Neuro-Imaging and Neuro-Modulation of Somatosensory Information and Phantom Limb Pain

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ATR

What makes haptic ~~affective~~ Pain

1. Brain makes sensation pain

2. Brain makes pain without somatosensory stimulus

Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. (International Association for the Study of Pain (IASP) definition)

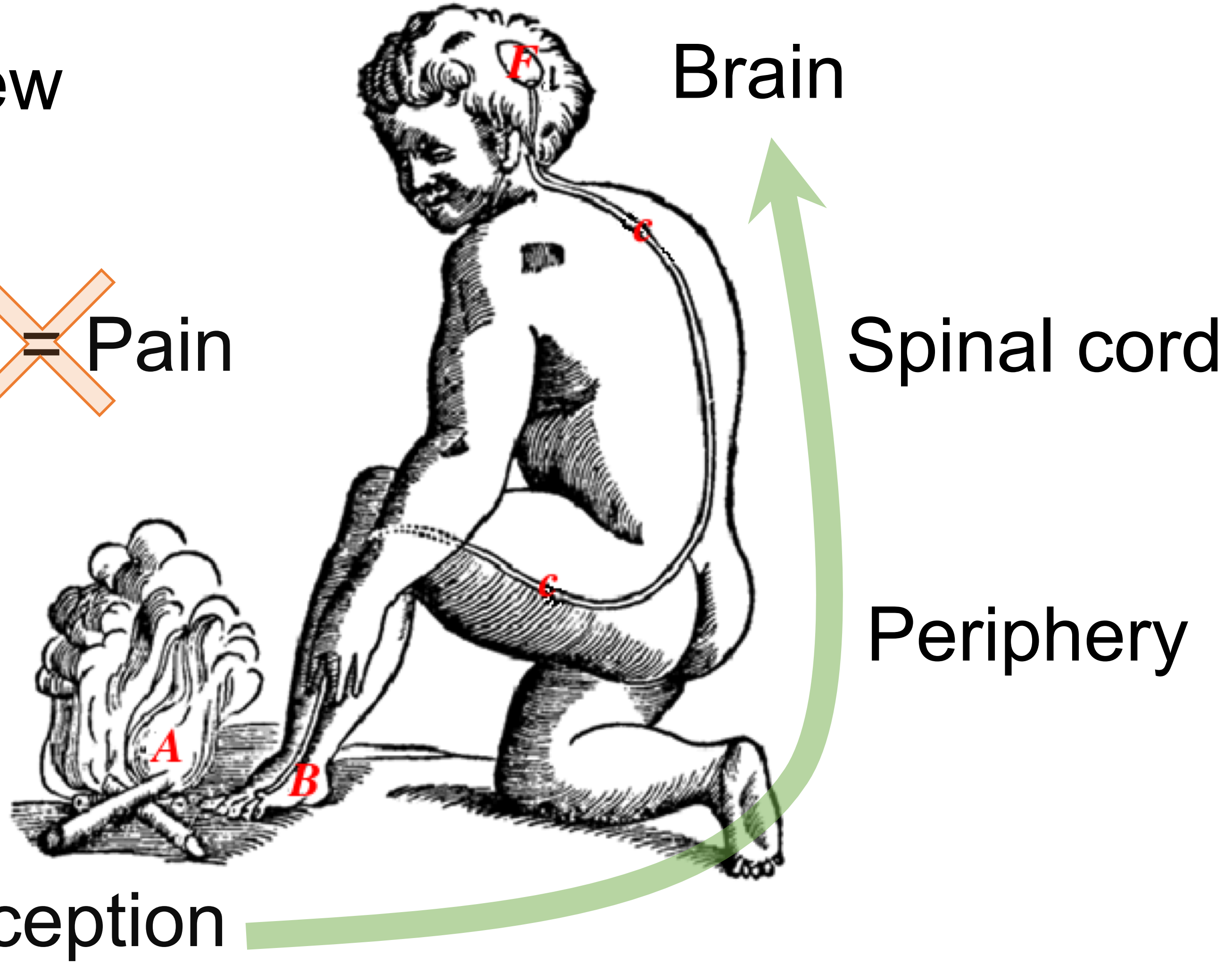
Note:

1. It is unquestionably a sensation
2. It is unpleasant and emotional experience.
3. It is not necessarily linking to the stimulus

How is pain perceived?

