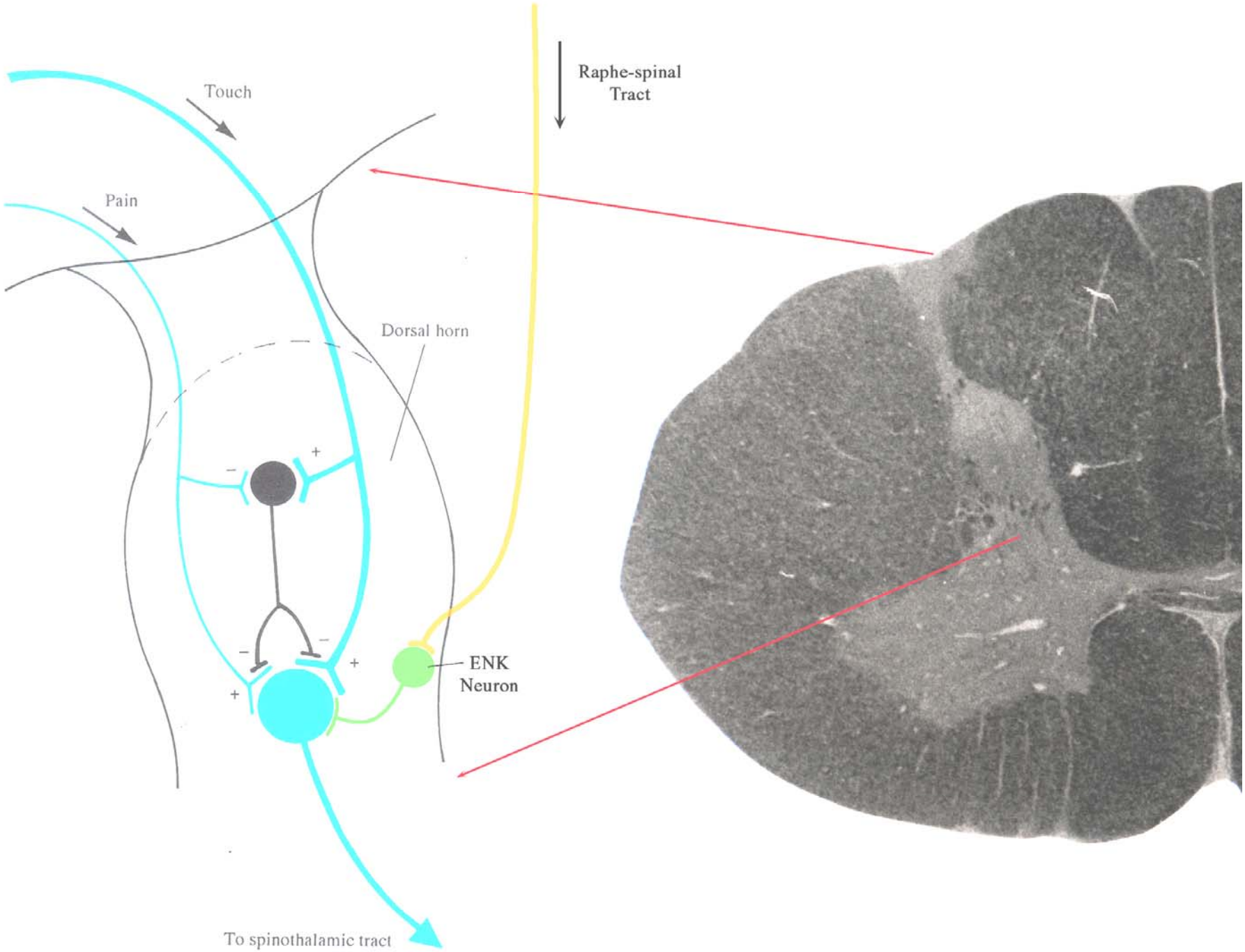

Tibia
Kidney 9
region
Cruciate
crural
ligament


Anterior
Cingulate
Cortex
Primary
Somatic
Sensory
Cortex
Insula
Am
Inflammation

Endogenous Control Pathways

- Limbic forebrain level
- Hypothalamic level
- Midbrain level
- Medullary level




Raphe-spinal
Tract
Touch
Pain
Dorsal horn
ENK
Neuron
To spinothalamic tract

Emotions

Limbic Forebrain

Hormones

Hypothalamus

Neuropeptides

PAG

Opioids

Raphe

Serotonin
Norepinephrine

Medullary or Spinal
Dorsal Horn

Emotions

Limbic Forebrain

Hormones

Hypothalamus

Neuropeptides

PAG

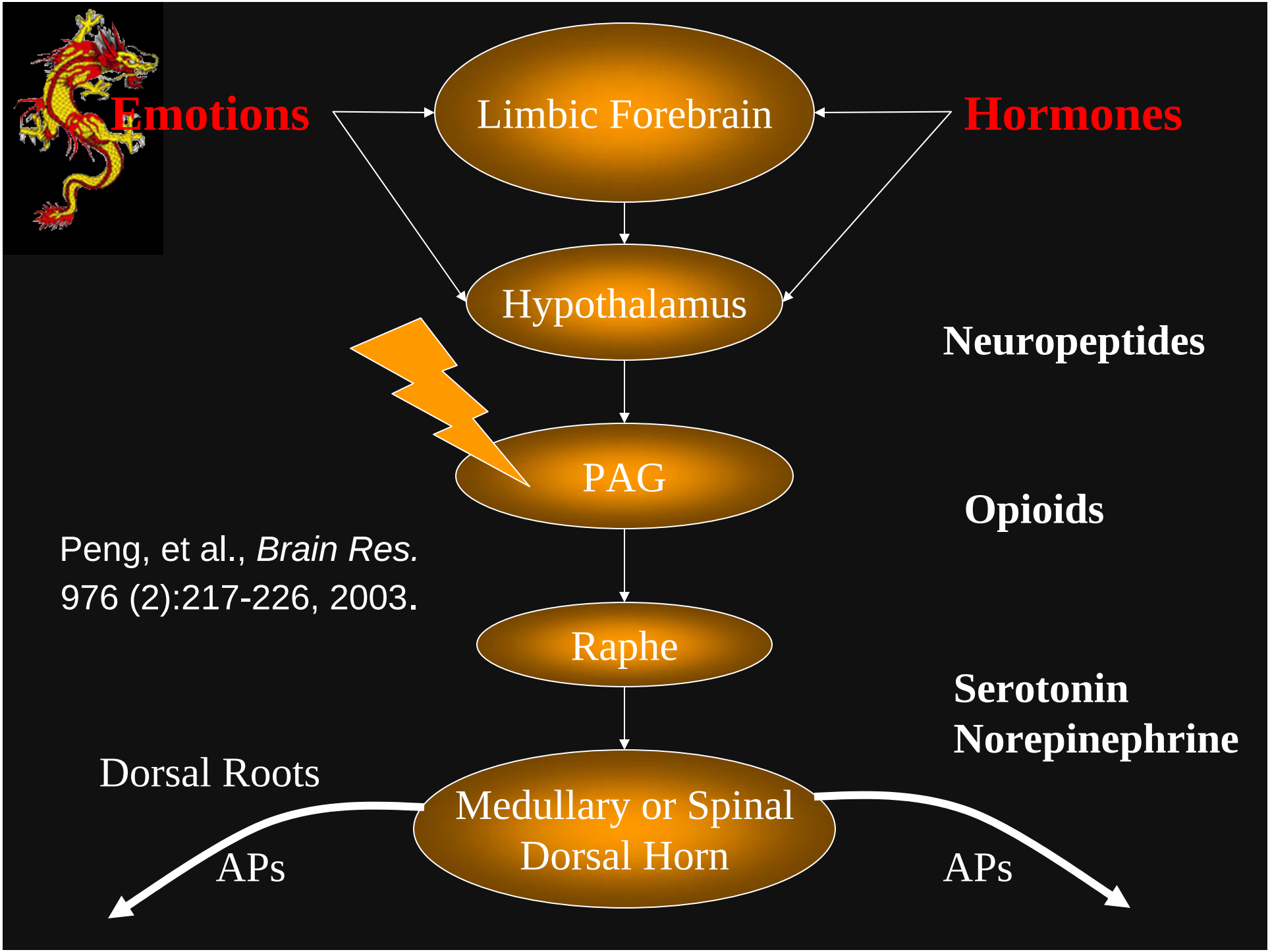
Opioids

Off Cells
On Cells

Raphe

Serotonin
Norepinephrine

Medullary or Spinal
Dorsal Horn


Emotions
Limbic Forebrain
Hormones
Hypothalamus
Neuropeptides
PAG
Opioids
Peng, et al., *Brain Res.* 976 (2):217-226, 2003.
Raphe
Serotonin
Norepinephrine
Dorsal Roots
Medullary or Spinal Dorsal Horn
APs
APs

