운동치료의 신경학적 의의

한림의대 재활의학과
온석훈

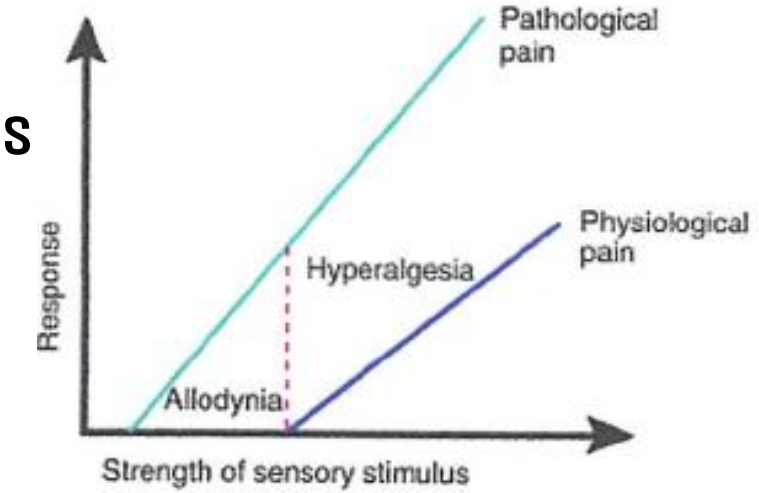
Contents

- Pain pathway and pain network
  1) Functional anatomy
  2) Changes in pain systems in chronic pain
  3) How to view the MRI coordinates

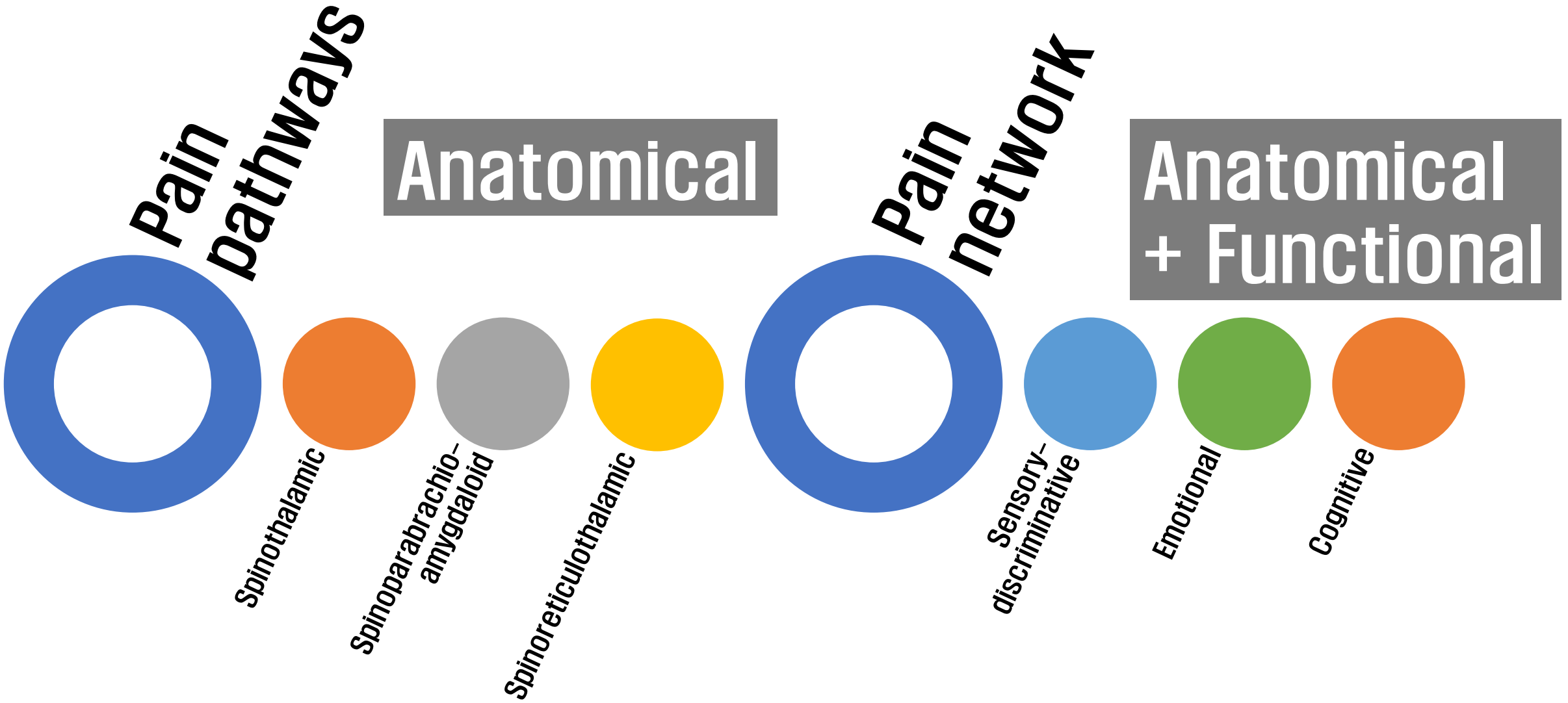
- Mechanism of exercise for pain control
  1) Exercise-induced hypoalgesia (EIH)
  2) Training-induced hypoalgesia (TIH)

Pain

- **Physiological pain**
  - Unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (IASP)
  - Important protective function
- **Pathological pain**
  - Inflammation, neuropathy, cancer, chemotherapy, diabetes
  - Hyperalgesia: increased sensitivity to painful stimuli
  - Allodynia: pain produced by normally innocuous stimuli
    example) stroking sunburned skin

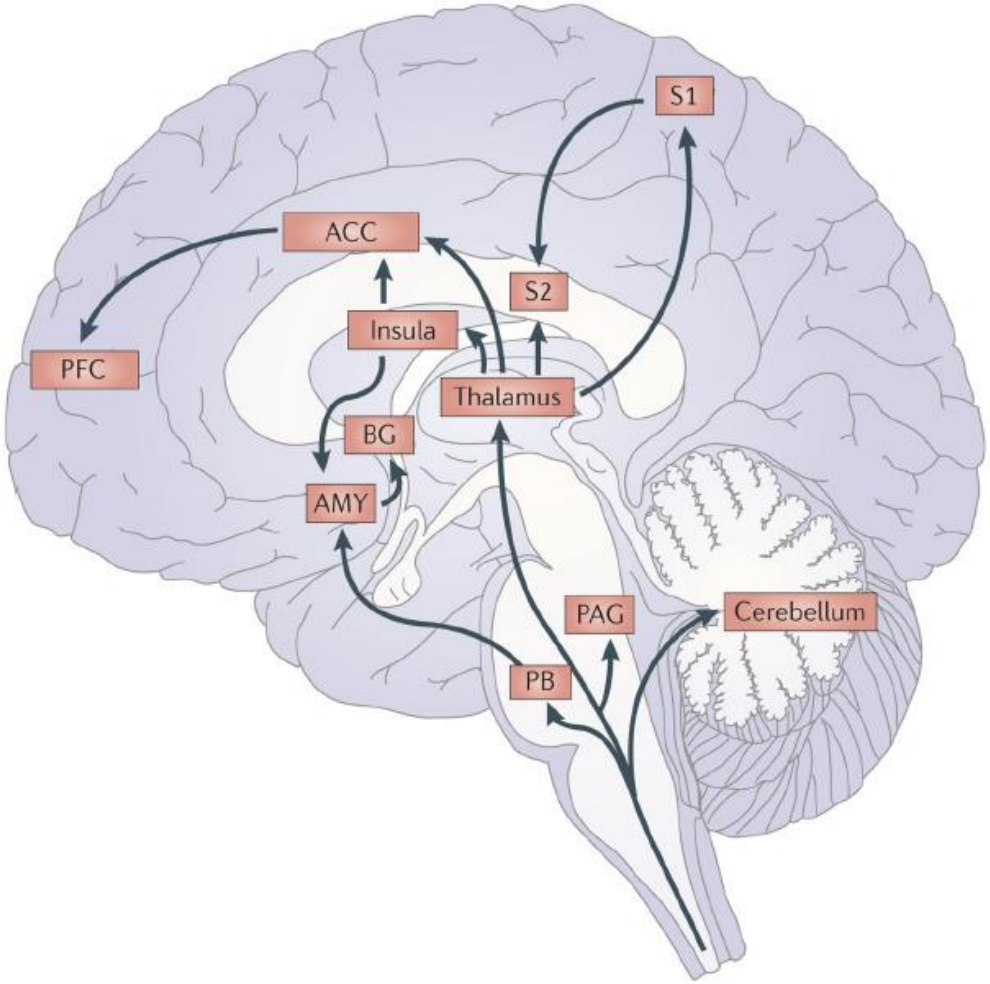


(Kuner, 2010)


Pain pathways
Anatomical
Spinothalamic
Spinoparabrachio-amygdaloid
Spinoreticulothalamic
Pain network
Anatomical + Functional
Sensory-discriminative
Emotional
Cognitive

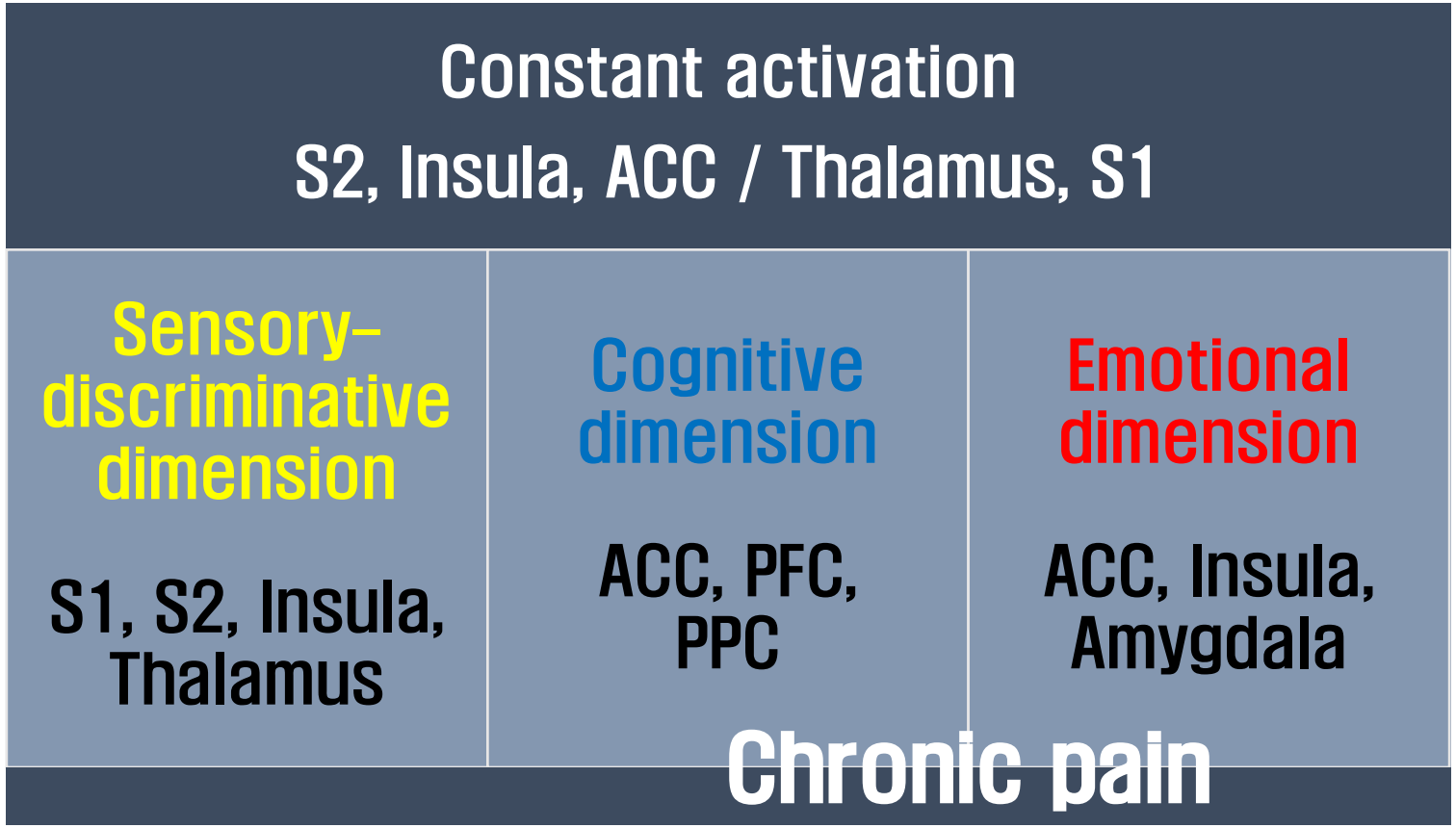
Pain Pathways & Networks

- Multiple pain pathways
  - Spinothalamic
    - Thalamus → Insula, ACC, S1, S2
  - Spinoparabrachio-amygdaloid
    - PB → AMY → BG
  - Spinoreticulothalamic
    - PAG → Thalamus
- Three different pain networks
  1) Sensory-discriminative
  2) Affective
  3) Cognitive



(Bushnell, 2013)

Pain Network



(Peyron, 2000)

Sensory-discriminative Dimension

- Sensation with pain qualities
  - Stinging, burning, aching
  - Location and duration of pain
- Somatosensory cortex (S1, S2), insula, thalamus

Emotional Dimension

- Emotional and motivational aspects of pain
  - Observing another individual in pain
  - Listening to unpleasant music
  - Smelling unpleasant odor
- What is real?
  - Even though it is not real pain, the affective pain sensation makes it real, and the opposite situation is possible (deep massage)
  - Priming of the affective dimension
    → Enhanced pain experience
- ACC, insula, amygdala