Classical view

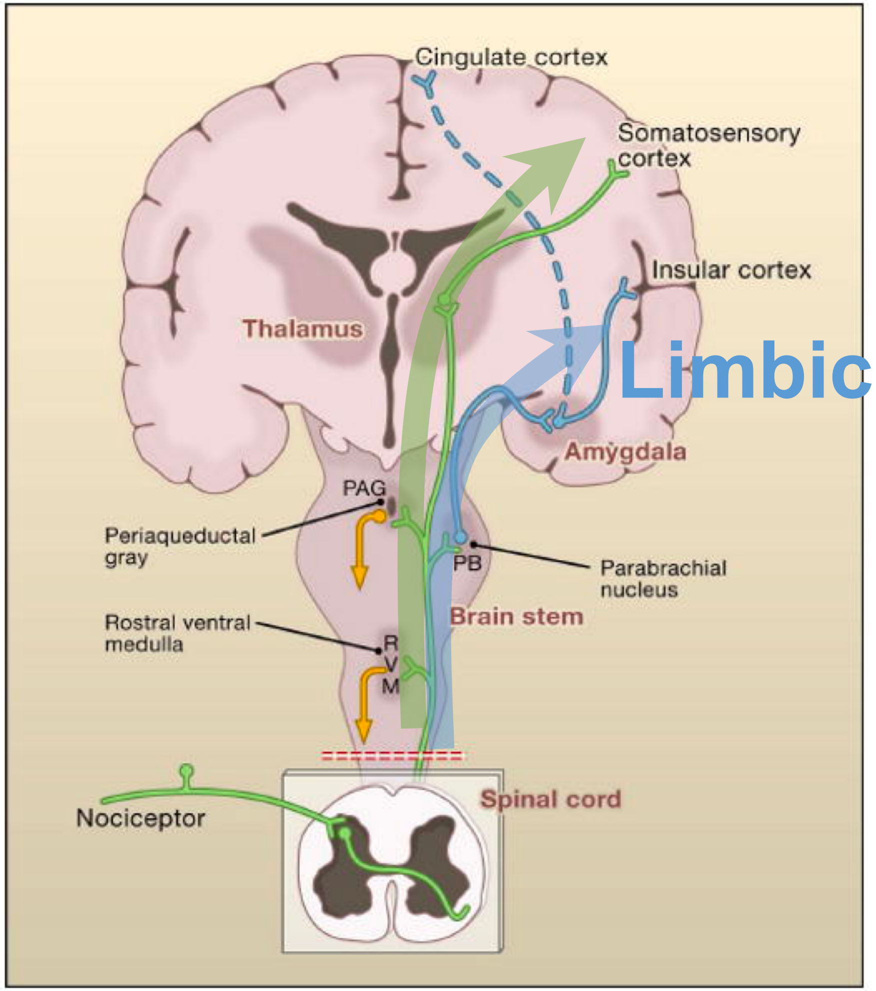
Nociception ~~=~~ Pain



http://plaza.umin.ac.jp/~beehappy/analgesia/pain-poly.html

Two pathways of pain

Somatosensory



Basbaum et al., Cell, 2009

1. Projection to somatosensory cortex via thalamus, providing information about the **location** and **intensity** of the stimulus