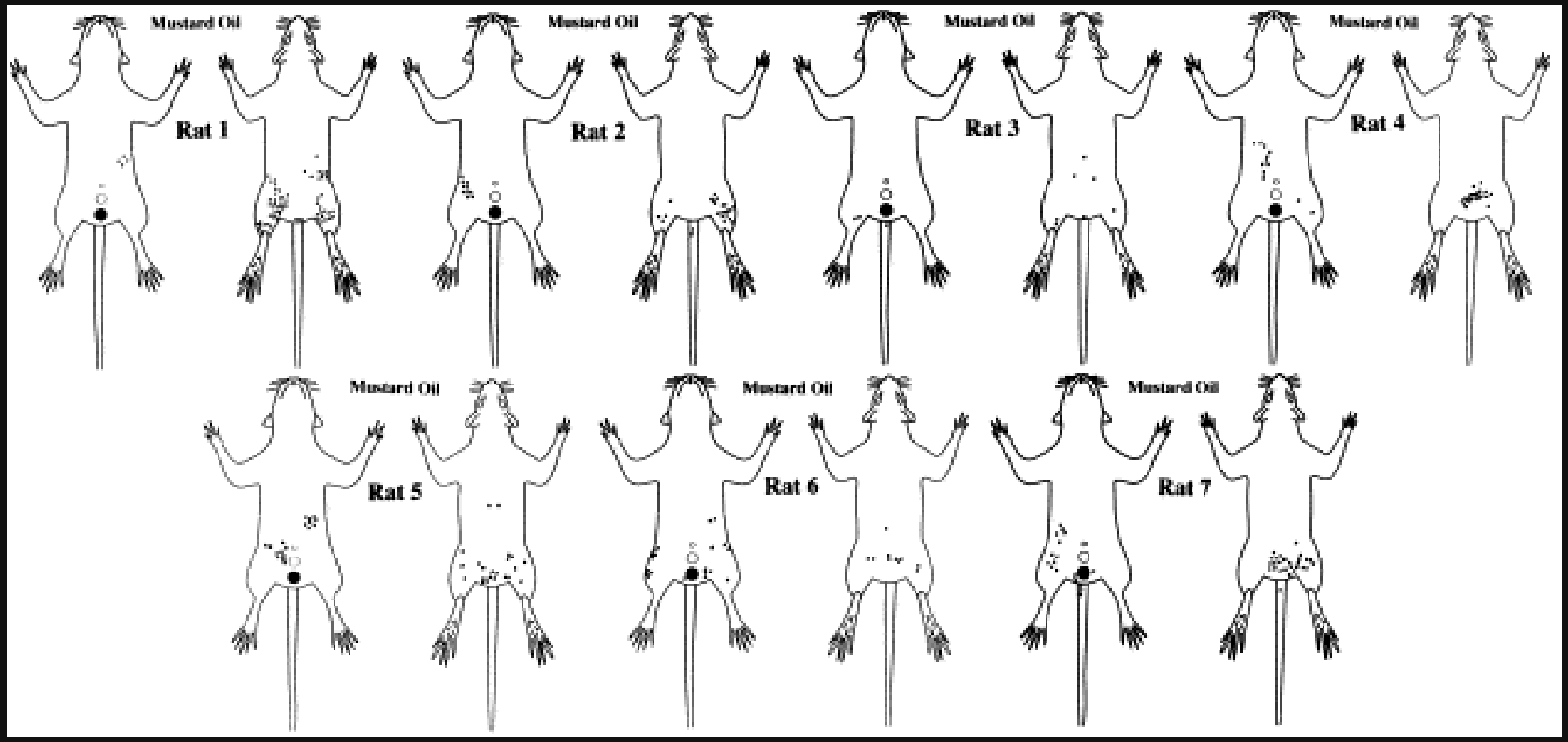
Response To Illness

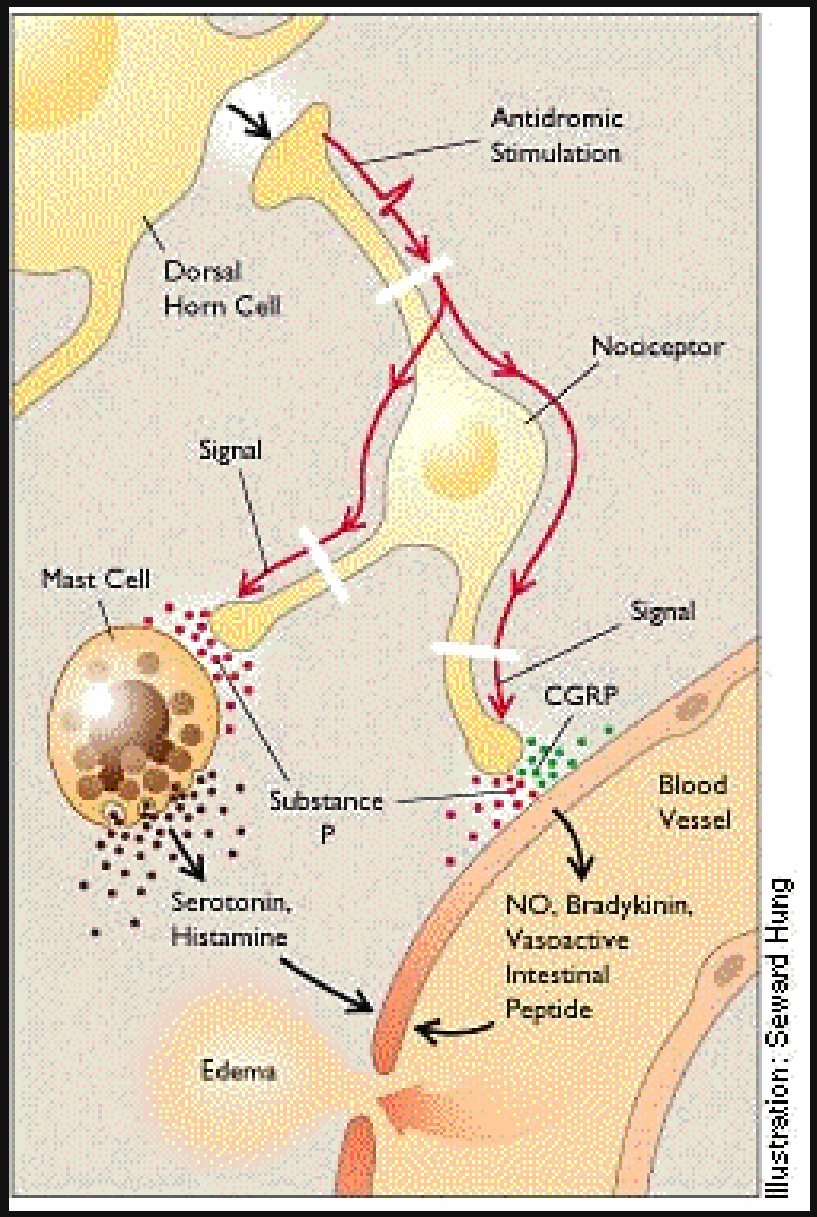
- Pool of Acupoints/TrP's that become activated relates to a complicated central map that integrates CNS and motor system.
- This pattern of activation follows Acupuncture Meridian pathways
- Myofascial Pain with a distinct pattern is endpoint of activation.

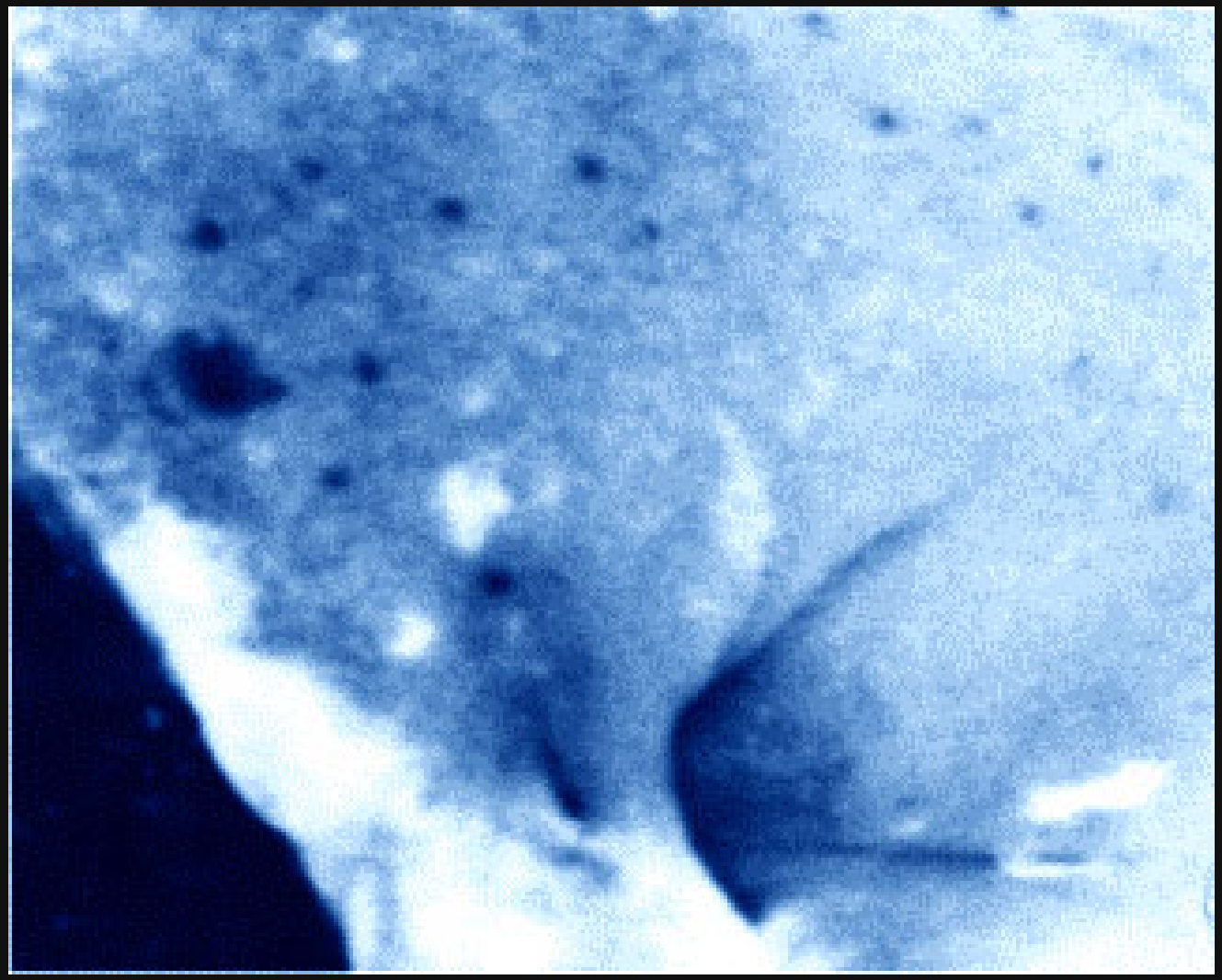
Animal Model of UteroSomatic Reflexes

- Rats pretreated with Evans Blue Dye
- Noxious Uterine stimulation
- Extravasation of dye in Skin
  - Lower abdomen
  - Sacrum
  - Perineum
- Due to neurogenic secretions in these regions causing plasma extravasation