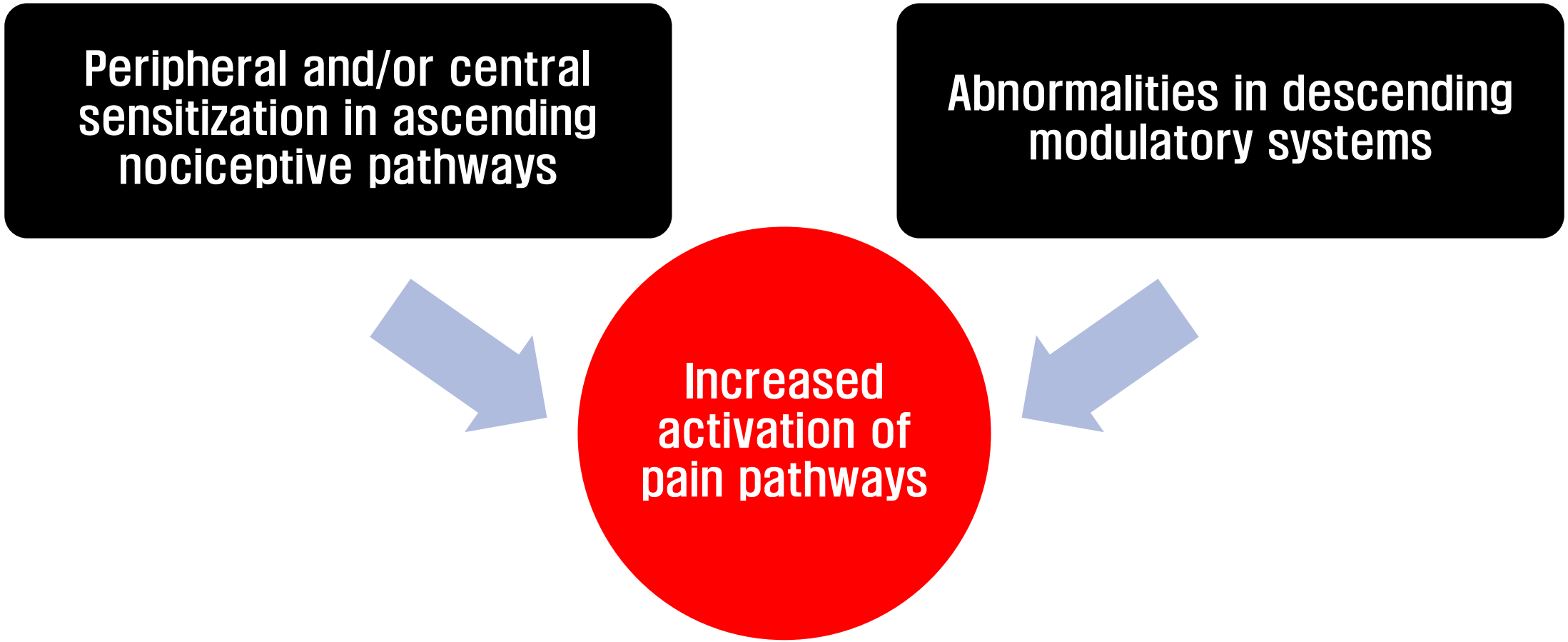
Negative emotional state

Positive emotional state

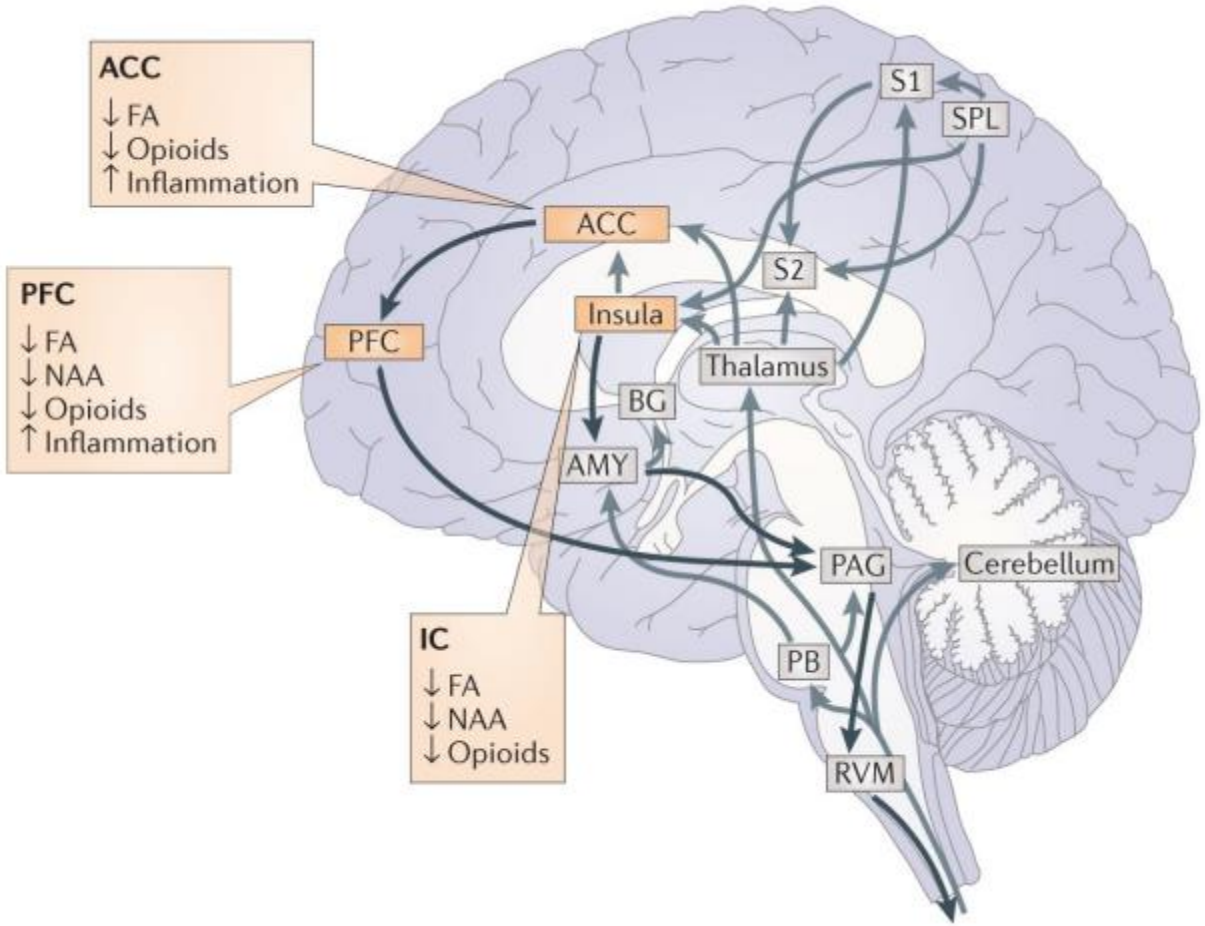
Cognitive Dimension

- Interaction with both sensory and affective dimensions
- Background
  - Wounded soldiers
  - Western medicine < Oriental medicine
- Top-down orienting of the attention system
  - ACC, PFC, PPC

Changes in Pain Systems in Chronic Pain

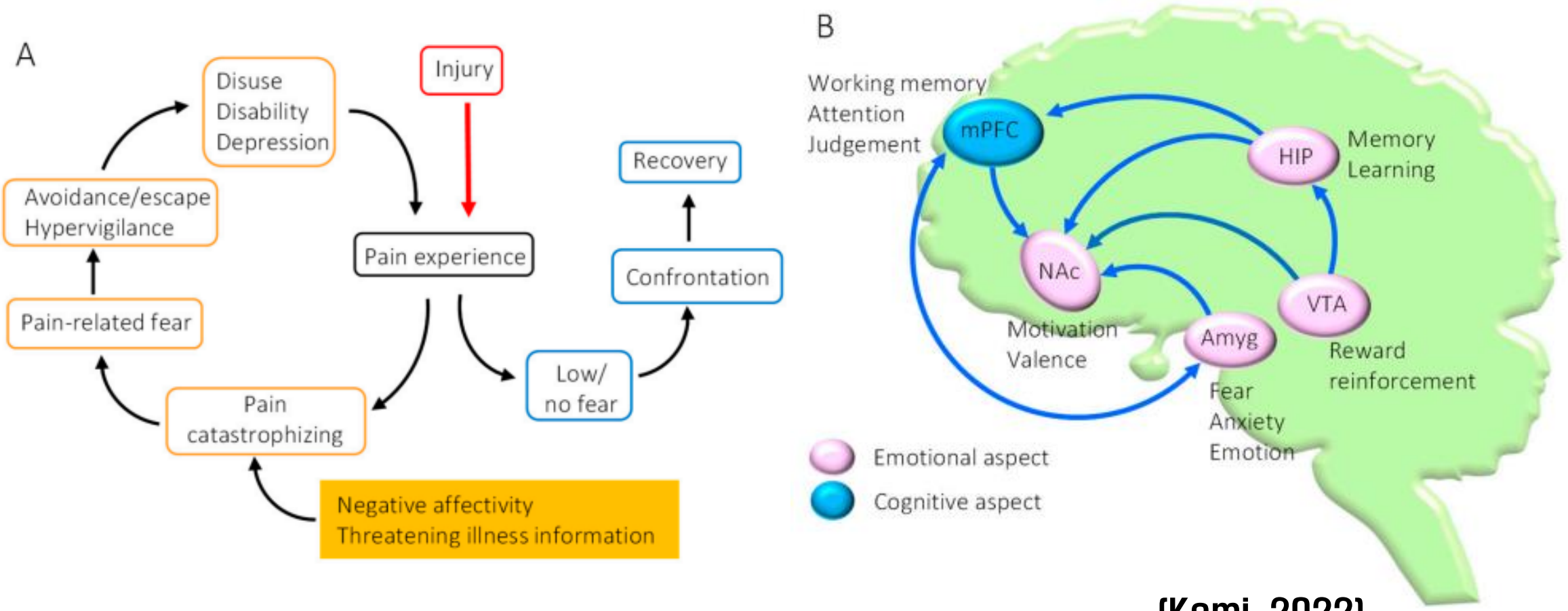


Changes in Pain Systems in Chronic Pain



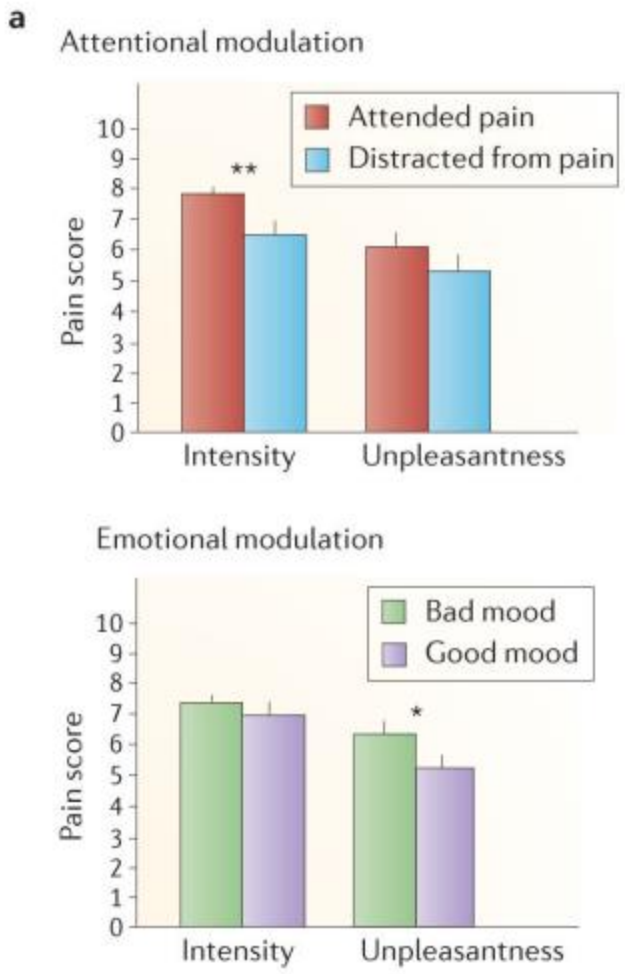
(Bushnell, 2013)

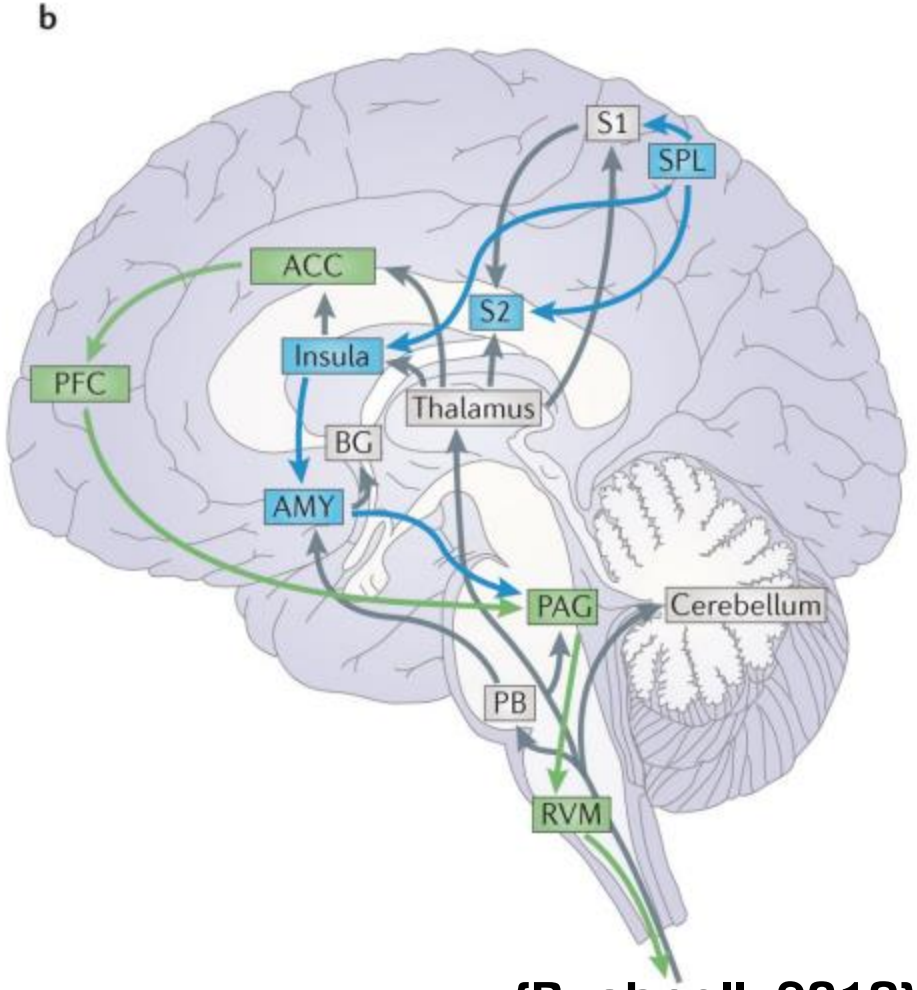
Simultaneous Action of Emotional and Cognitive Dimensions