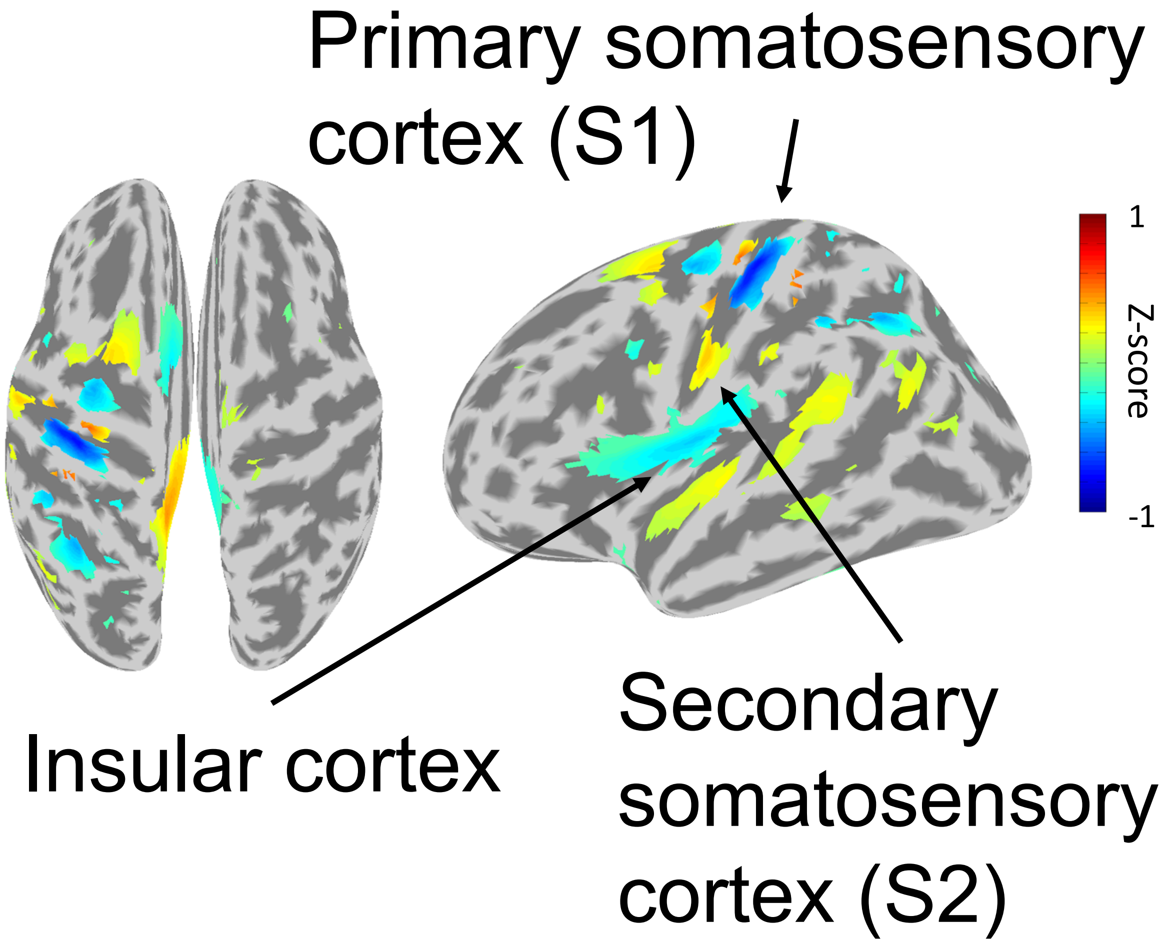
2. Projection to the cingulate, insular and amygdala, contributing to the **affective** component of the pain