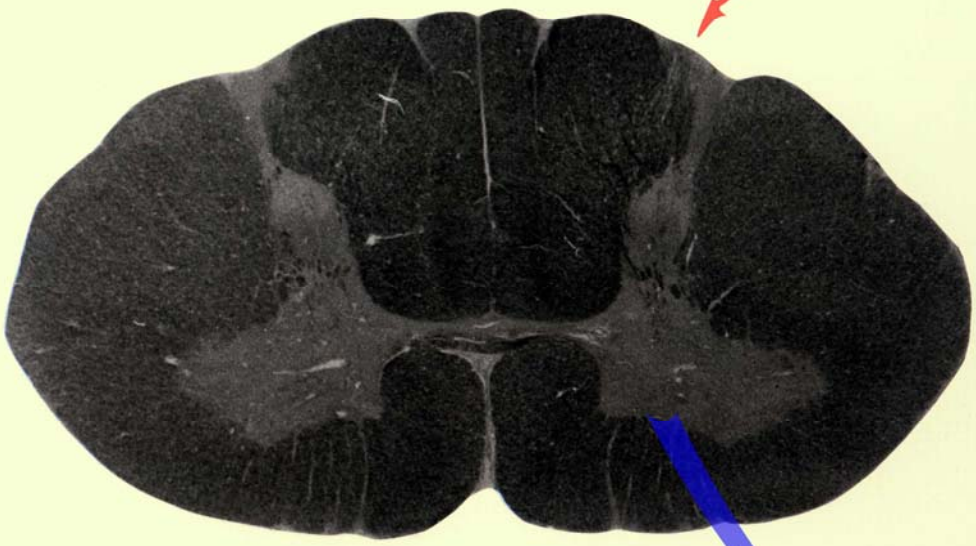
Wesselmann U, Lai Pain 1997;73(3):309-317.


Mustard Oil
Rat 1
Mustard Oil
Rat 2
Mustard Oil
Rat 3
Mustard Oil
Rat 4
Mustard Oil
Rat 5
Mustard Oil
Rat 6
Mustard Oil
Rat 7

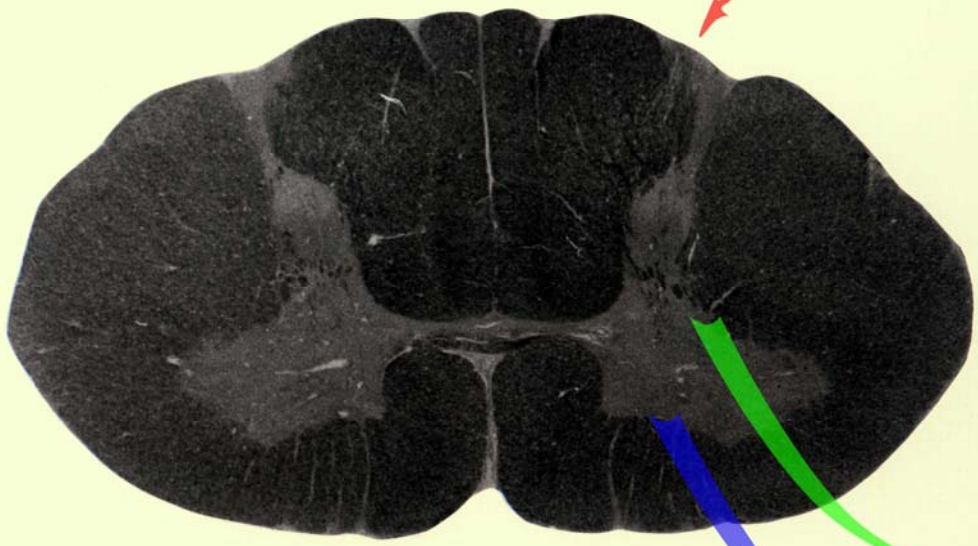

Antidromic
Stimulation
Dorsal
Horn Cell
Nociceptor
Signal
Mast Cell
Signal
CGRP
Substance
P
Blood
Vessel
Serotonin,
Histamine
NO, Bradykinin,
Vasoactive
Intestinal
Peptide
Edema
Illustration: Seward Hung



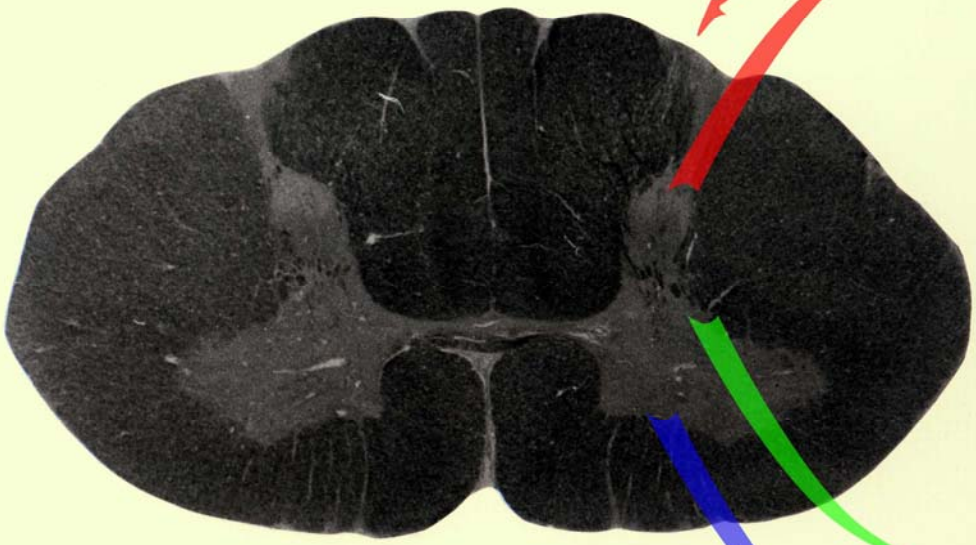
Spinal Facilitation



Spinal Facilitation



Spinal Facilitation



Primary Afferernt Nociceptors

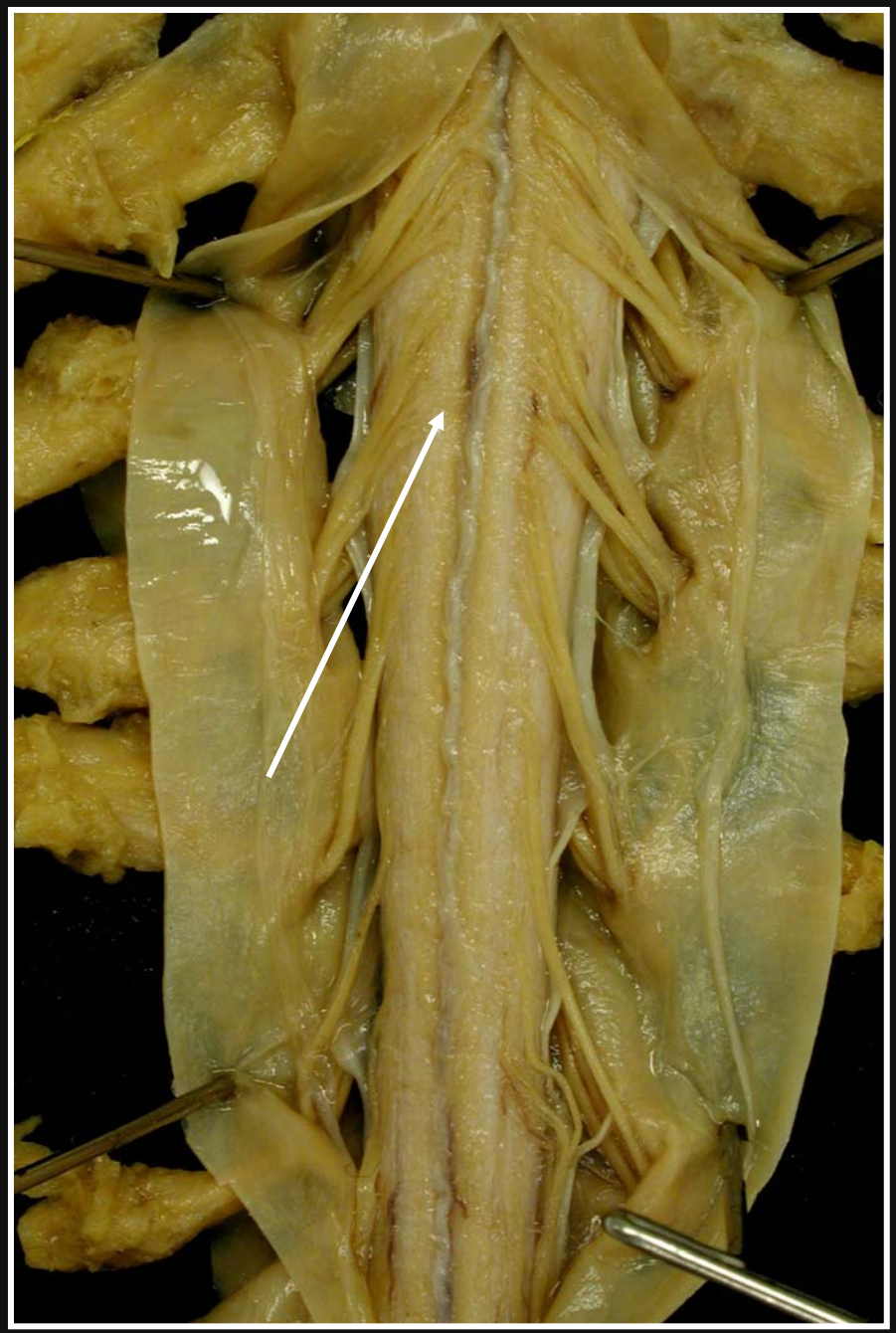
Dorsal Horn Outflow

Lateral Horn Outflow

Ventral Horn Outflow

Dorsal Root Reflexes

- Outflow on dorsal roots
- Initial C-fiber activity
- Tissue-level peptide release