(Kami, 2022)

Simultaneous Action of Emotional and Cognitive Dimensions

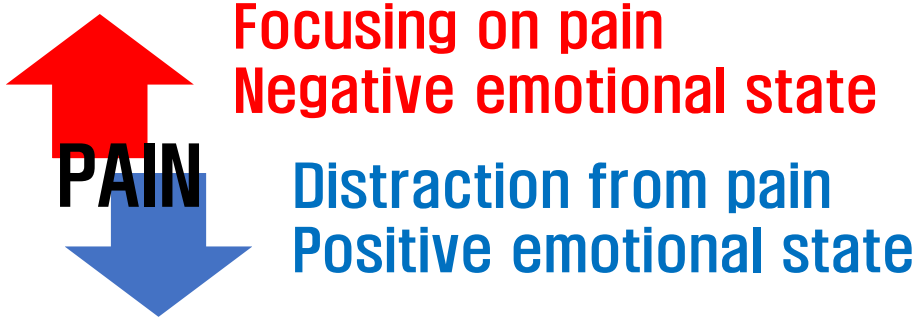




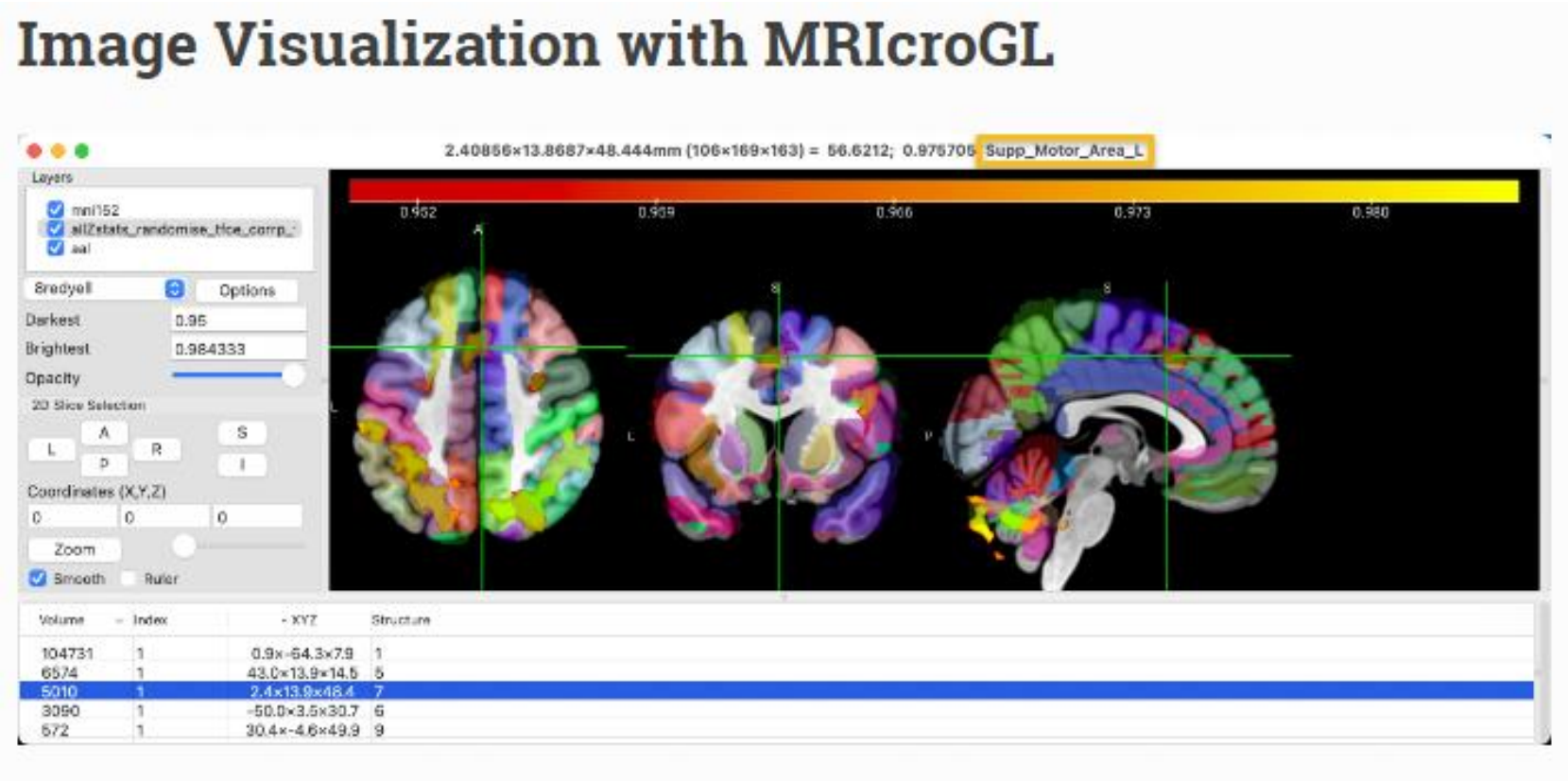
(Bushnell, 2013)

Simultaneous Action of Emotional and Cognitive Dimensions

- Fear–Avoidance Model
  - e.g., Mind–Body Techniques
  - Techniques for controlling pain
  - Use of attentional and emotional factors for pain control
  - Work individually via different pathways
  - Cognitive behavioral therapy, yoga, meditation, hypnosis



MRIcroGL



- MRIcroGL allows you to view 2D slices and renderings of your brain imaging data. It can display many image formats and includes a graphical interface for dcm2nii to convert DICOM images to NIfTI format. It allows you to draw regions of interest which can aid lesion mapping and fMRI analysis. It provides sophisticated rendering.

MRIcroGL

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version 20-July-2022 (v1.2.20220720)	2022-08-11 13:15					
	MRIcroGL_linux1804.zip	62.06 MB	19	Linux	.zip	
	MRIcroGL_linux.zip	67.54 MB	22	Linux	.zip	
	MRIcroGL_macOS.dmg	67.68 MB	90	macOS Universal Binary (x86/ARM)	Other	
	MRIcroGL_windows.zip	64.69 MB	243	Windows	.zip	

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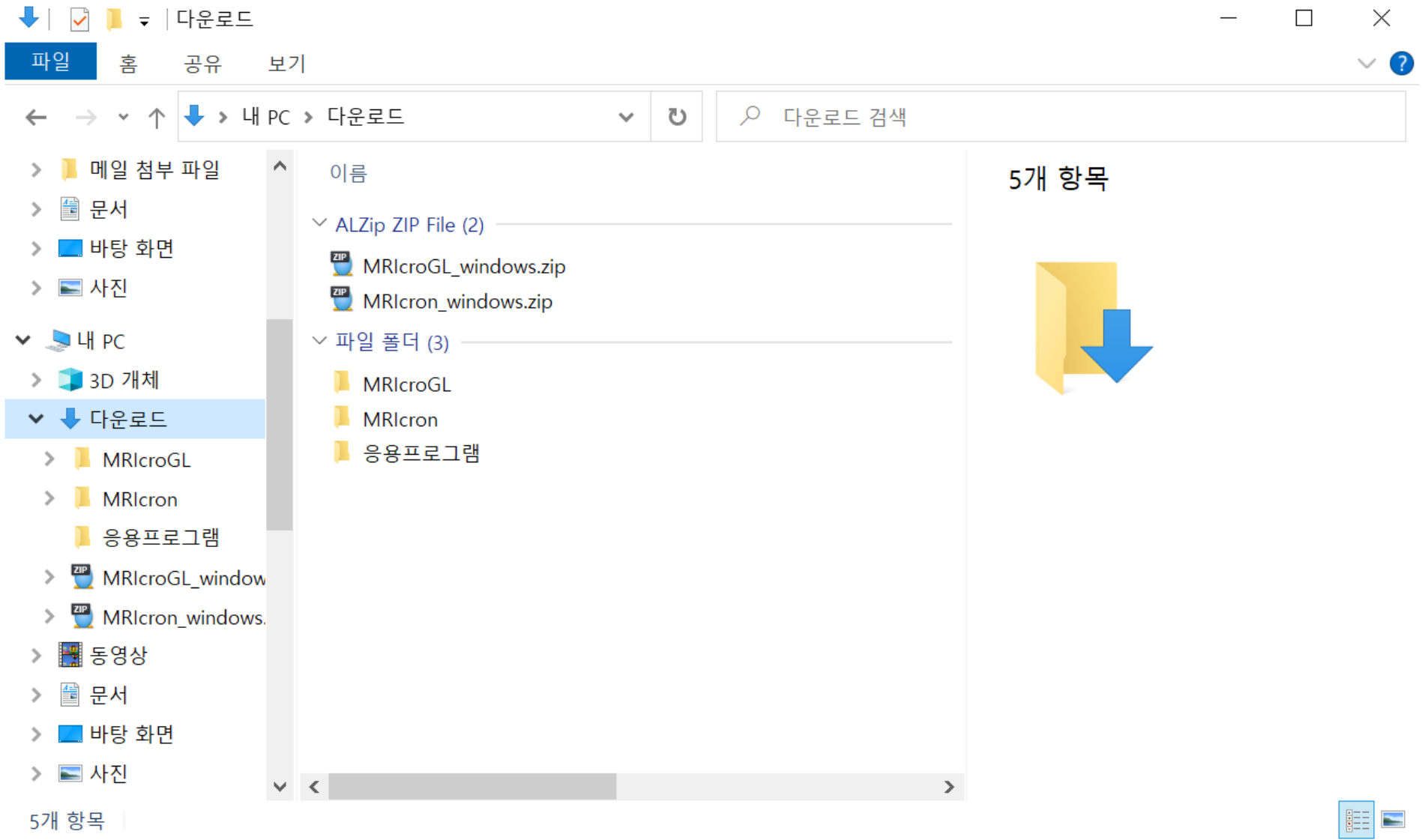
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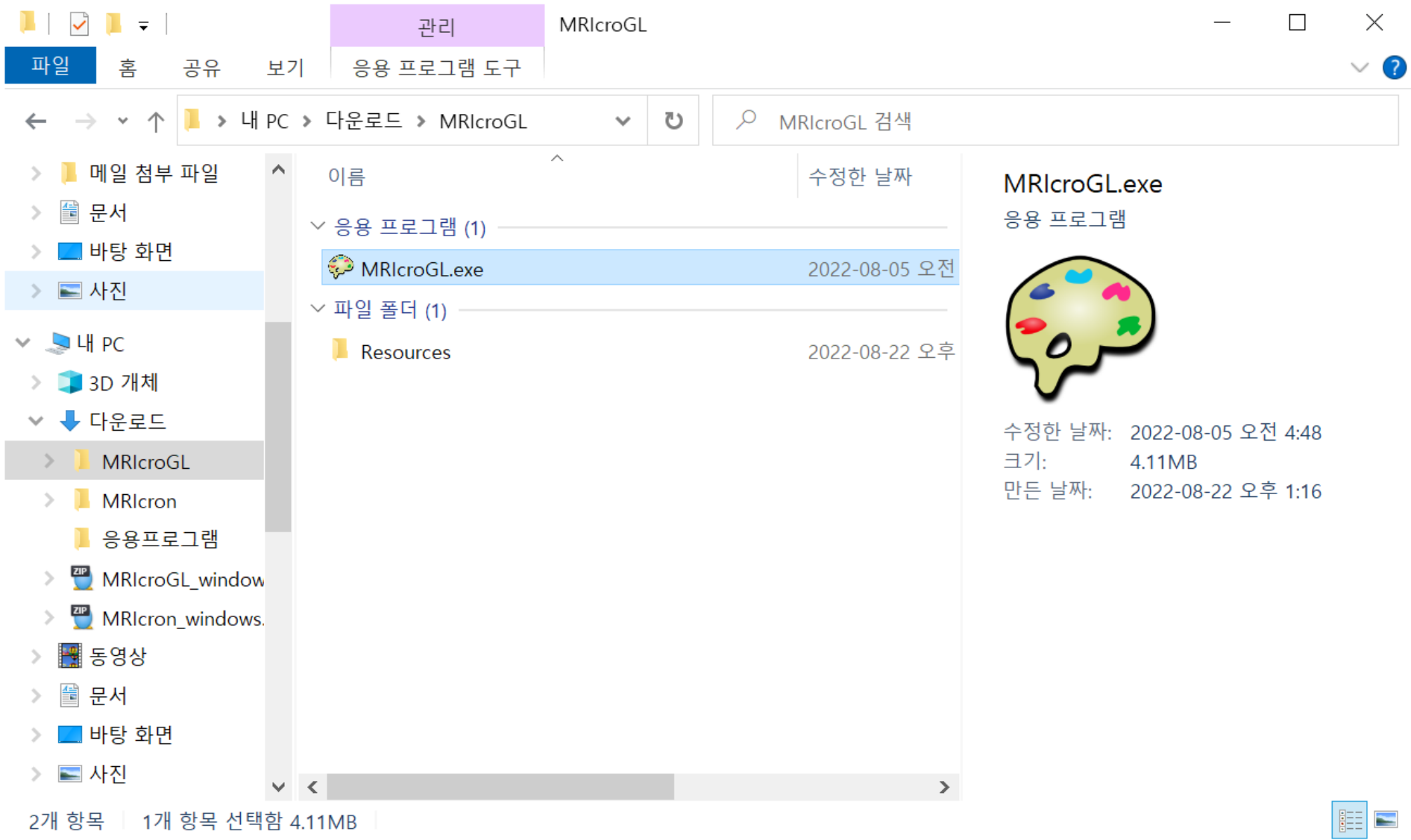
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2022-08-05 오전
파일 폴더 (1)
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크기: 4.11MB
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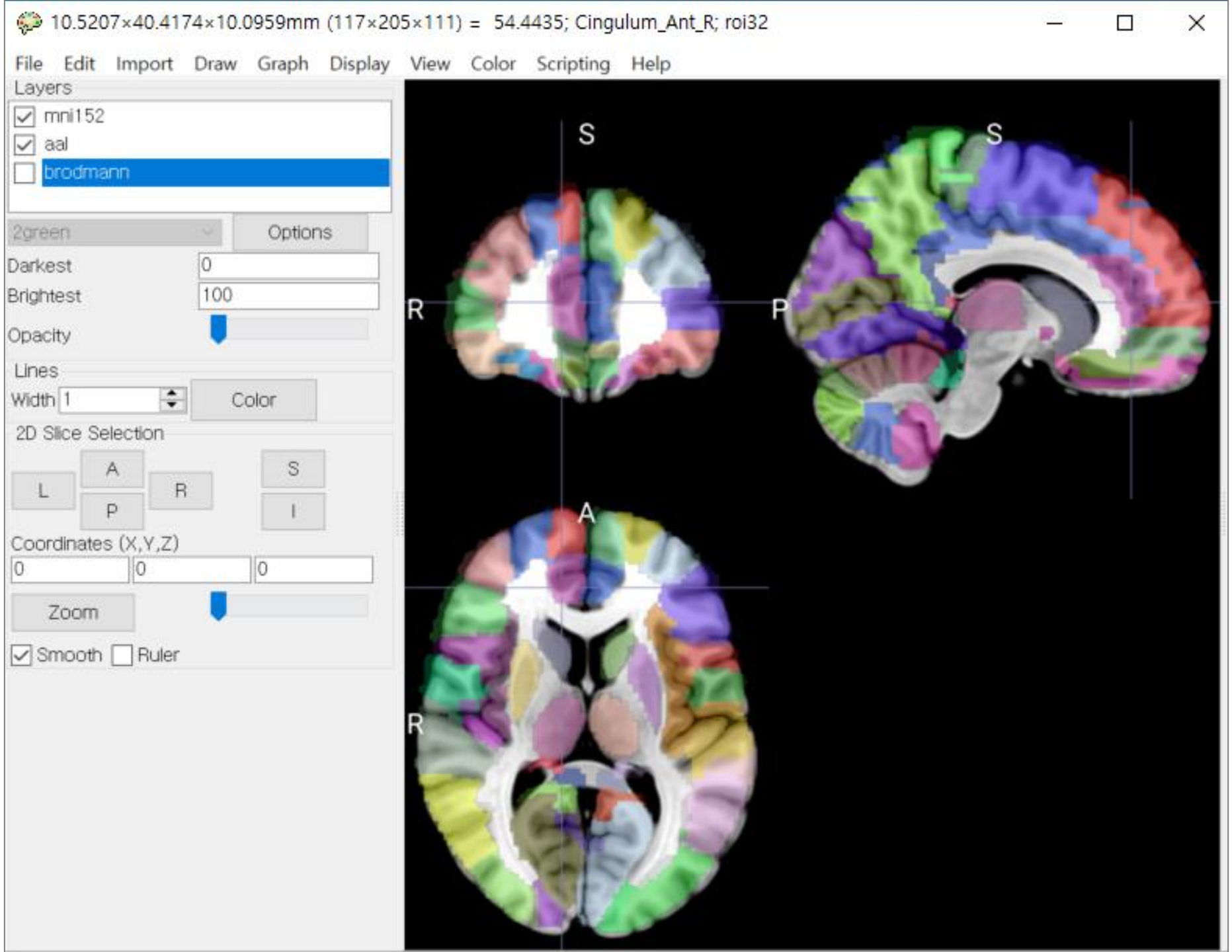
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Coordinates (X,Y,Z)
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Zoom
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Ruler
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R
P
S
A
R