Cortical responses after somatosensory stimulation

Magnetoencephalography, MEG

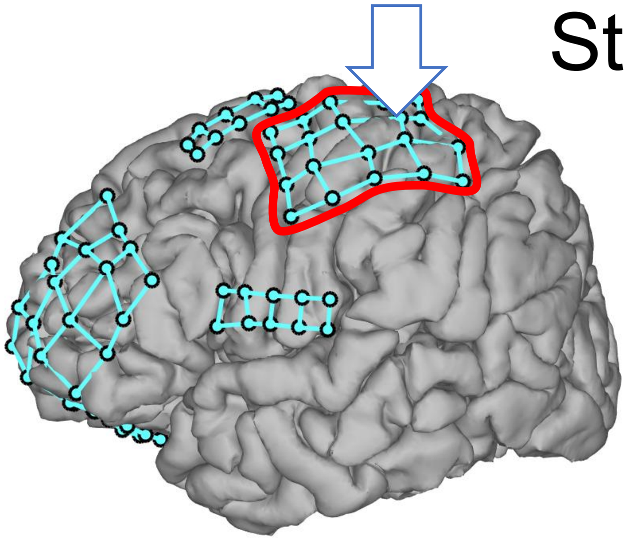
Electrical stimulation on right arm

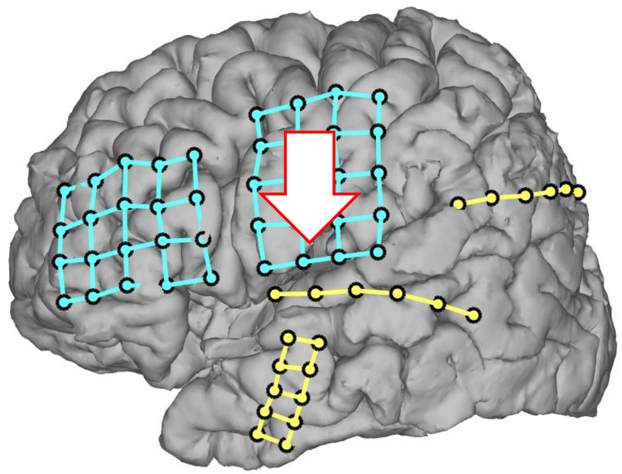
Averaged currents of 50-80ms



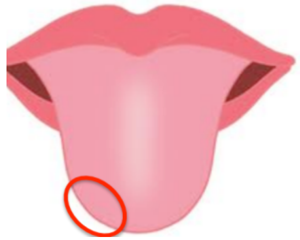
Artificial sensation by electrical stimulation

Stim (50Hz, 5s)



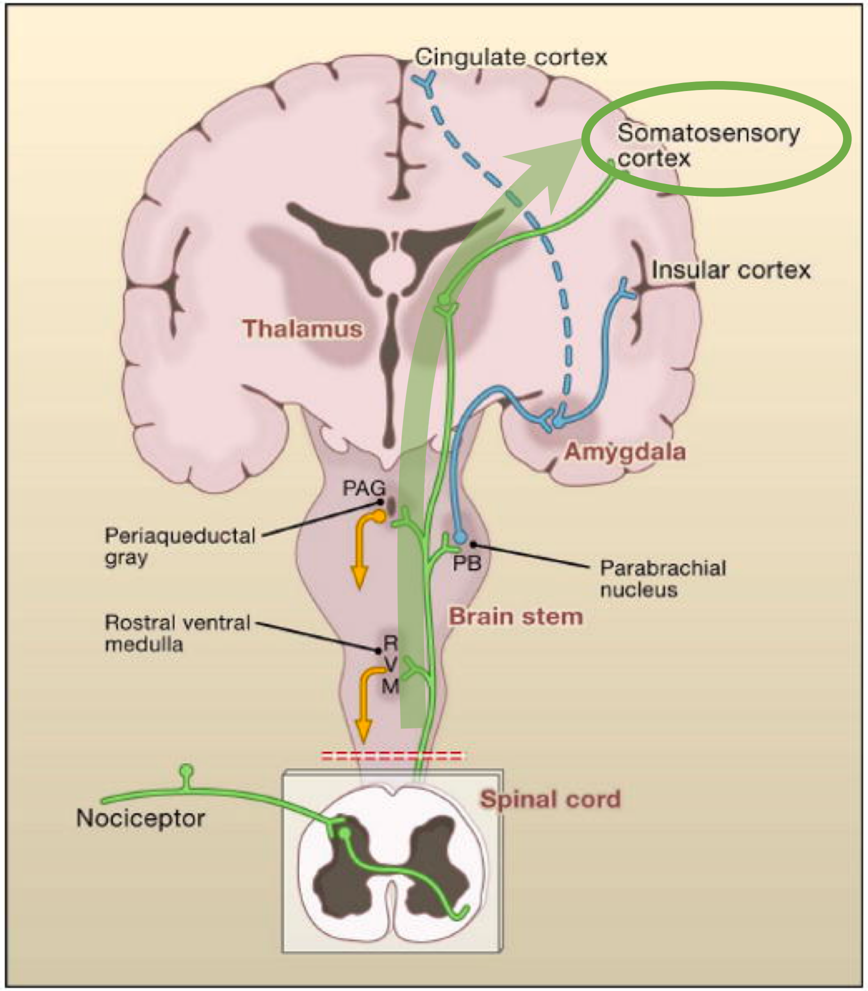


No pain



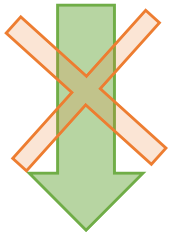
It's as if I'm eating pineapple, but there's no taste
It feels like my tongue is swollen like after being bitten