Dorsal Root Reflexes

- Outflow on dorsal roots
- Initial C-fiber activity
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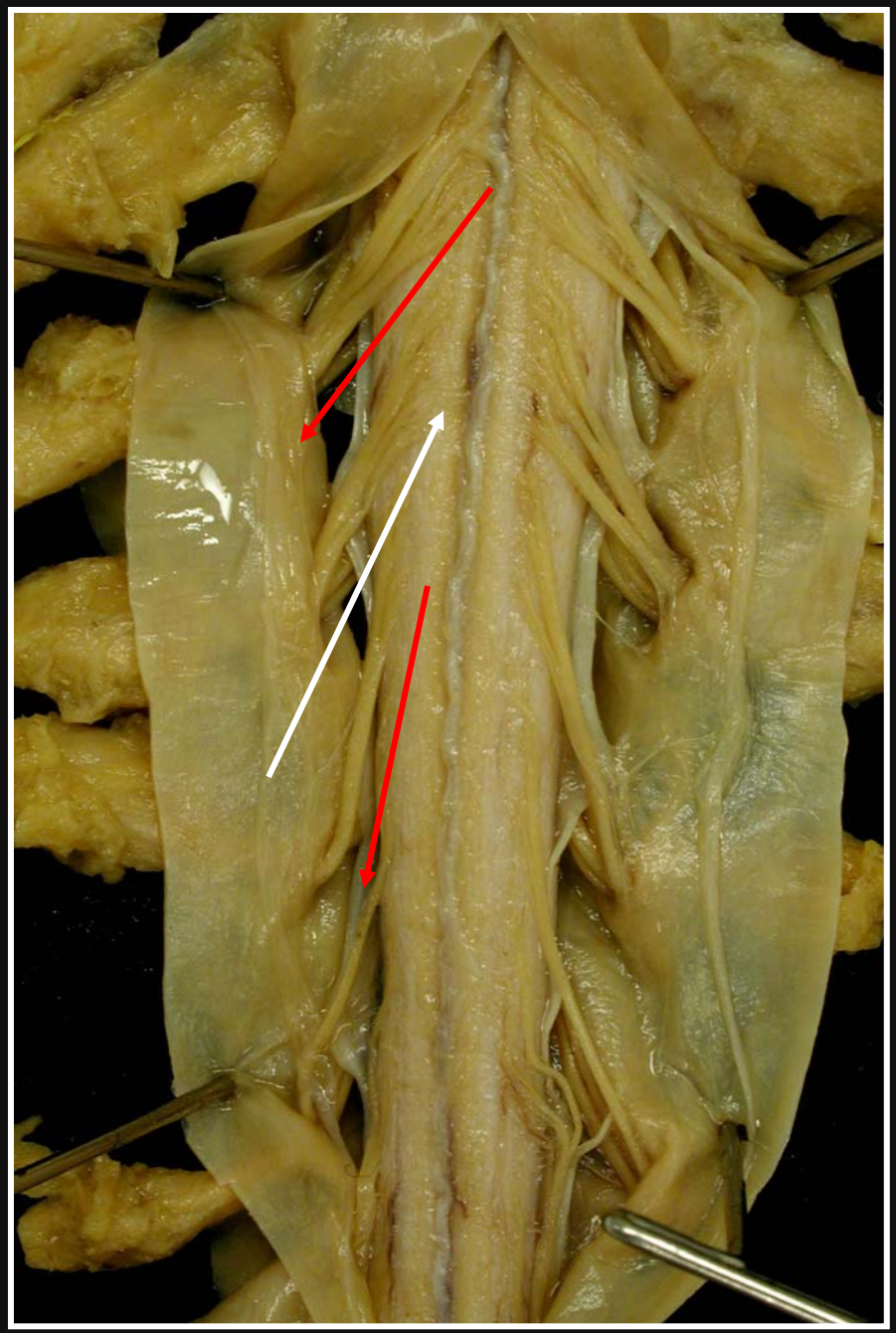
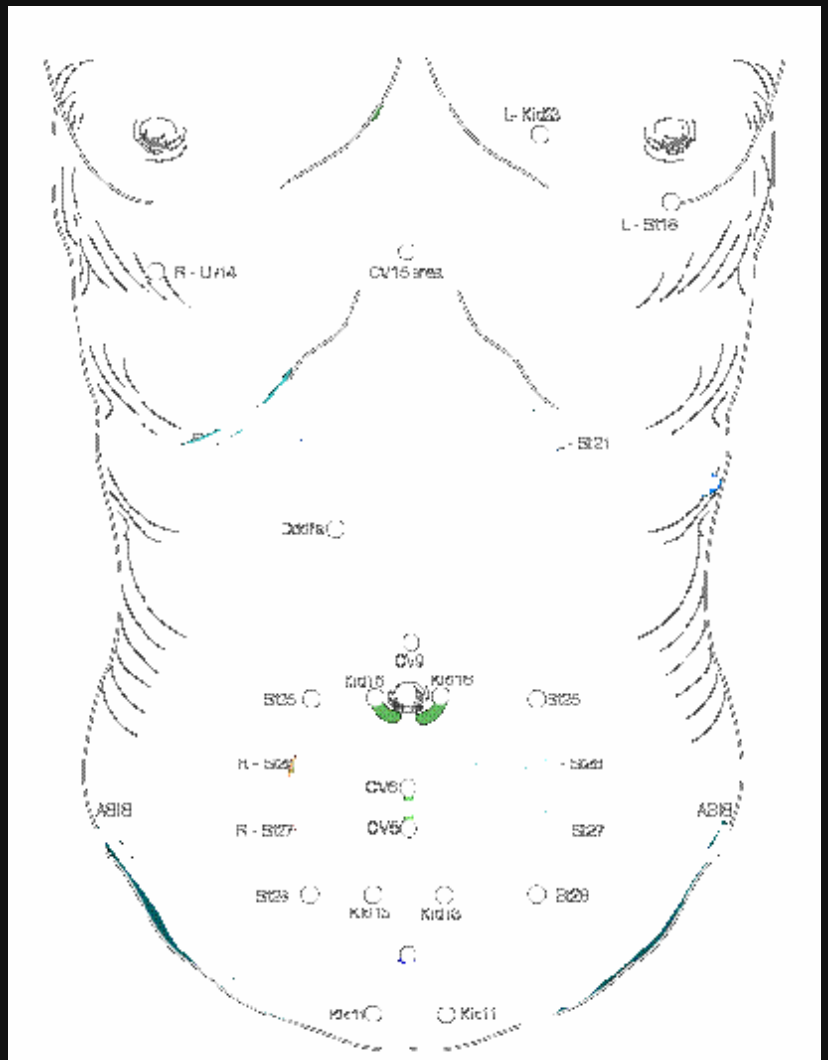
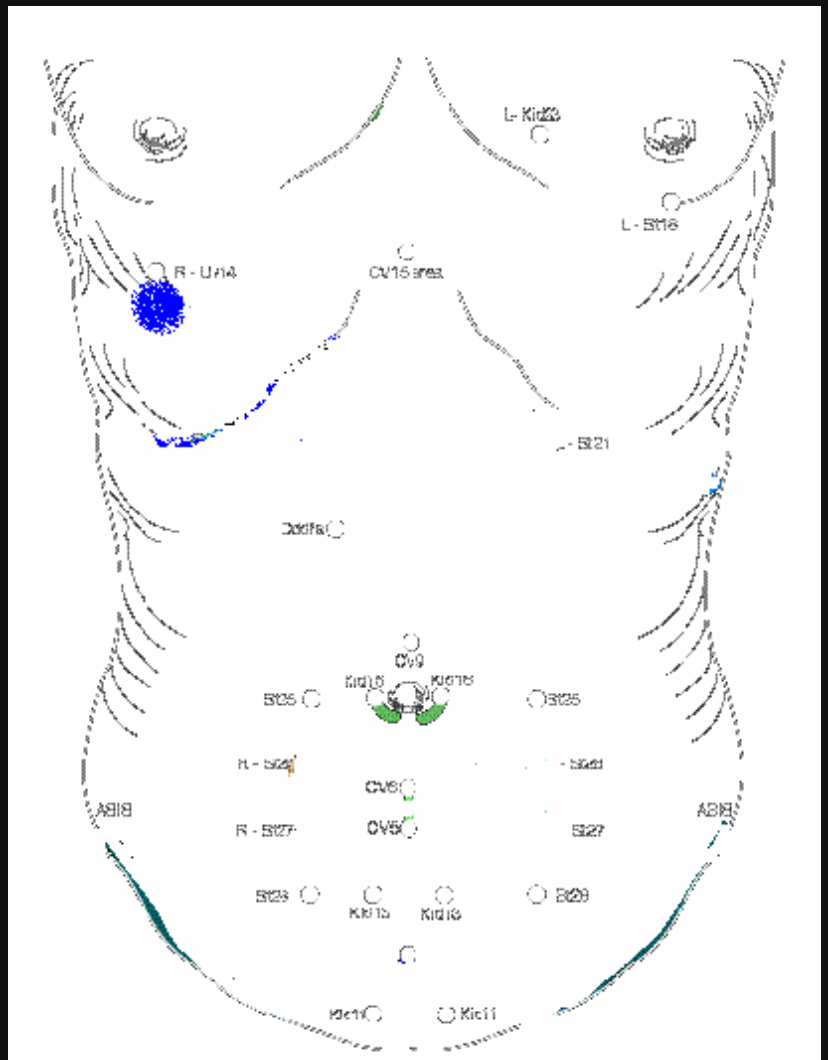
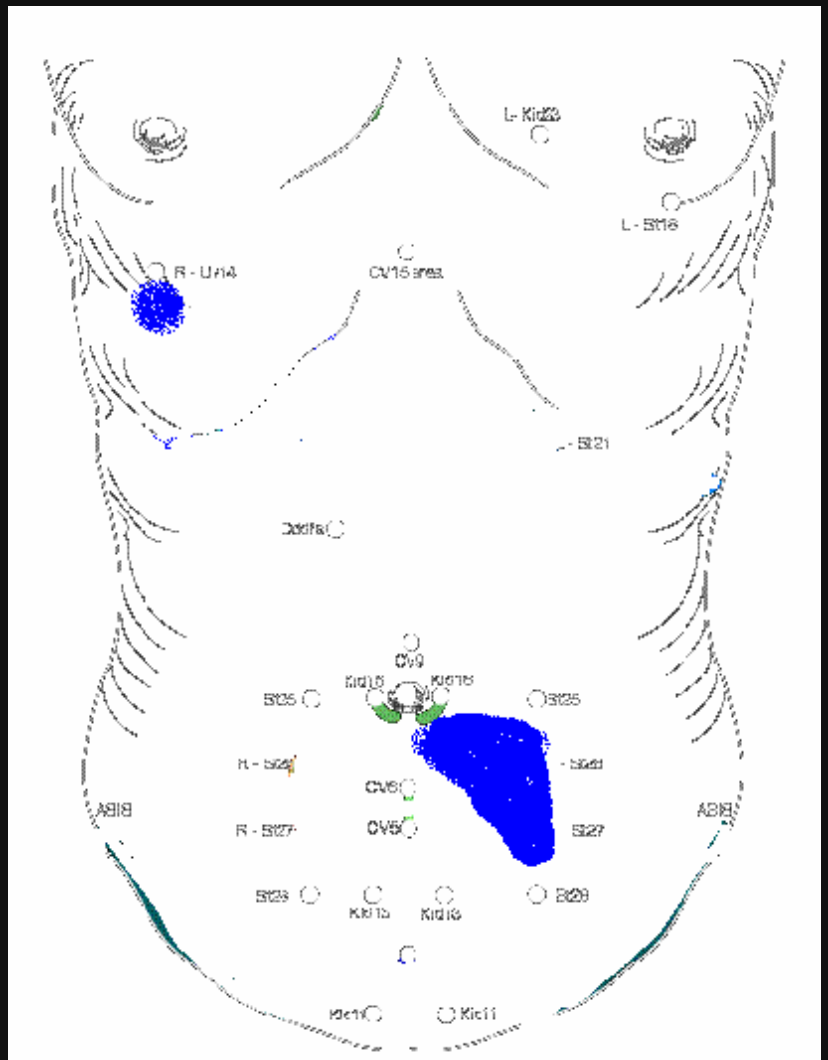
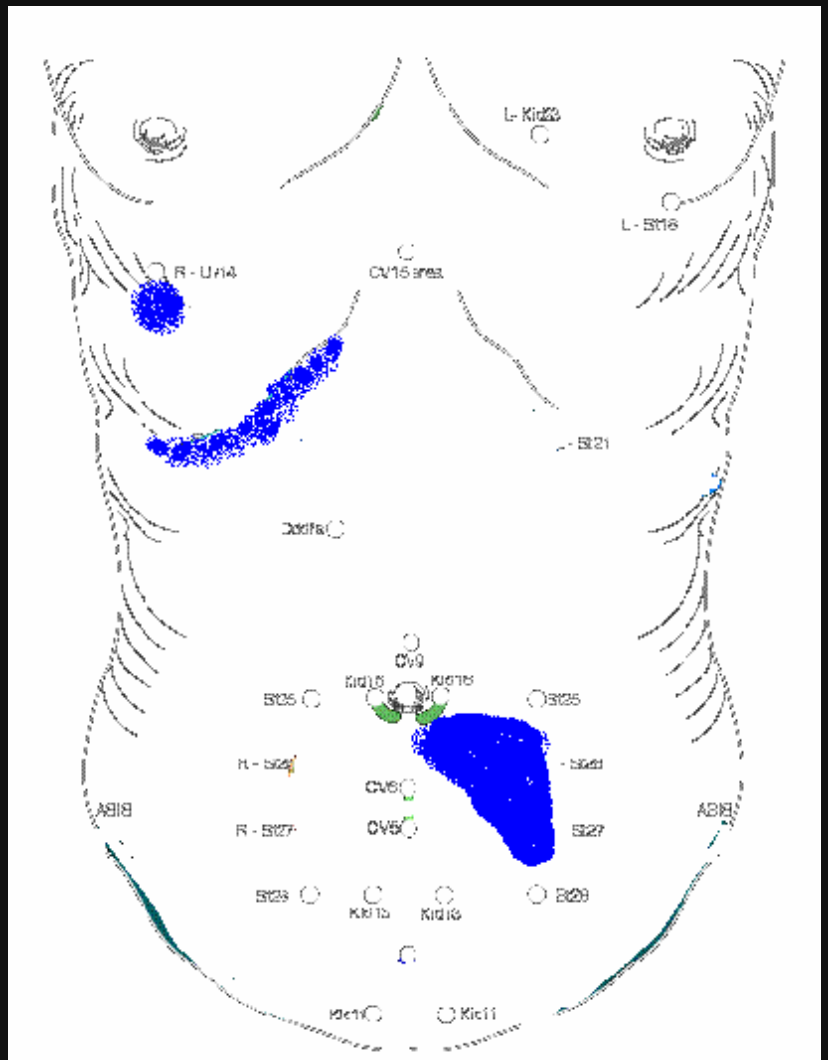
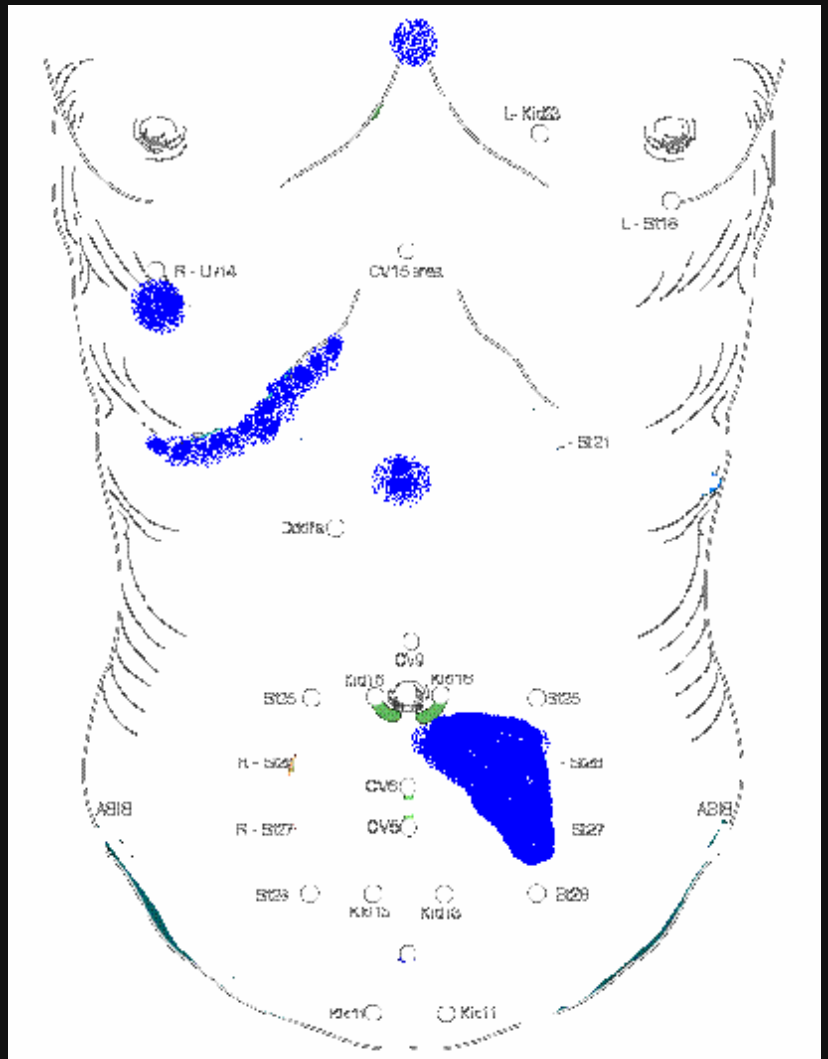