Coordinate: A × B × C

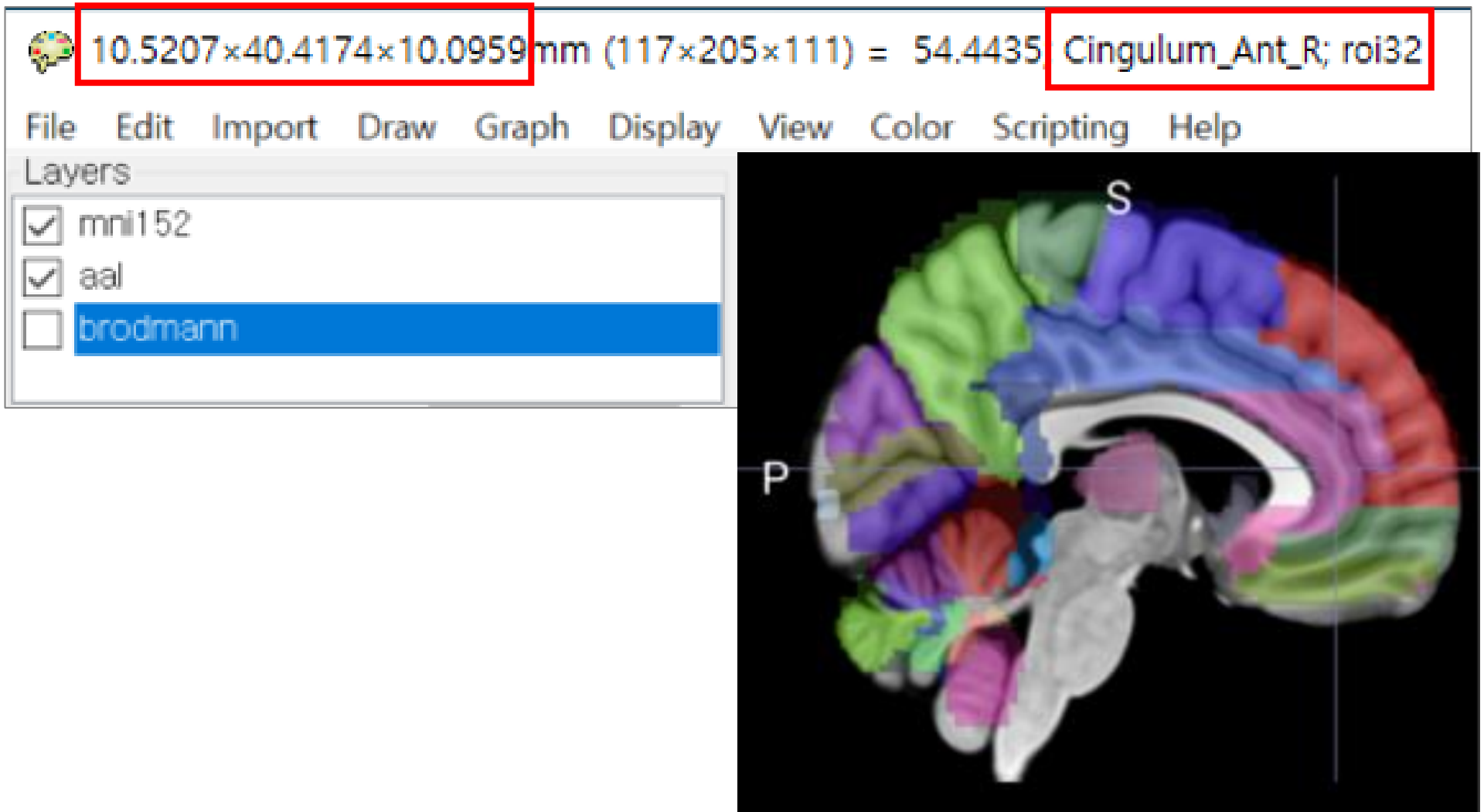
(0,0,0) Anterior commissure

A: RL → R (+) L (–)

B: AP → A (+) P (–)

C: UD → U (+) D (–)

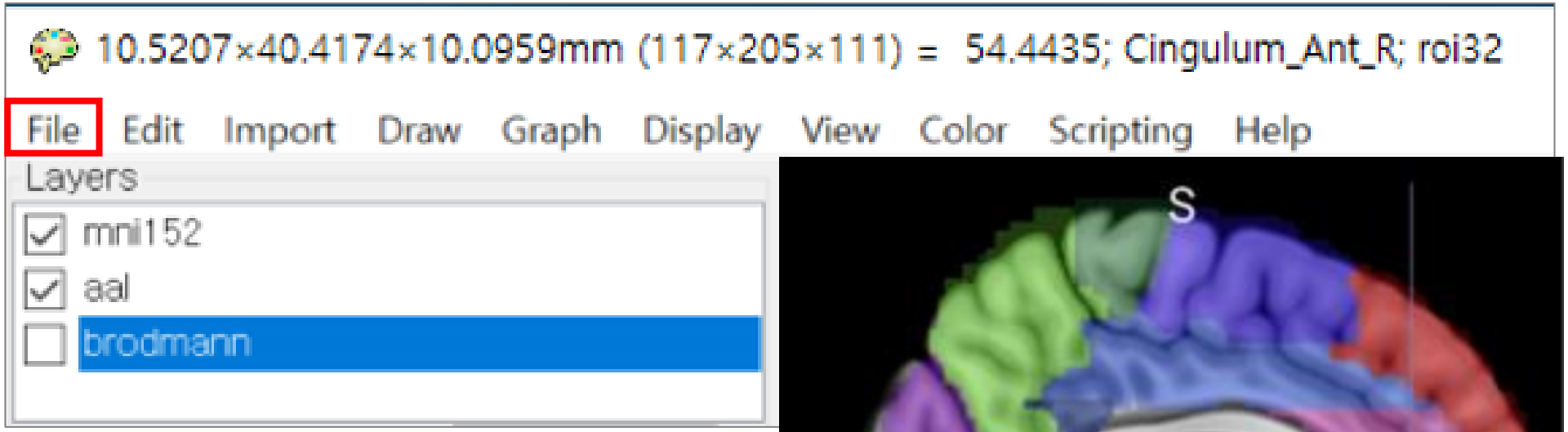
Anatomical designation; Brodmann area (ACC_R; B 24, 32, 33)



File

Open standard

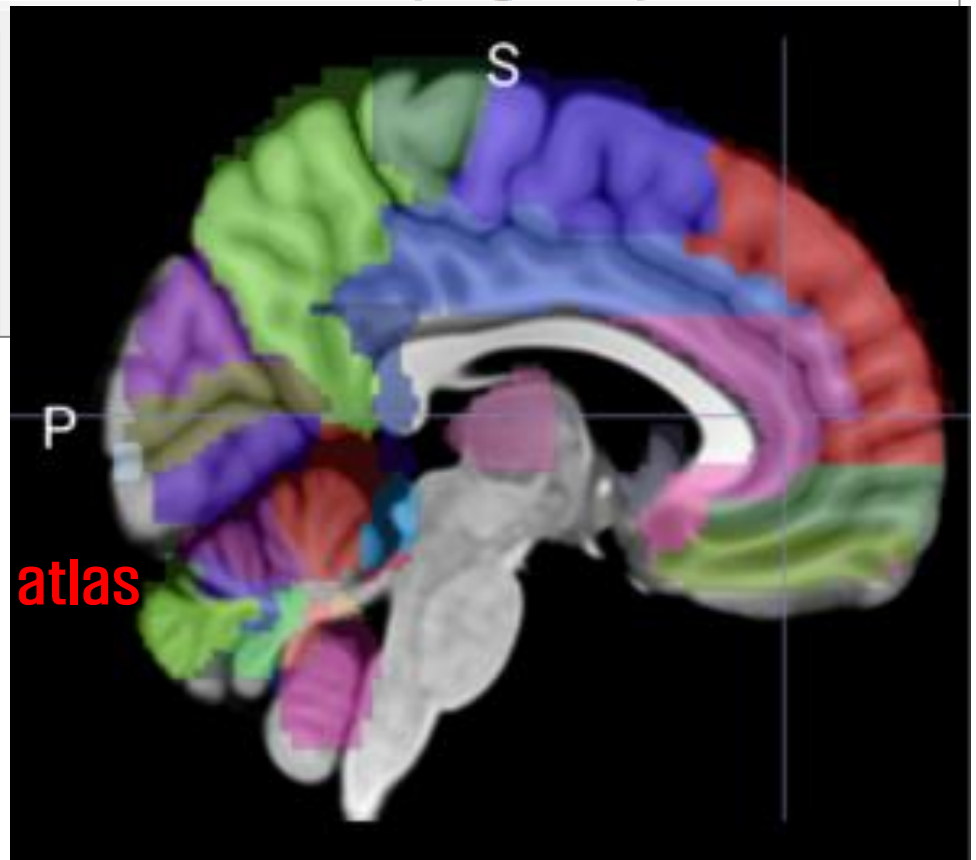
- T1: useful for studying anatomy
- MNI or SPM: useful for writing papers
- Visual human: brain dissection