Pain is not a result of sensation



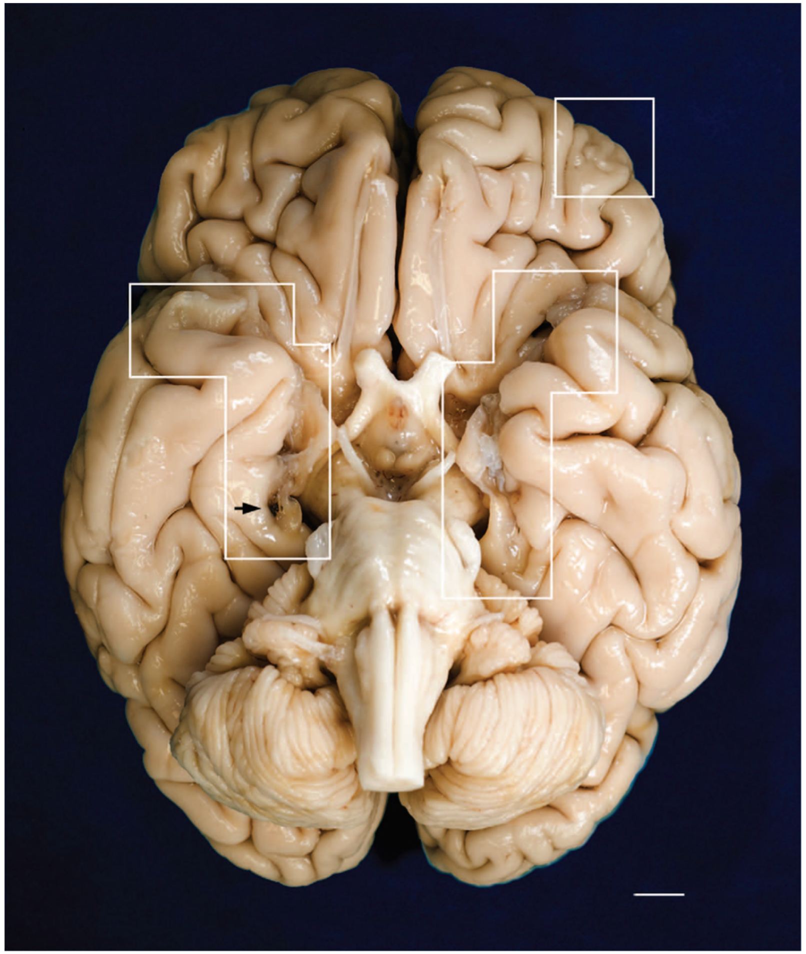
Basbaum et al., Cell, 2009

Somatosensory information



Pain

Limbic system is necessary to perceive pain



Annese et al., Nat. Comm., 2013

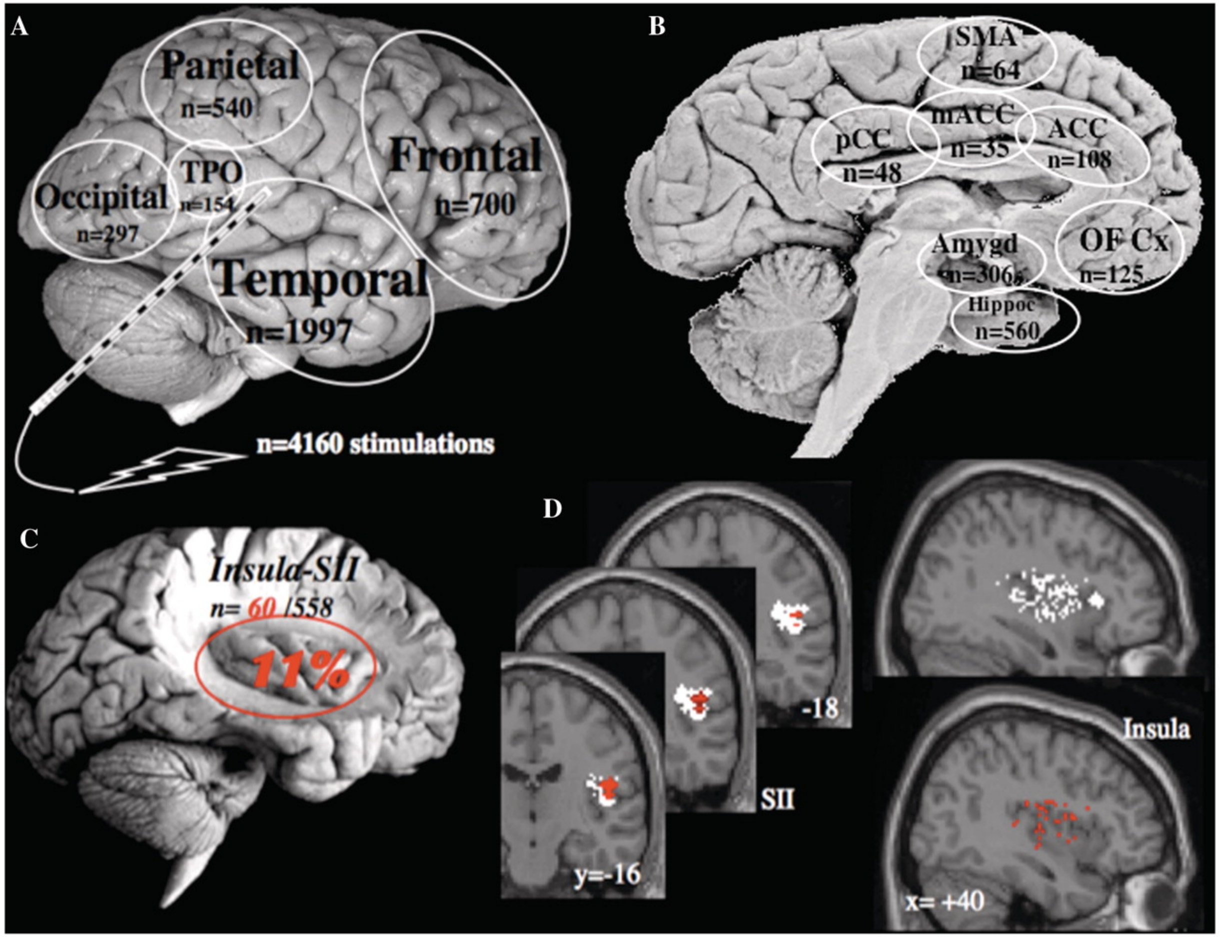
Bilateral resection of amygdala and hippocampus