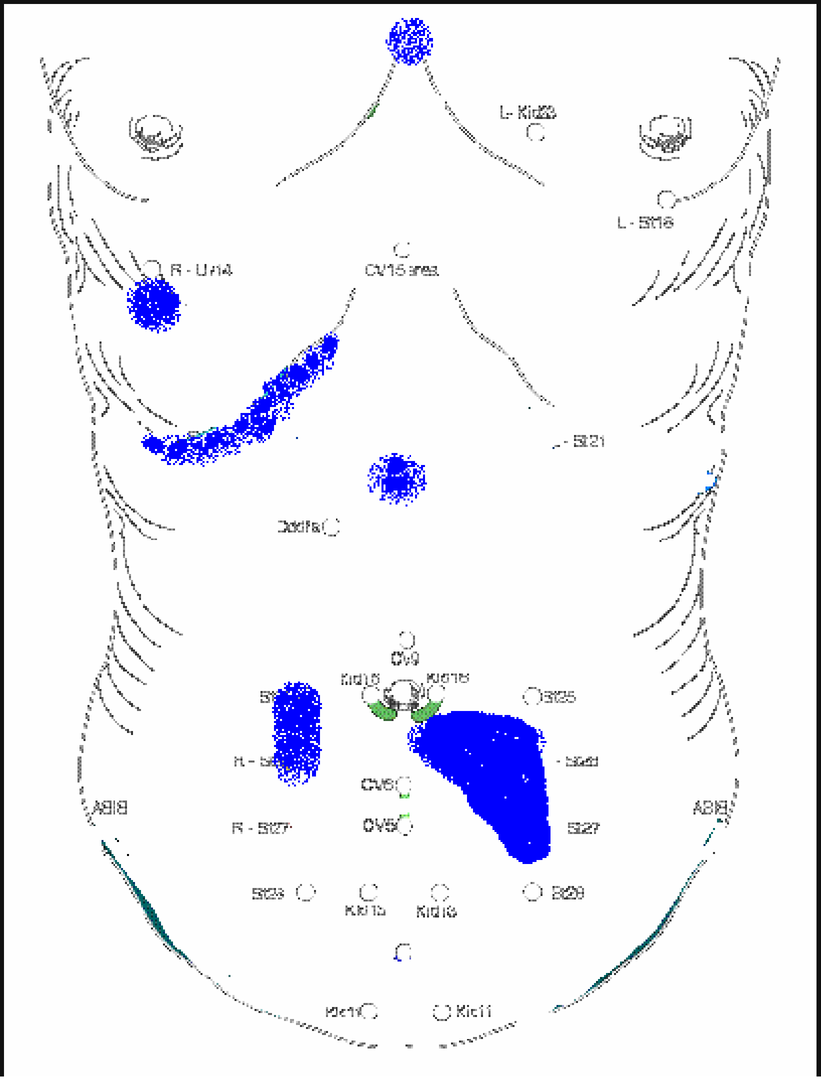

L- Kid23
L - St16
R - U.14
CV15 area
- St21
3ddfa
CV9
Kid16
Kid15
St25
St25
R - St24
- St24
CV6
ASIS
ASIS
R - St27
CV5
St27
St28
St29
Kid13
Kid19
Kid14
Kid11