File

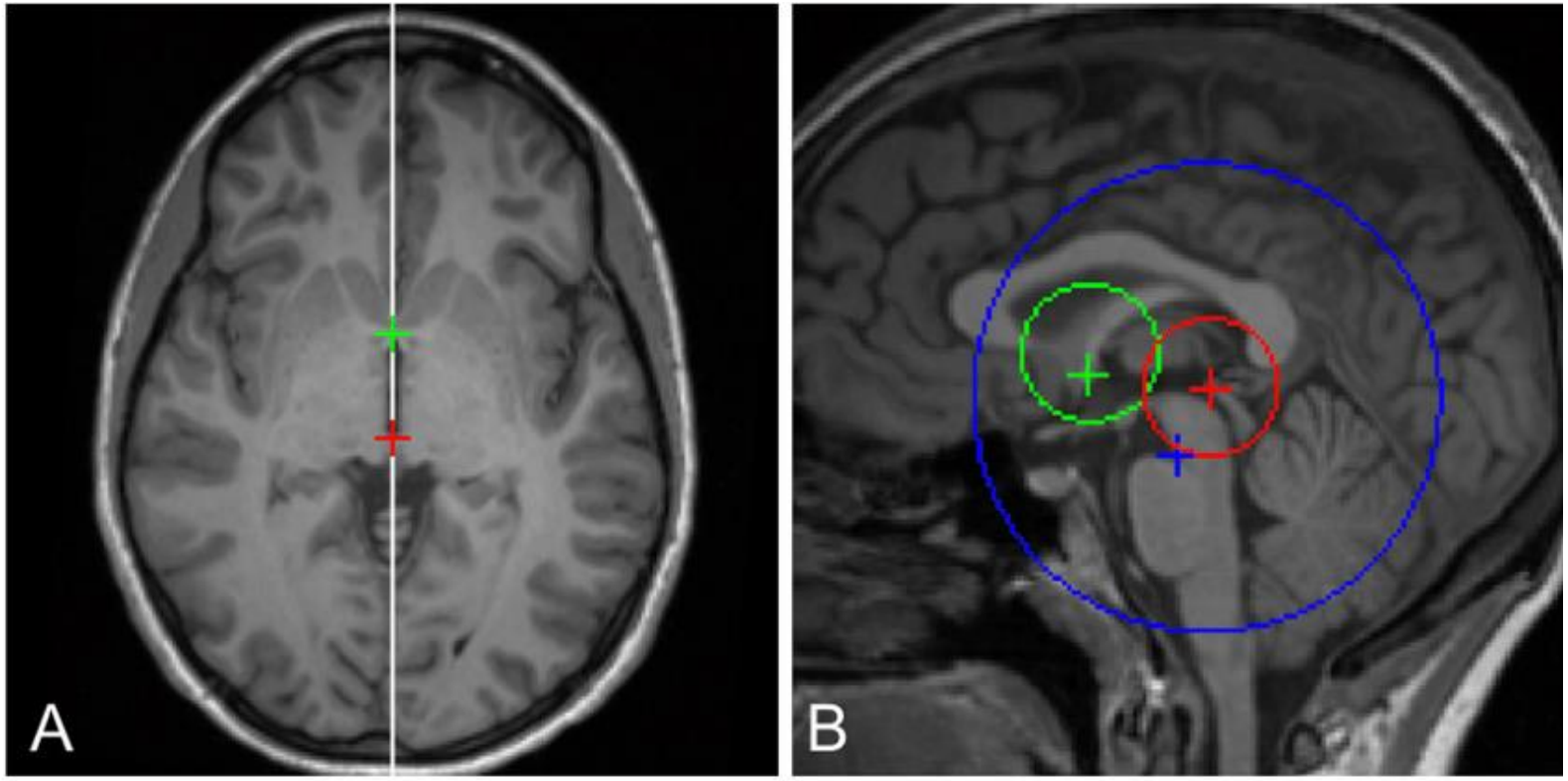
Add Atlas

- AAL (automated anatomical labeling) atlas
- Broadmann atlas



AC–PC Line

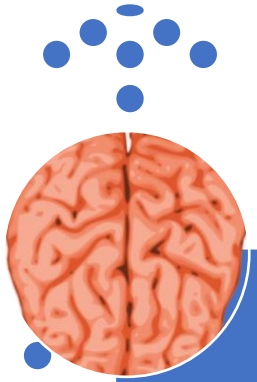
Anterior commissure: connecting the two temporal lobes in front of the fornix, (0,0,0)
Posterior commissure: dorsal to the cerebral aqueduct



Lindsey (2015)

- Ex effect
  - EIH, TIH 개념
  - 통증에 대한 운동 효과는 Cognition model (Jenin El-Sayes review, 슬라이드 4장)처럼 잘 정립되지 못했음
- EIH
- TIH
- Considerations

Exercise-Induced Neuroplasticity



Cognitive function
Motor function

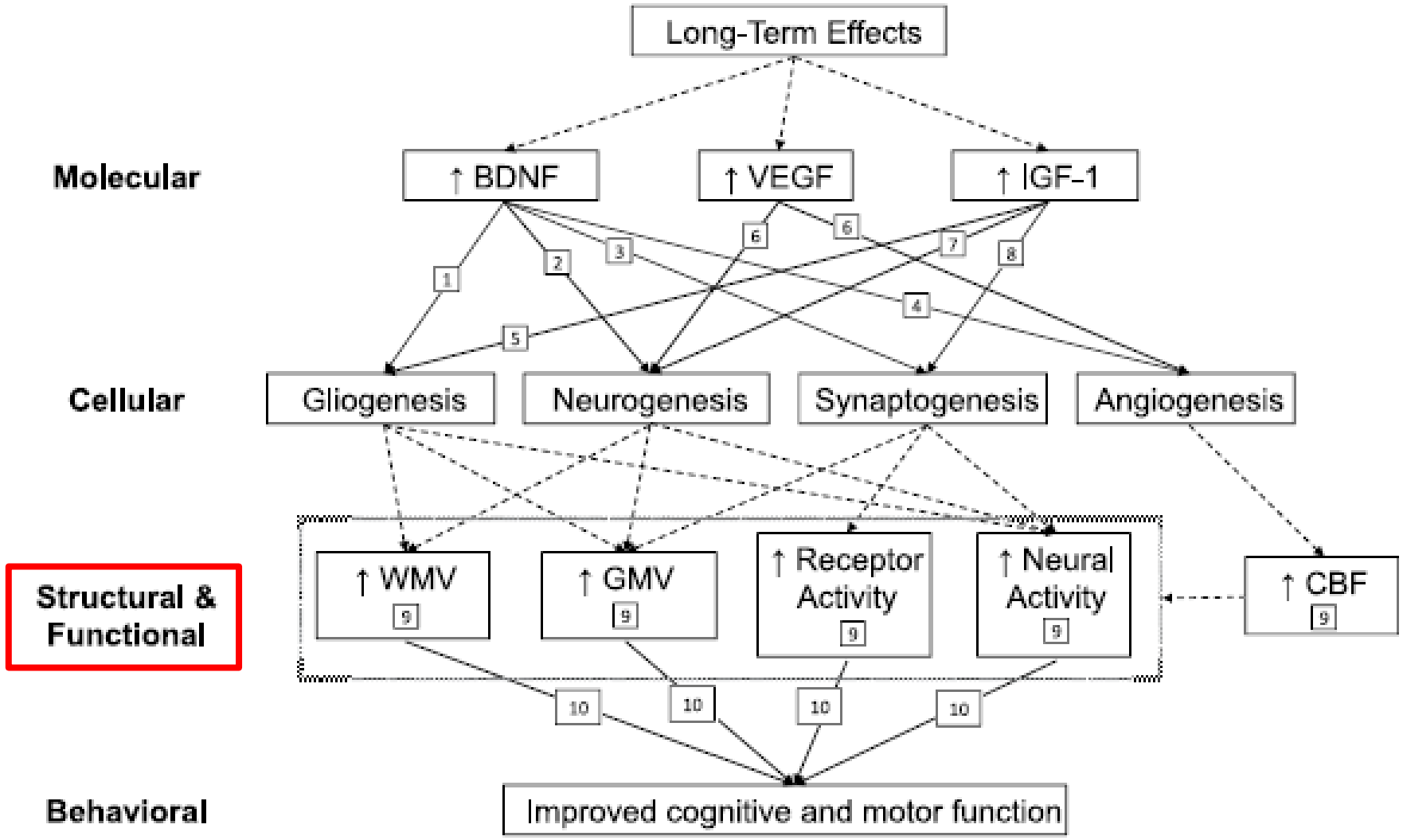
Aerobic exercise

Systematic level

Cellular level

Molecular level

Chronic Aerobic Exercise

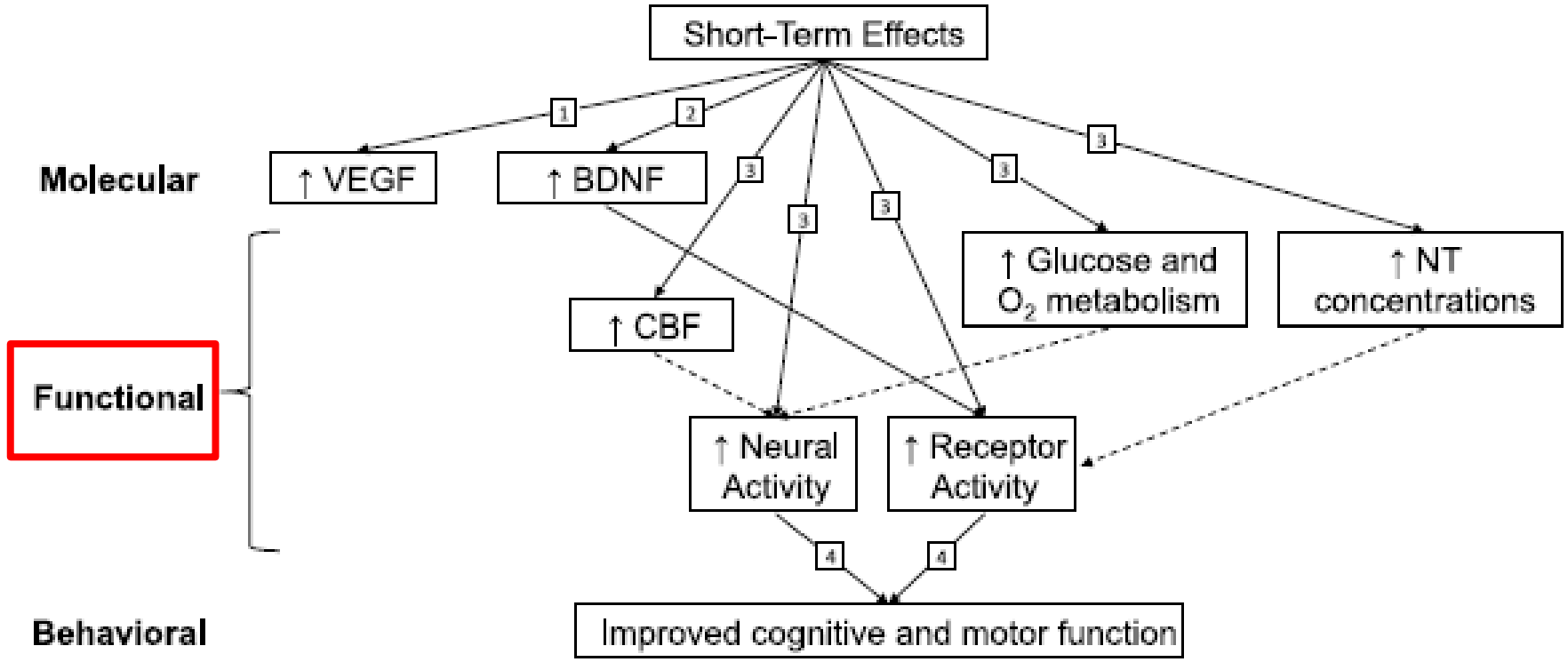


El-Sayes (2019)

Chronic Aerobic Exercise

Brain region	GM volume	WM volume	Perfusion	[GABA/Glu]	Receptor activity	Neural activity (activity-related)	Neural connectivity
Hippocampus	↑*(1)		↑(11)			X(17)	↑(25)
Cingulate	↑(2)		↑(12)			X(18)	
Frontal	↑(3)	↑(10)	↑(13)			↑*(19)	↑*(26)
Prefrontal	↑(1,2)						
Primary Motor	↑(4)				↑*(16)	↑(20)	↓(26)
Parietal	↑(2)	↑(10)	↑(14)			↑*(21)	↑(26)
Occipital	↑(6)	↑(10)		X(15)		↑*(22)	↓(26)
Temporal	↑(2)					↑*(23)	
Cerebellum	↑(7)						
Insular	↑(8)					↑*(23)	
Basal ganglia	↑*(9)					↑*(24)	
Thalamus						↑(20)	

Acute Aerobic Exercise



El-Sayes (2019)

Acute Aerobic Exercise

Brain region	Perfusion	[GABA/Glu]	Glucose metabolism	Oxygen metabolism	Neural activity (resting)	Neural activity (task-related)	Receptor activity	Neural connectivity
Hippocampus	↓(1)							
Cingulate						↓(15)		
Frontal					↑(11)	↓(15)		
Prefrontal				↑(10)		↑(16)		
Supplementary motor			↑(5)					
Premotor			↑(6)					
Primary motor	↑(2)		↑(7)				↑(18)	
Parietal					↑(12)	↓(17)		↑(19)
Secondary sensory								↑(19)
Occipital		↑(4)	↑(8)		↑(13)	↑(15)		
Temporal					↓(14)			
Cerebellum			↑(9)					
Insular	X(3)							

Exercise Effects on Pain

Exercise-induced hypoalgesia (EIH)

- Reduction in pain sensitivity by a single bout of exercise
- EIH after acute (or single) exercise
- Mostly experimental

Training-induced hypoalgesia (TIH)

- Reduction in pain sensitivity after repeated bouts of exercise
- EIH after regular exercise
- Mostly clinical (exercise for controlling chronic pain)