Patient H.M. did not feel acute thermal pain applied over diverse body parts but he had normal sensory encoding of noxious stimuli.

(Baliki et al., Neuron, 2015),

Pain region?

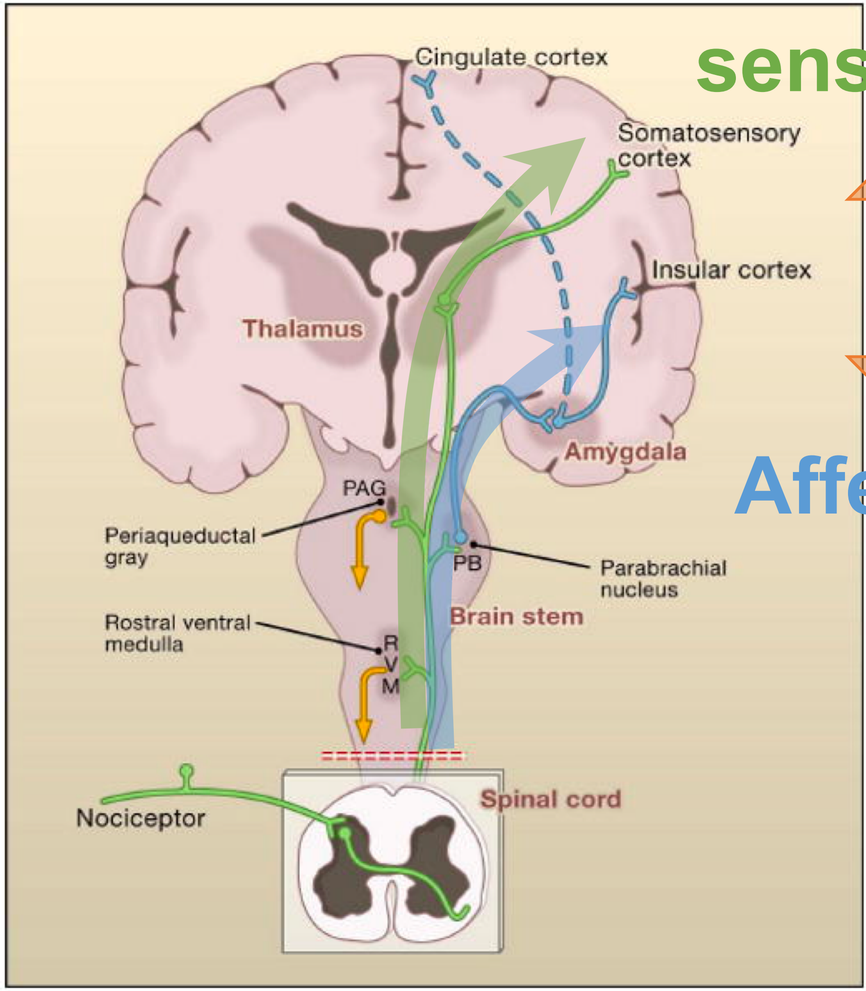
Electrical stimulation of the insular and S2 sometimes (11%) induced pain, although it is still controversy.