L- Kid23
L - St16
R - Ut14
CV15 area
- St21
Dd/Ra
CV9
Kid16
Kid15
St25
St25
R - St24
- St24
CV6
ASIS
ASIS
R - St27
CV5
St27
St28
St29
Kid13
Kid12
Kid1
Kid 1

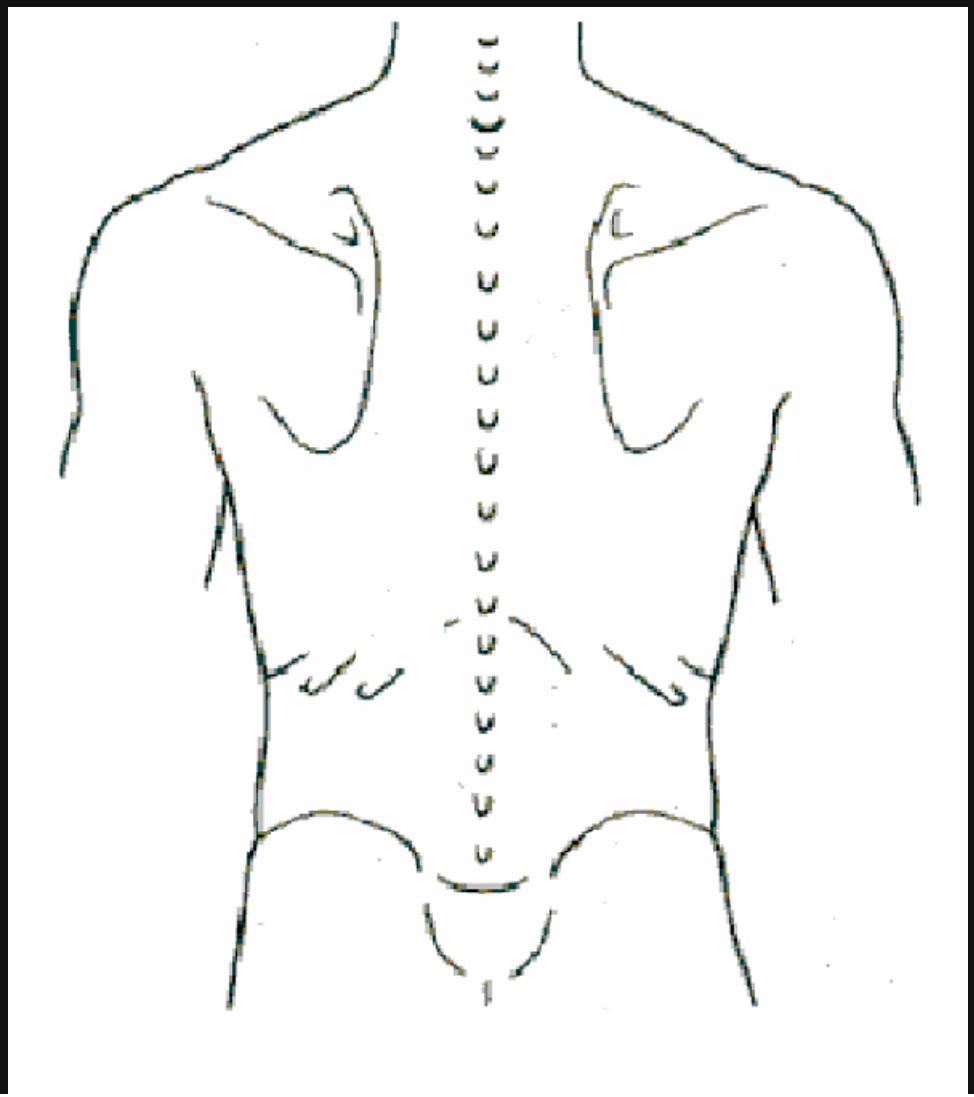

L- Kid23
L - St16
R - UH4
CV15 area
- St21
3dd Pa
CV9
Kid16
Kid15
St25
St25
- St24
CV6
ASIS
ASIS
R - St27
CV5
St27
St29
St23
Kid13
Kid12
Kid1
Kid 1

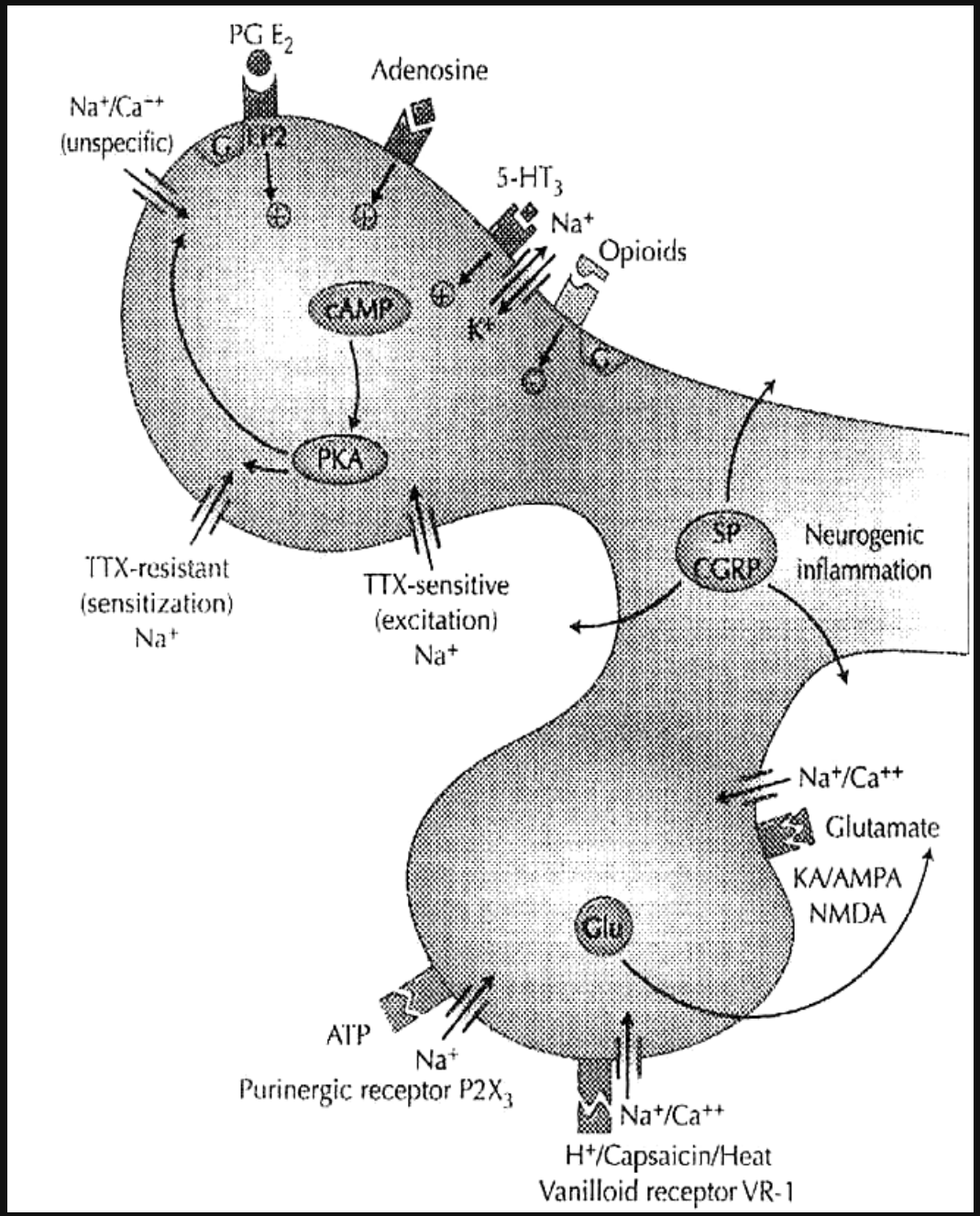

L- Kid23
L - St18
R - U.14
CV15 area
- St21
3dd Pa
CV9
Kid16
Kid15
St25
St25
- St26
R - St24
CV6
ASIS
ASIS
R - St27
CV5
St27
St28
St29
Kid13
Kid19
Kid14
Kid11