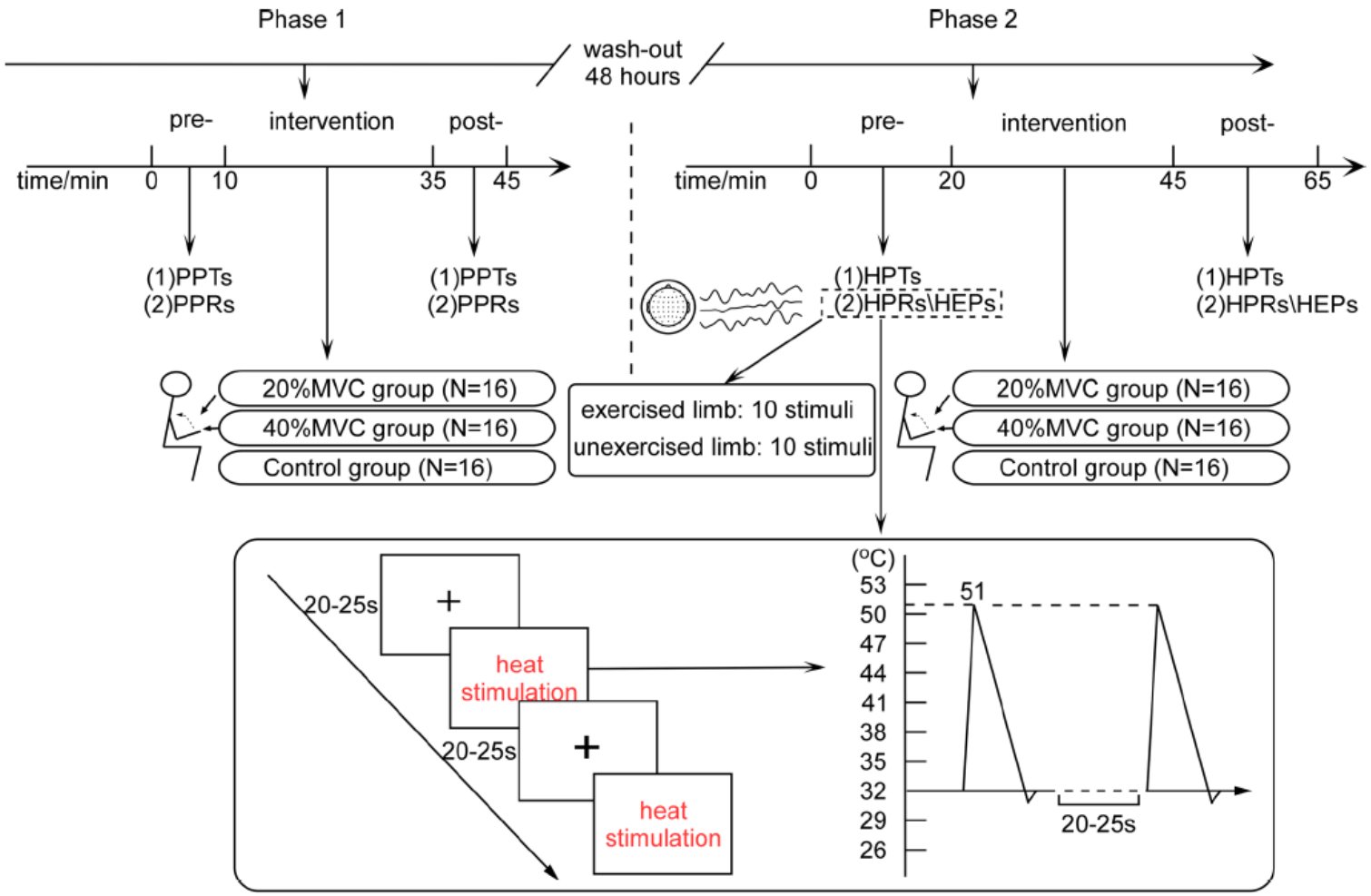
Exercise-induced Hypoalgesia (EIH)

- EIH
  - Common in healthy people
  - Often impaired in patients with chronic pain (e.g., absent or hypoalgesia)
- Experimental measurements
  - Parameters
    - Pain threshold (minimal noxious stimulus intensity perceived as painful)
    - Pain tolerance (maximum noxious stimulus intensity that one can tolerate)
  - Noxious stimulus
    - Thermal, electrical stimulation, pressure

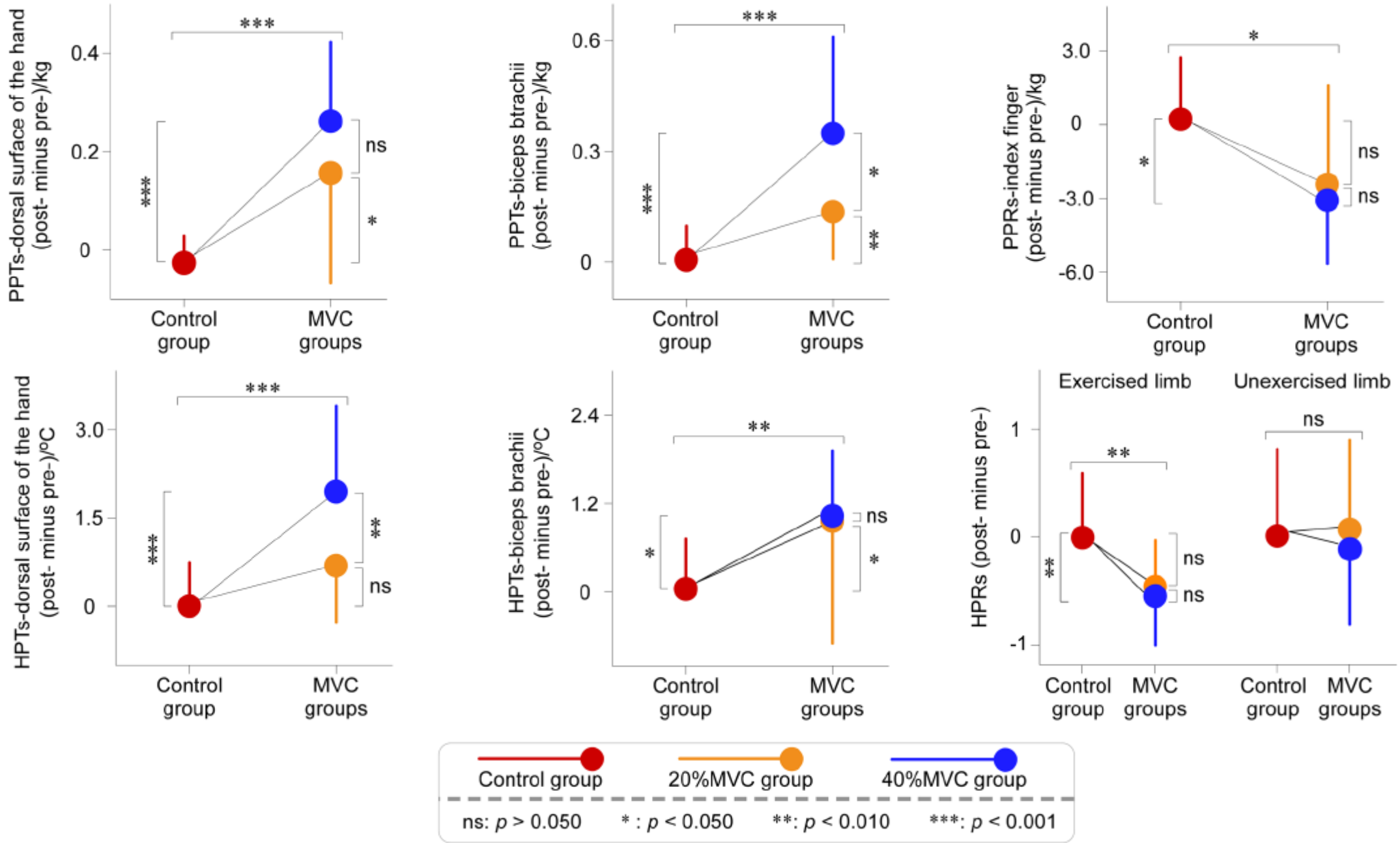
EIH

- Simultaneous analgesic effect
  - Targeted exercising muscles (local effect)
  - Small magnitude in non-exercising muscles (systemic effect)
- Affected by its intensity and duration, not by its type (dynamic OR isometric exercise)
  - unsuitable for individuals who are incapable or unwilling to exercise at high intensities or for long durations (e.g. patients undergoing rehabilitation and/or elderly populations).

EIH Research



Wu (2022)


PPTs-dorsal surface of the hand (post- minus pre-)/kg
0.4
0.2
0
***
***
ns
*
Control group
MVC groups
PPTs-biceps btrachii (post- minus pre-)/kg
0.6
0.3
0
***
***
*
**
Control group
MVC groups
PPRs-index finger (post- minus pre-)/kg
3.0
0
-3.0
-6.0
*
*
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ns
Control group
MVC groups
HPTs-dorsal surface of the hand (post- minus pre-)/ºC
3.0
1.5
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Control group
MVC groups
HPTs-biceps brachii (post- minus pre-)/ºC
2.4
1.2
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*
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Control group
MVC groups
HPRs (post- minus pre-)
Exercised limb
Unexercised limb
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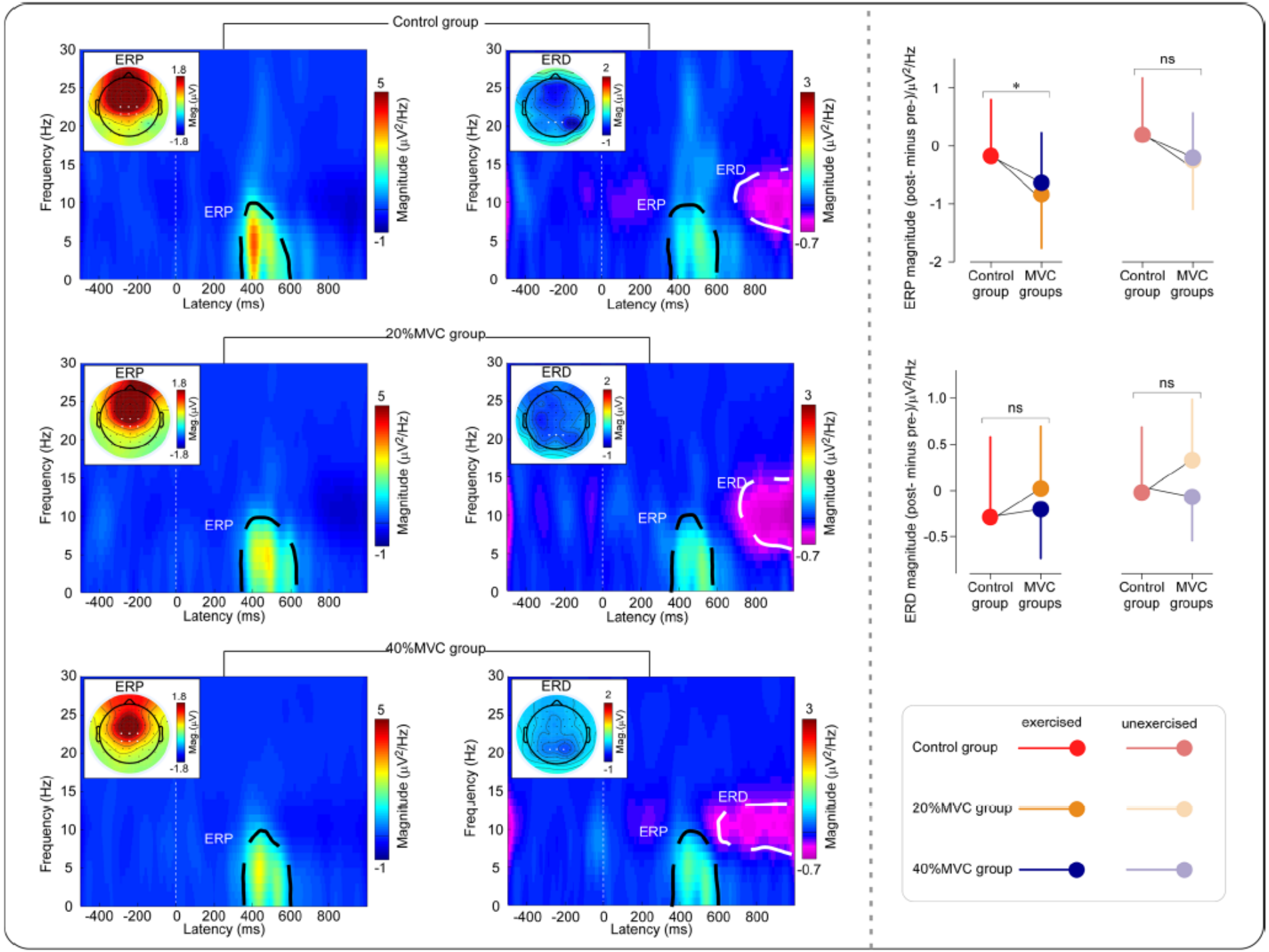
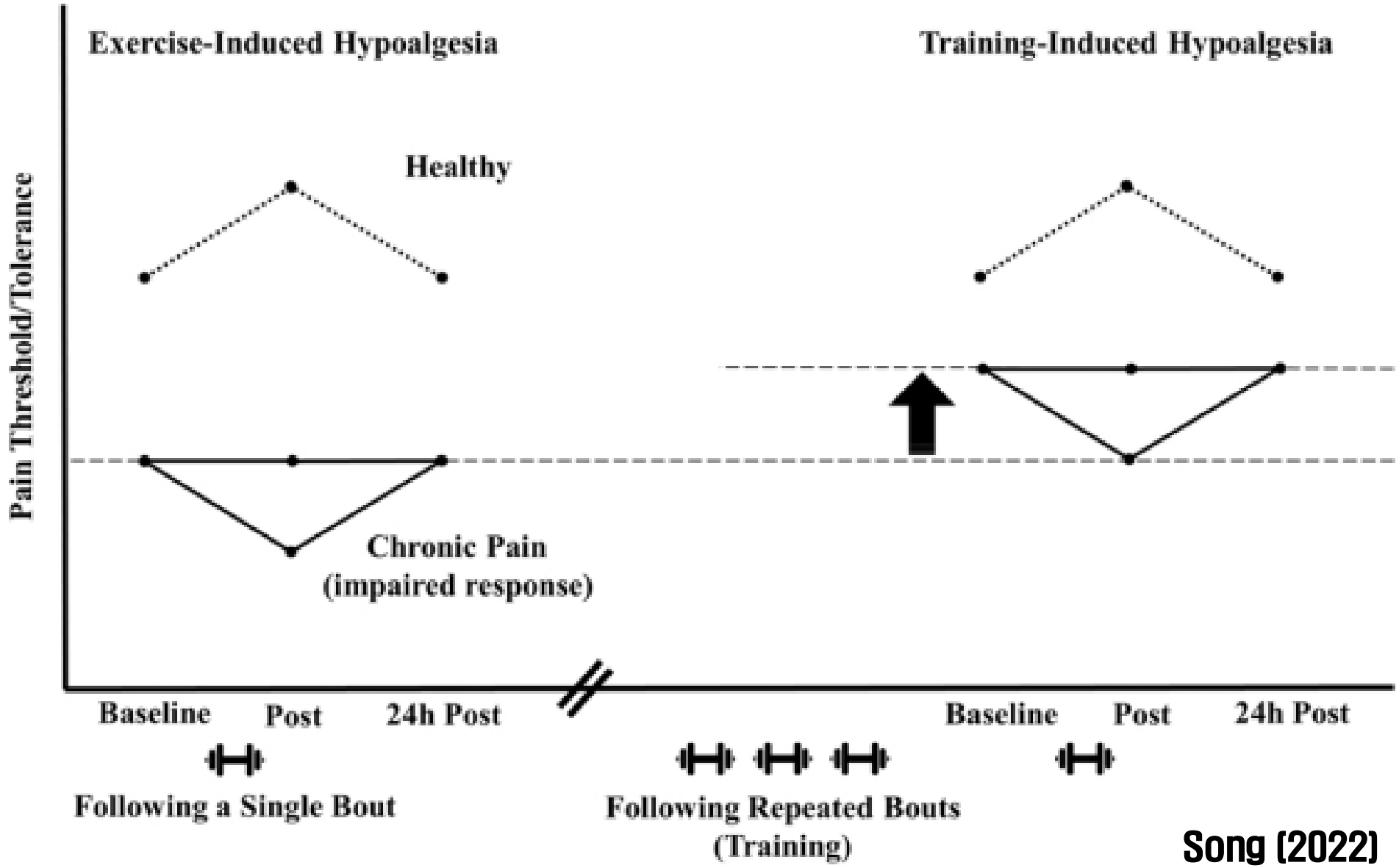
0
-1
**
**
ns
ns
ns
Control group
MVC groups
Control group
MVC groups
Control group
20%MVC group
40%MVC group
ns: p > 0.050
* : p < 0.050
**: p < 0.010
***: p < 0.001