Mazzola et al., Brain, 2012

Stimulation of insular

Limbic system makes sensation pain



Basbaum et al., Cell, 2009

sensory information of stimulus

Pain

Affective dimension of pain

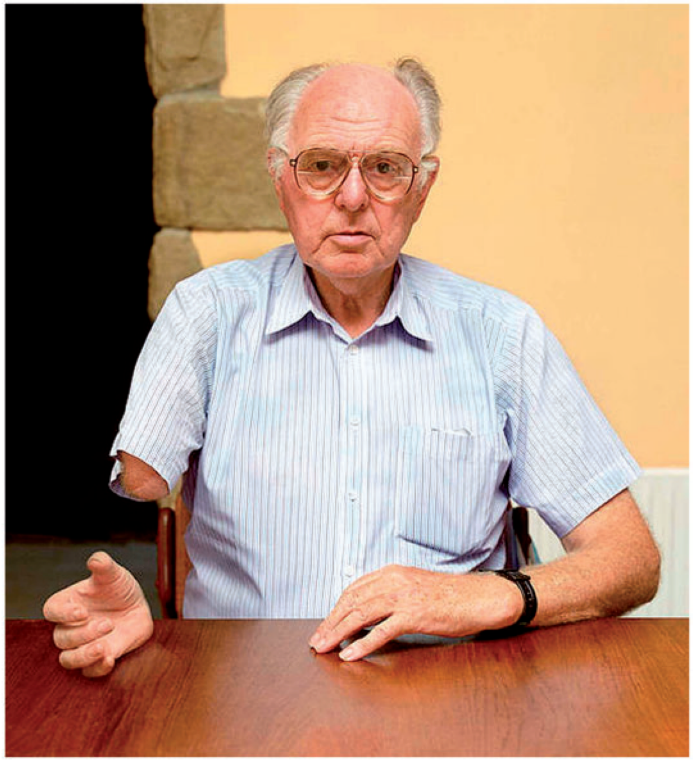
The pain originates from the interaction among somatosensory pathways and limbic pathway.