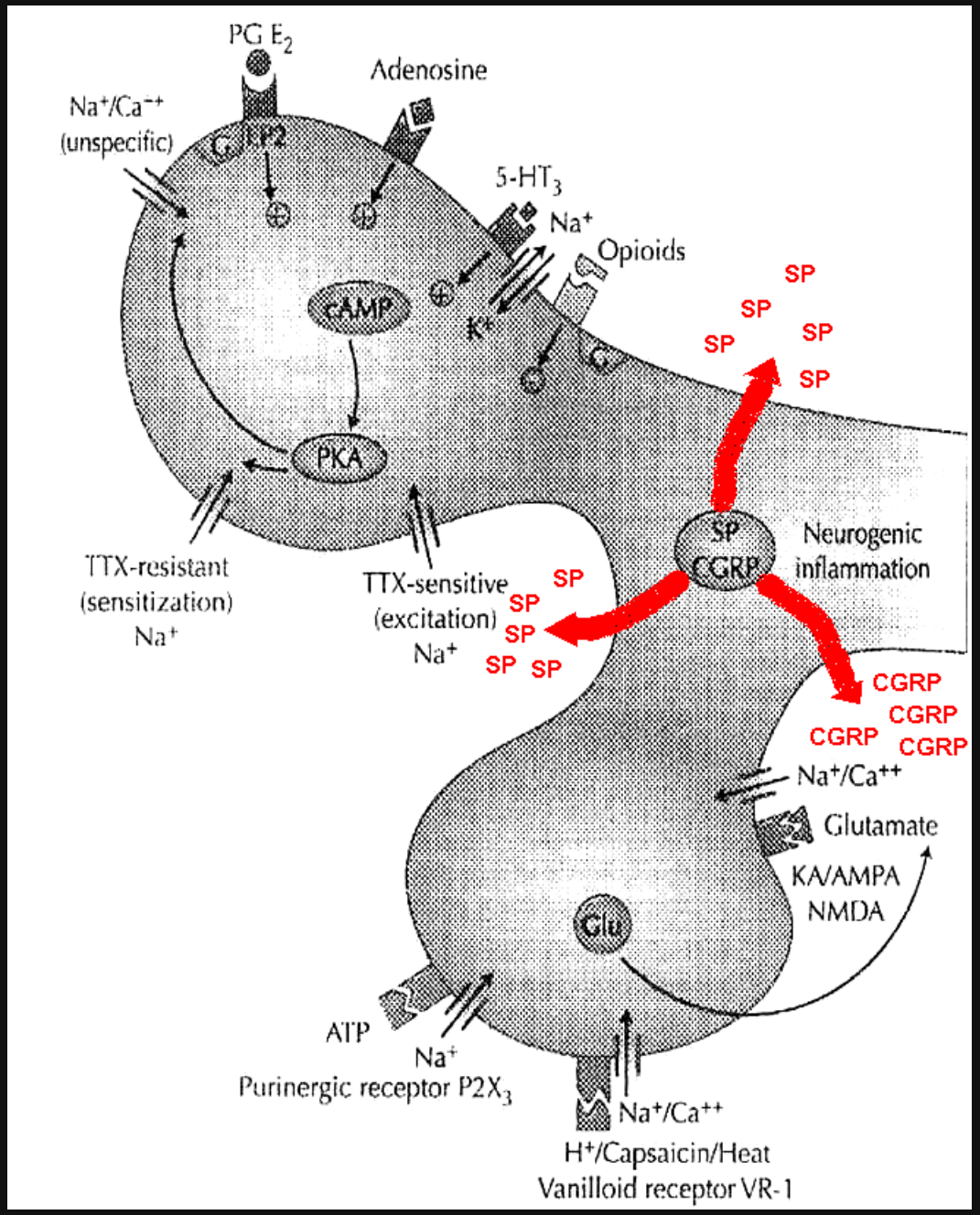

L- Kid23
L - St18
R - U/14
CV15 area
- St21
Dddfa
CV9
Kid16
Kid15
St25
St25
- St24
CV6
ASIS
ASIS
R - St27
CV5
St27
St29
St23
Kid13
Kid12
Kid1
Kid 1

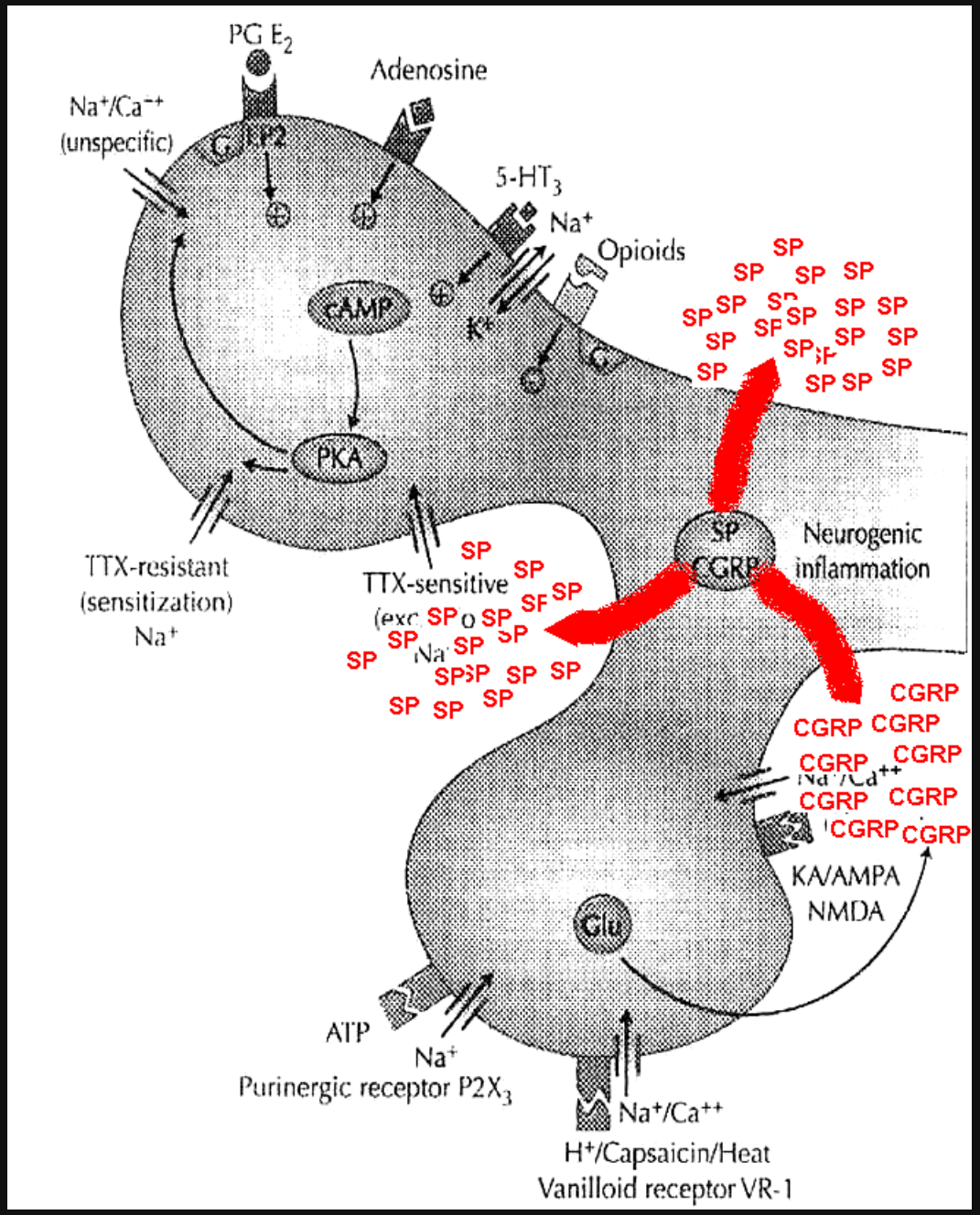


L- Kid22
L - St16
CV15 area
L - St21
CV9
Kid16
St25
St27
R - St27
CV6
CV5
St28
Kid15
Kid11




PG E_2
Adenosine
Na^+/Ca^{-+}
(unspecific)
P_2
5-HT_3
Na^+
Opioids
cAMP
K^+
PKA
TTX-resistant
(sensitization)
Na^+
TTX-sensitive
(excitation)
Na^+
SP
CGRP
Neurogenic
inflammation
Na^+/Ca^{++}
Glutamate
KA/AMPA
NMDA
Glu
ATP
Na^+
Purinergic receptor $P2X_3$
Na^+/Ca^{++}
H^+/Capsaicin/Heat
Vanilloid receptor VR-1


PG E_2
Adenosine
Na^+/Ca^{-+}
(unspecific)
5-HT_3
Na^+
Opioids
cAMP
K^+
PKA
SP
CGRP
Neurogenic
inflammation
TTX-resistant
(sensitization)
Na^+
TTX-sensitive
(excitation)
Na^+
CGRP
Na^+/Ca^{++}
Glutamate
KA/AMPA
NMDA
Glu
ATP
Na^+
Purinergic receptor $P2X_3$
Na^+/Ca^{++}
H^+/Capsaicin/Heat
Vanilloid receptor VR-1