Control group
20%MVC group
40%MVC group
ERP
ERD
Frequency (Hz)
Latency (ms)
Magnitude (μV²/Hz)
Mag.(μV)
ERP magnitude (post- minus pre-)/μV²/Hz
ERD magnitude (post- minus pre-)/μV²/Hz
Control group
MVC groups
ns
*
exercised
unexercised
Control group
20%MVC group
40%MVC group

Training-induced Hypoalgesia (TIH)

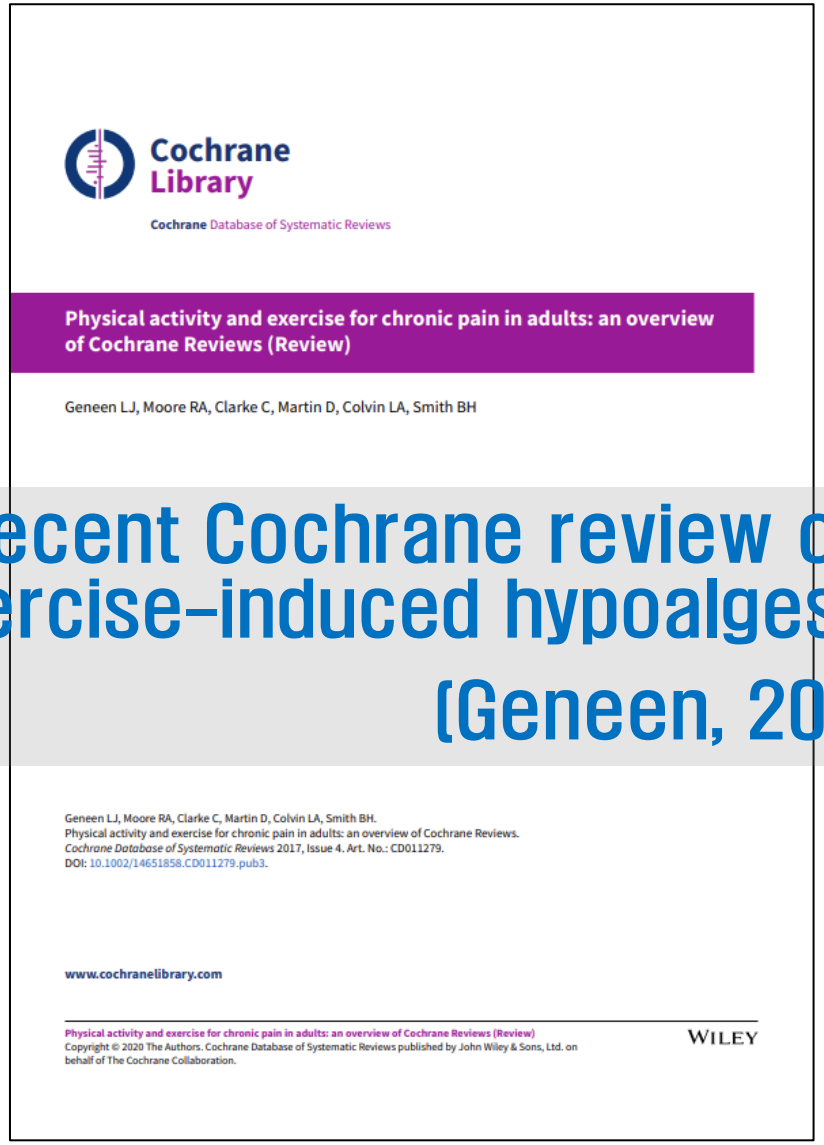
- Exercise aimed at controlling pain
  - Multifaceted effects on cardiorespiratory function, mental health & pain
  - Increasing evidence in chronic neck/back pain, OA & fibromyalgia
  - Particularly advantageous in chronic pain comorbid with psychiatric illness
- Dose
  - American College of Sports Medicine: 30 minutes of moderate-intensity exercise five days per week (or 150 MET-minutes) in order to maintain cardiorespiratory, musculoskeletal, and neuromotor fitness for healthy adults

EIH & TIH



Song (2022)

Recent Analysis of TIH



Cochrane Library

Cochrane Database of Systematic Reviews

Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review)

Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH

Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH.
Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews.
Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011279.
DOI: 10.1002/14651858.CD011279.pub3.

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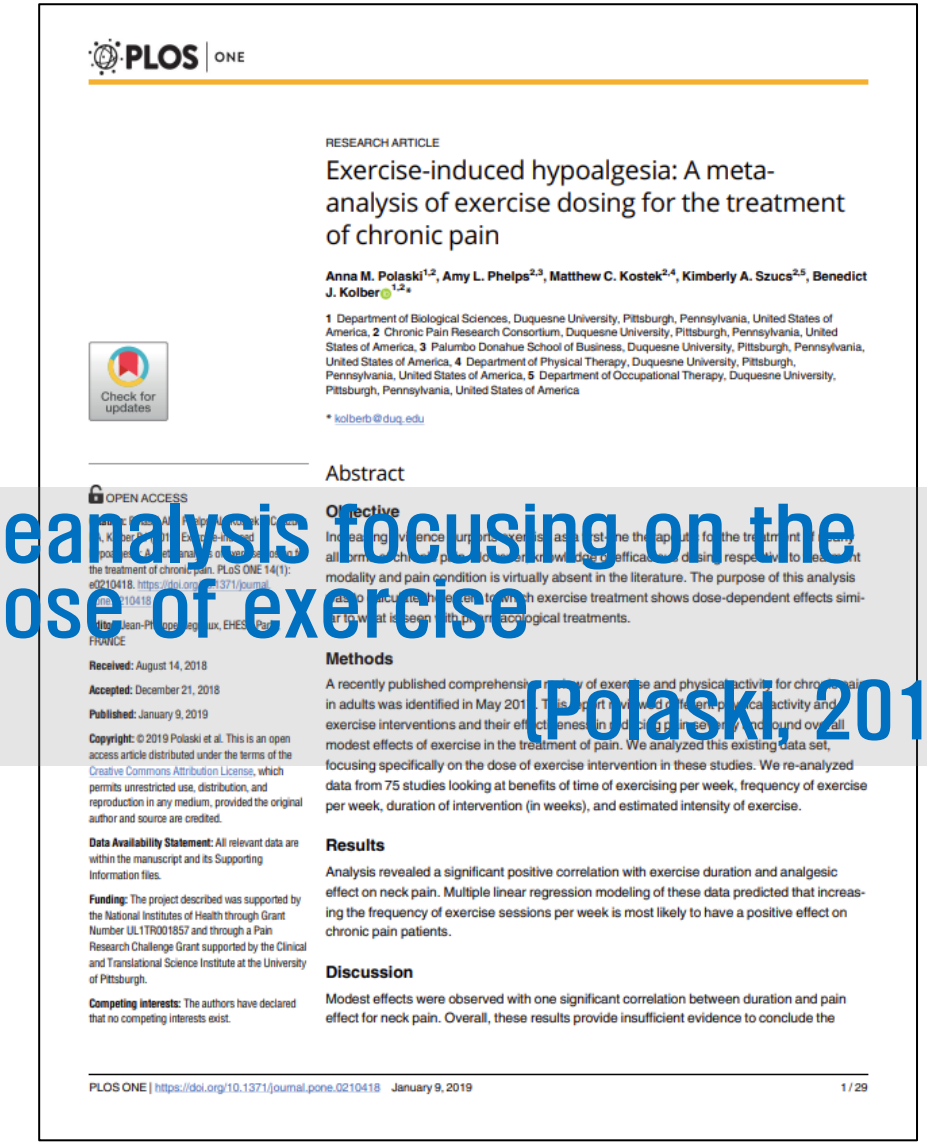
A recent Cochrane review of exercise-induced hypoalgesia (Geneen, 2017)



PLOS ONE

RESEARCH ARTICLE

Exercise-induced hypoalgesia: A meta-analysis of exercise dosing for the treatment of chronic pain

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Competing interests: The authors have declared that no competing interests exist.

Abstract

Objective

Increasing evidence supports exercise as a first-line therapeutic for the treatment of many all[illegible] chronic pain conditions. However, knowledge of efficacy of dosing respective to treatment modality and pain condition is virtually absent in the literature. The purpose of this analysis is to focus on the effect of [illegible] with exercise treatment shows dose-dependent effects similar to what is seen with pharmacological treatments.

Methods

A recently published comprehensive review of exercise and physical activity for chronic pain in adults was identified in May 201[illegible]. The primary outcome was physical activity and exercise interventions and their effectiveness in decreasing pain. We found overall modest effects of exercise in the treatment of pain. We analyzed this existing data set, focusing specifically on the dose of exercise intervention in these studies. We re-analyzed data from 75 studies looking at benefits of time of exercising per week, frequency of exercise per week, duration of intervention (in weeks), and estimated intensity of exercise.

Results

Analysis revealed a significant positive correlation with exercise duration and analgesic effect on neck pain. Multiple linear regression modeling of these data predicted that increasing the frequency of exercise sessions per week is most likely to have a positive effect on chronic pain patients.

Discussion

Modest effects were observed with one significant correlation between duration and pain effect for neck pain. Overall, these results provide insufficient evidence to conclude the

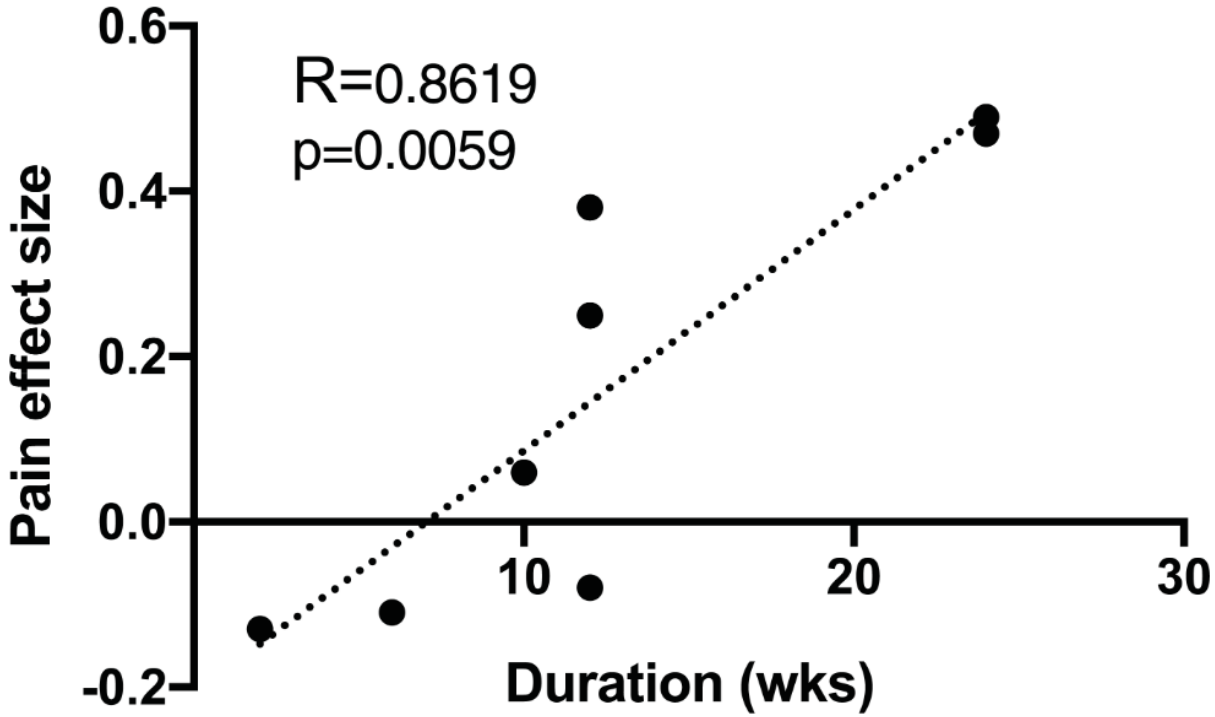
Reanalysis focusing on the dose of exercise (Polaski, 2019)

Recent Cochrane Review (2017)

- Pain conditions
  - RA, OA, fibromyalgia, LBP, intermittent claudication, dysmenorrhoea, mechanical neck disorder, SCI, postpolio synd, and patellofemoral pain
- Low quality of evidence
  - 21 reviews (381 studies / 37,143 participants)
  - Small sample sizes and potentially underpowered studies
- Conclusion
  - Some favorable effects in a reduction in pain severity and improved physical function (mostly of small-to-moderate effect)
  - Variable effects on psychological function and QOL

Reanalysis Focusing Dose (2019)