PG E_2
Adenosine
Na^+/Ca^{-+}
(unspecific)
P2
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Opioids
SP
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K^+
PKA
TTX-resistant
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TTX-sensitive
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CGRP
Neurogenic
inflammation
CGRP
Na^+/Ca^{++}
KA/AMPA
NMDA
Glu
ATP
Na^+
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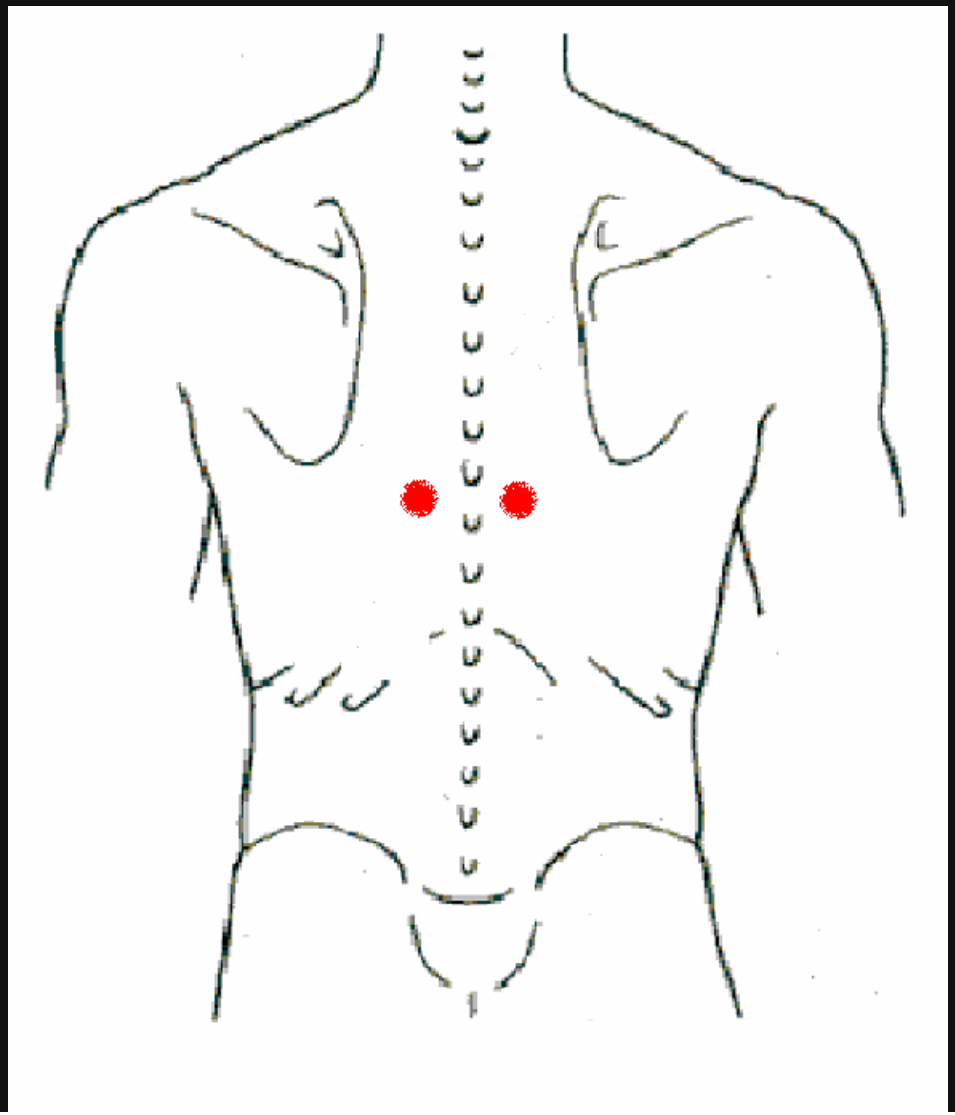

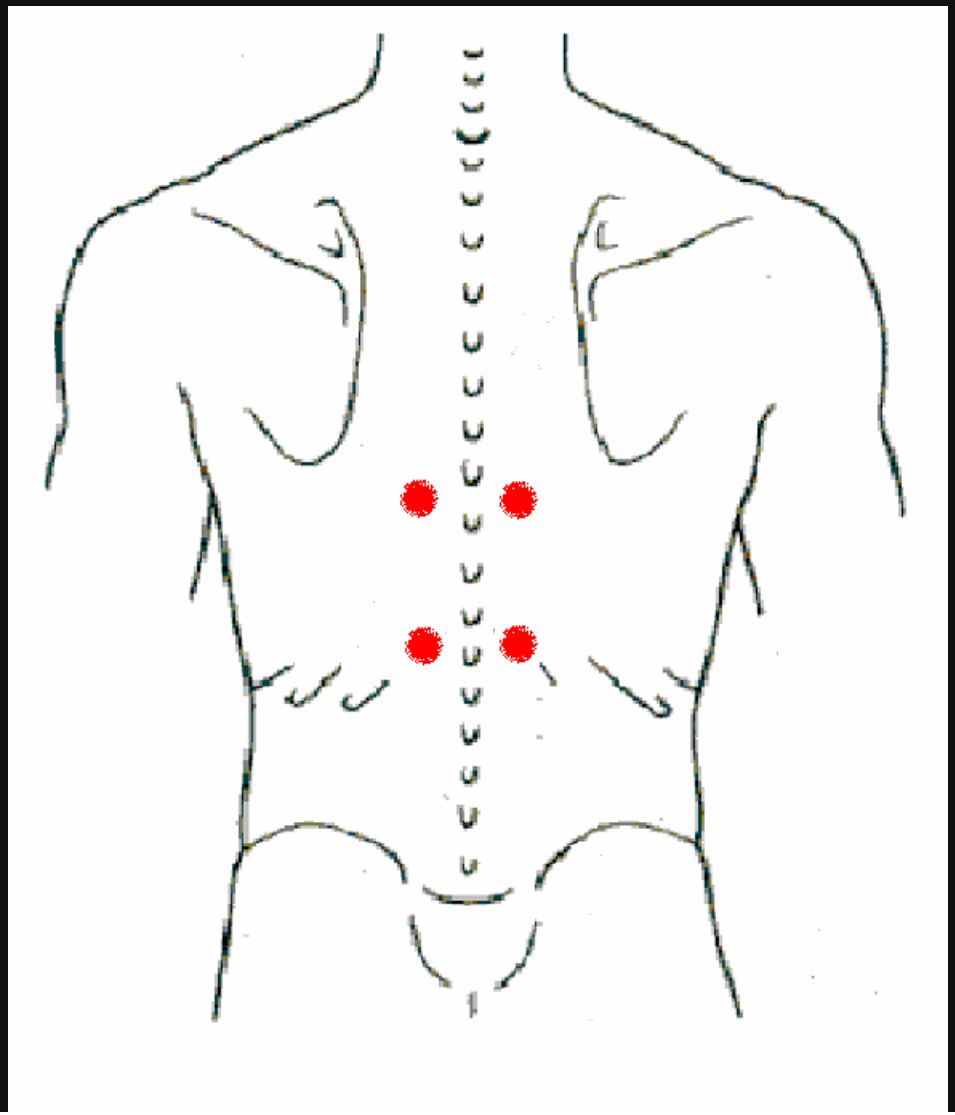

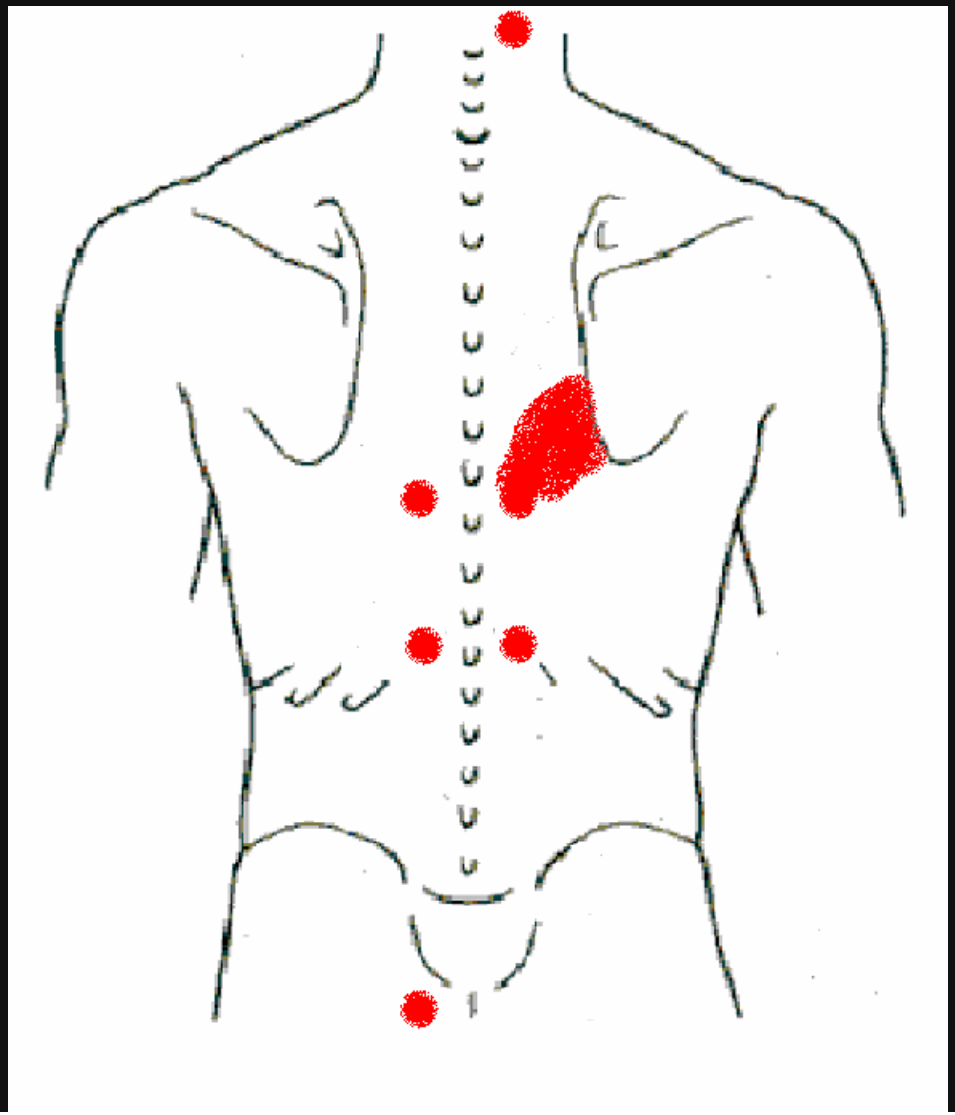

REVERSAL OF DISEASE PROCESS

- Stimulation of active points leads to central neuromodulation
  - Changes in Sympathetic Tone
  - Changes in gamma-motor neuron excitability
  - Changes in alpha-motor neuron activation
  - Reverses neuroplastic changes in pain modulation back to a homeostatic pattern
- Disease Modification

c-Fos Expression in CNS

- c-Fos gene expression in CNS occurs in cells felt to be activated after noxious peripheral stimulation
- Fos Protein is the nuclear product of the immediate-early gene c-Fos
- Couples transient intracellular signals to long term changes in gene expression.
- Heralds neuroplastic changes in CNS

c-FOS AND ACUPUNCTURE

- Differential expression in CNS when comparing noxious input vs. EA.
- EA shown to suppress expression of c-Fos in Dorsal Horn in response to mechanical noxious input.
- Question: Evidence of reverse neuroplasticity

Wang H et al. Acupuncture Electrother Res. 1995;20:163-172.

FUTURE RESEARCH

- Neurobiology of Acupoints/TrP's
  - Cytokines
- Neuroplastic Changes in CNS with disease states
  - c-Fos
  - fMRI
- Assess if Needle Stimulation of Active Points can reverse these changes