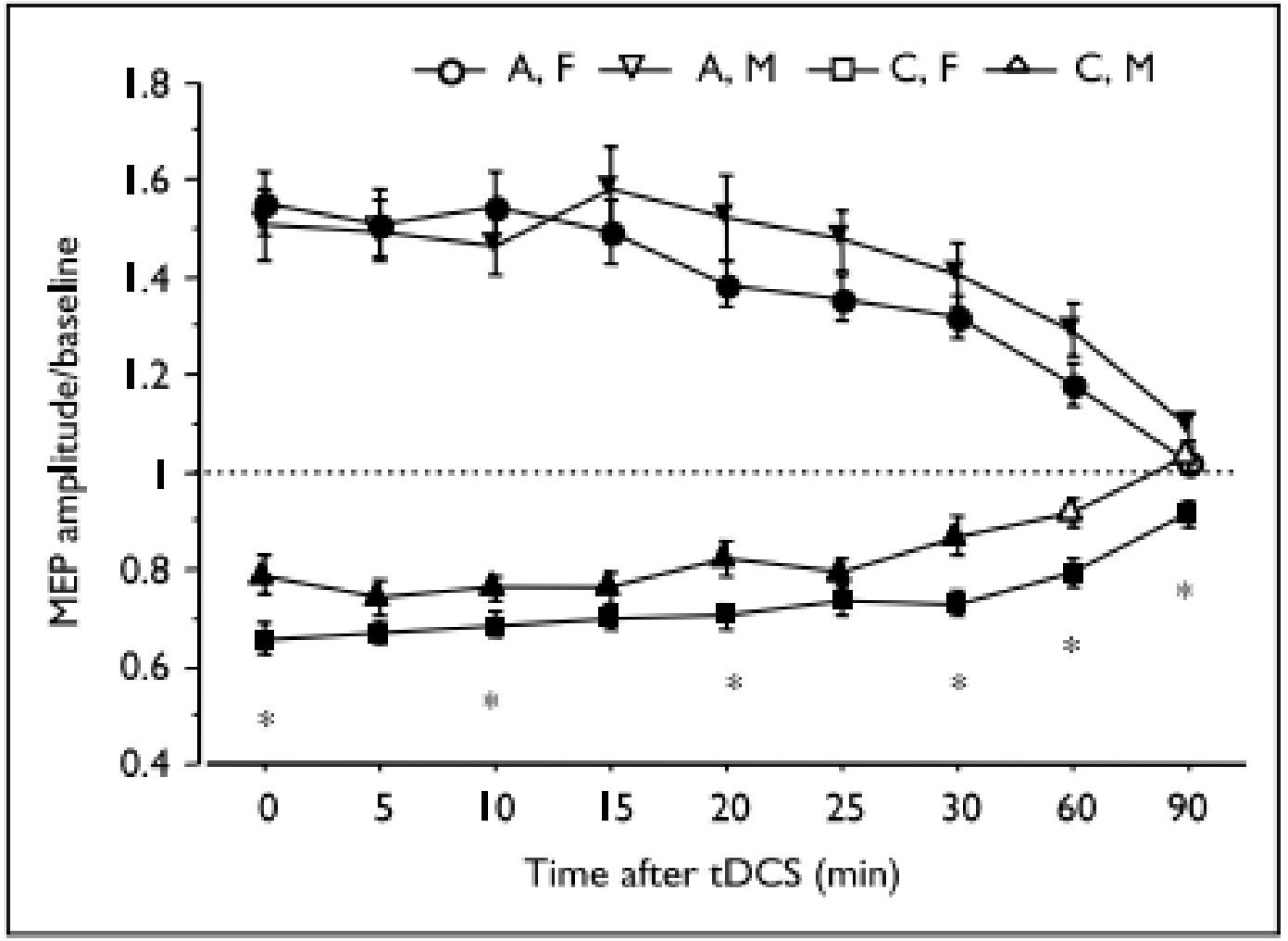
- Pain effect size vs. DURATION of exercise for neck pain patients for all exercise modalities
- Insufficient evidence to conclude the presence of a strong dose effect of exercise on pain



Potential Influencer for TIH
(from the perspective of brain plasticity)

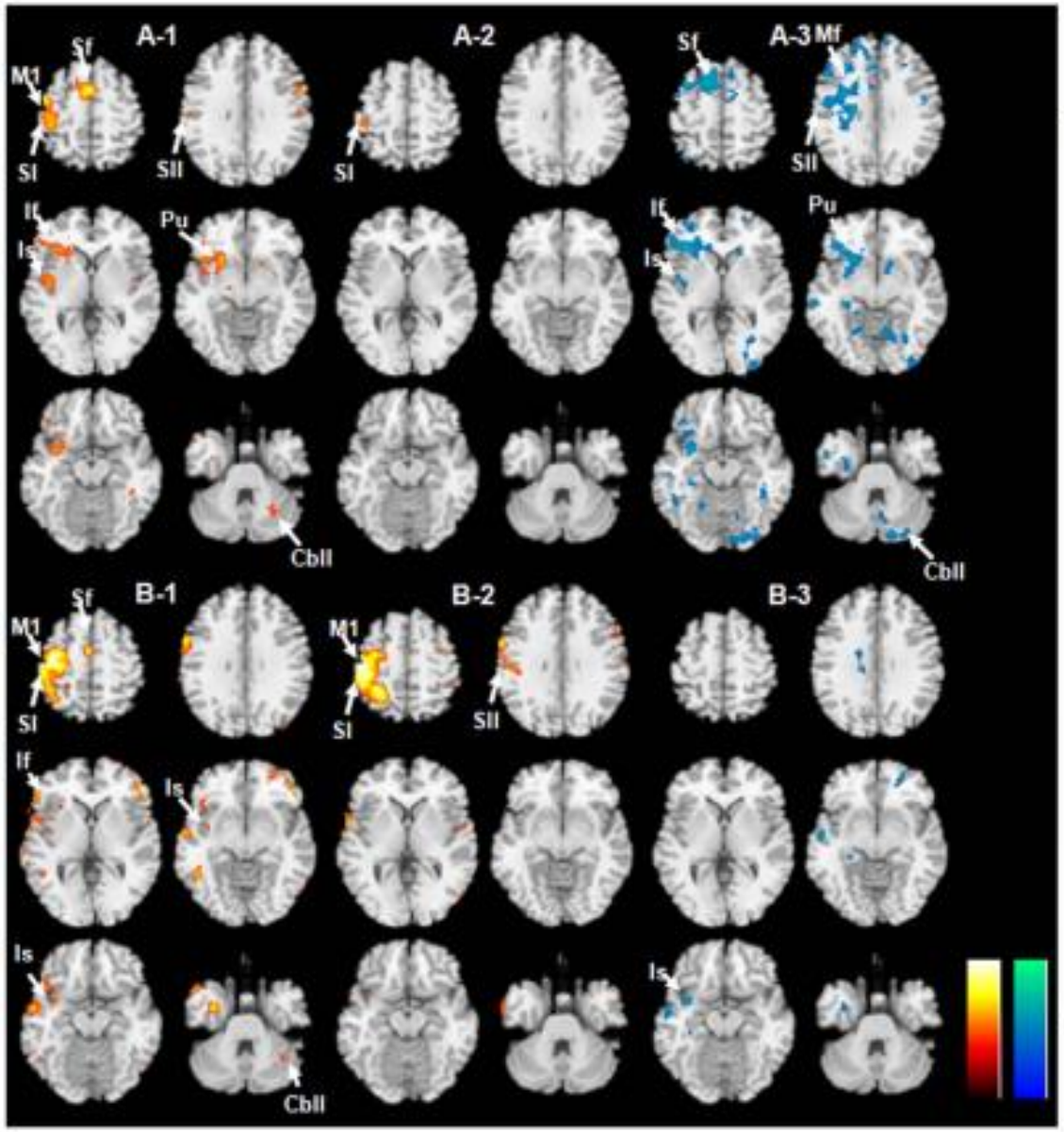
- Biological sex
- Depressive mood
- Negative expectation

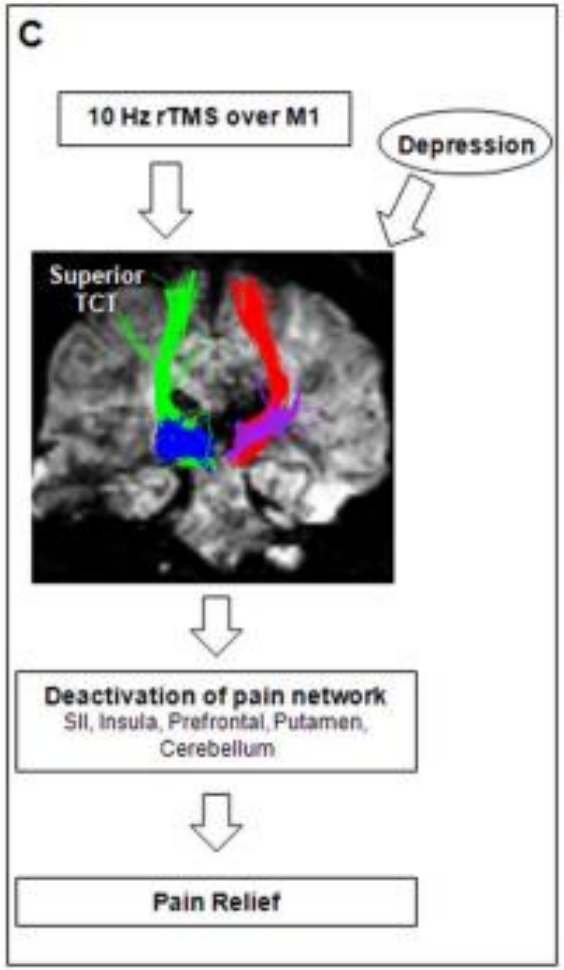
Biological Sex



El-Sayes (2019)

Depressive Mood





Ohn (2012)

Negative Expectations About TIH

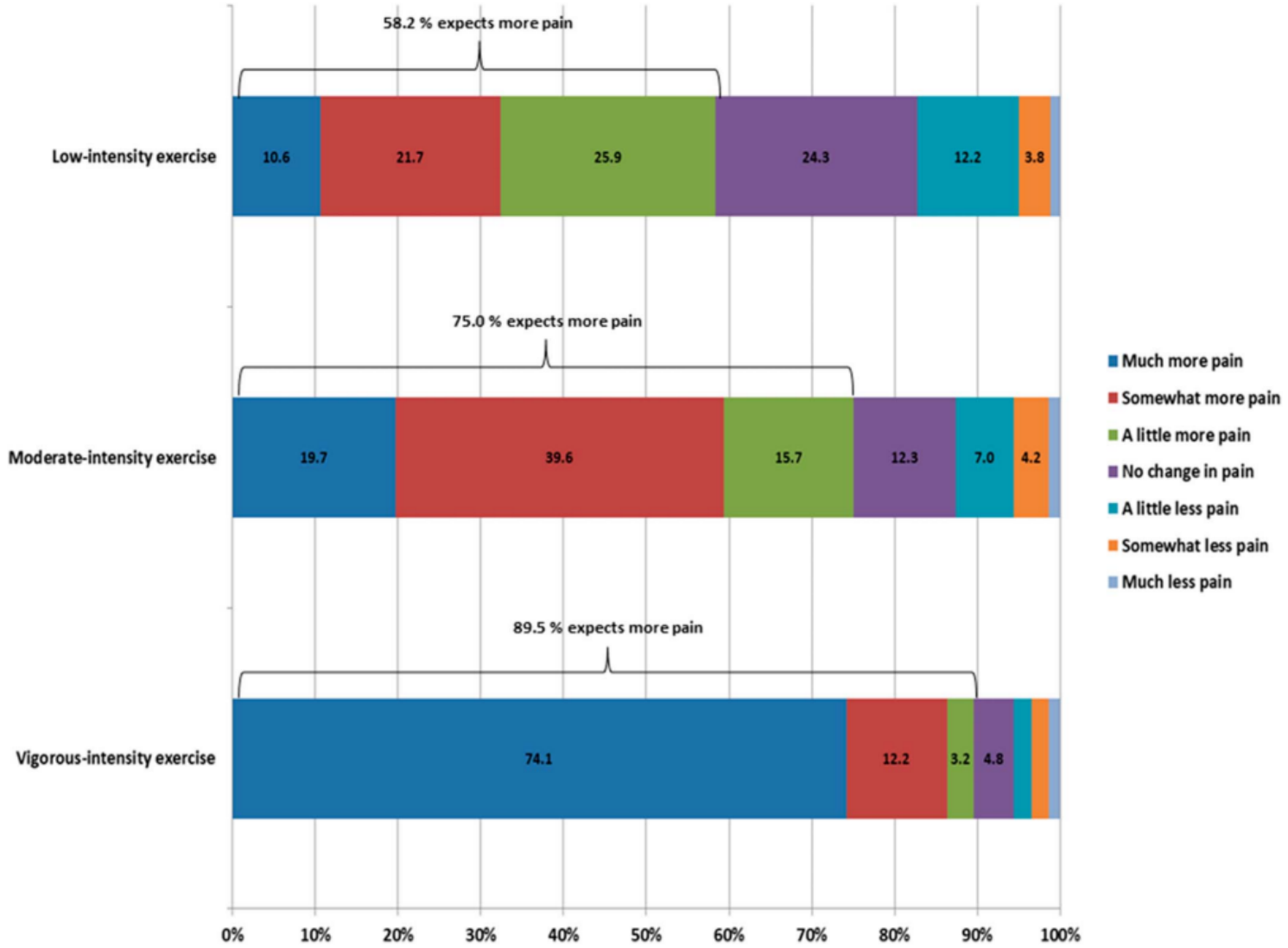


Figure 1. Expectations about the effects of low-intensity exercise, moderate-intensity exercise, and vigorous-intensity exercise on pain reported by patients (n = 500) referred for interdisciplinary pain treatment at a University Hospital Pain Center in Denmark (unpublished data from the clinical pain registry, PainData).

Vaegter (2020)

Conslusion

- Pain Network
  - Sensory-discriminative dimension
  - Emotional dimension
  - Cognitive dimension
- Chronic pain
  - Changes in the pain network change
  - Pain network-level approach for the control of chronic pain
- Exercise effects on pain
  - EIH: single, mostly experimental
  - TIH: repeated, mostly clinical, ex-duration dependent, LoE: not high