What makes haptics affective

1. Brain makes sensation pain
2. Brain makes pain without somatosensory stimulus

Phantom limb pain

Chronic pain without sensory input

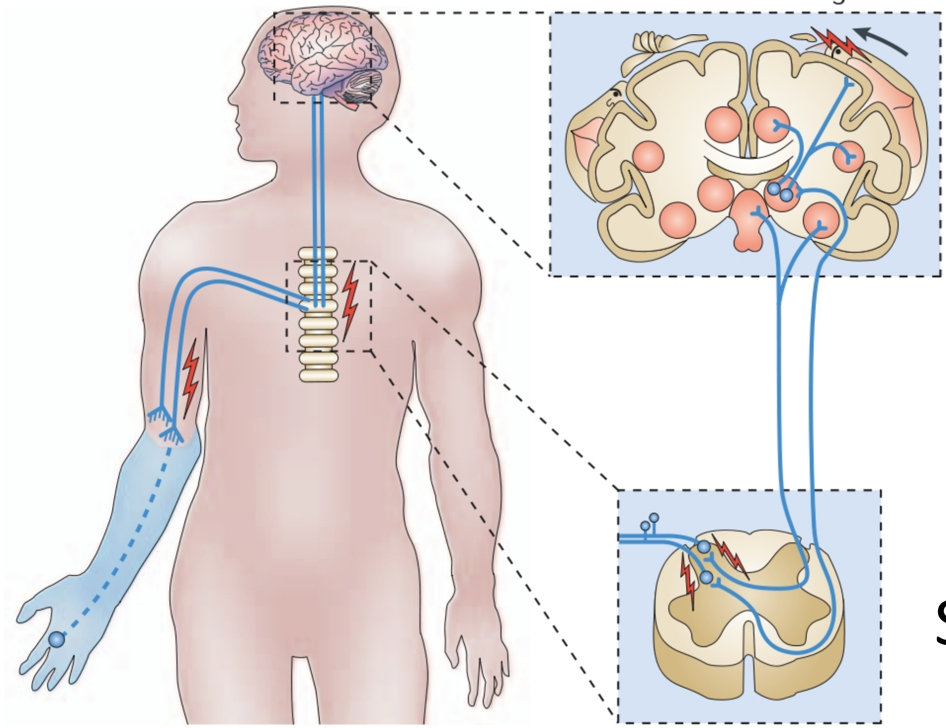


G. D. Schott, Brain 2014: 137; 960–969

Phantom limb pain belongs to a group of neuropathic pain syndromes that is characterized by pain in the amputated limb or pain that follows partial or complete deafferentation
(H.Flor et al. Nat Rev Neurosci., 2006)

5,000 amputees/yr in Japan
Phantom pain **50-80%**

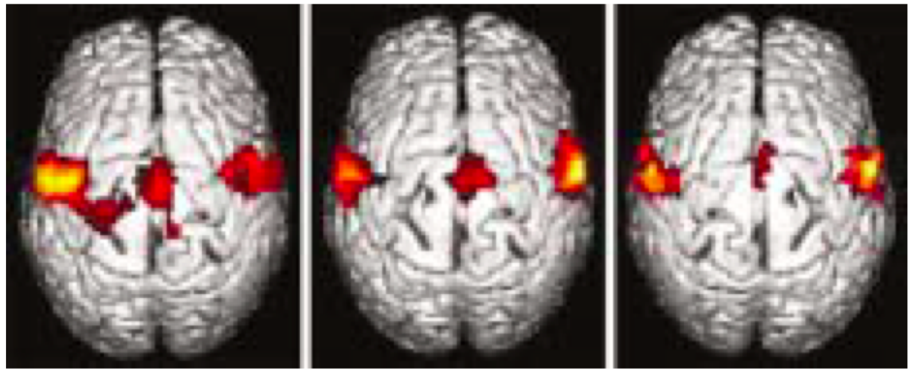
Pain from brain?



H.Flor et. al, Nat. Rev. Neurosci., 2006

Phantom hand representation should be strengthen or weaken?

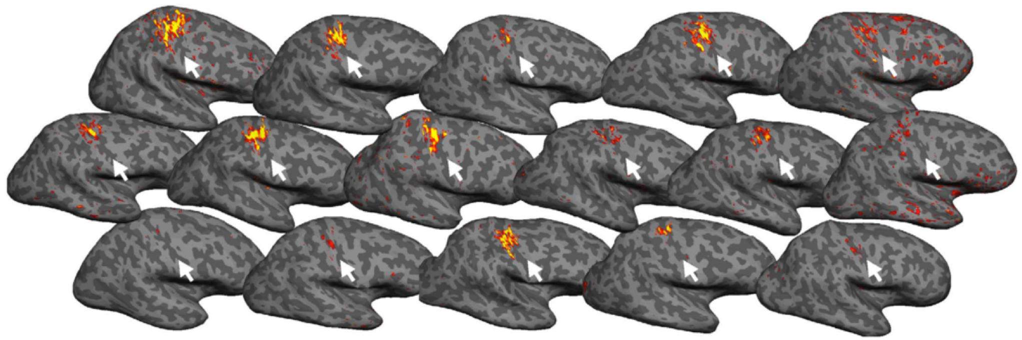
Activation during lip movements（fMRI)



Phantom pain	Amputee without pain	Normal

M. Lotz et al, Brain, 2001

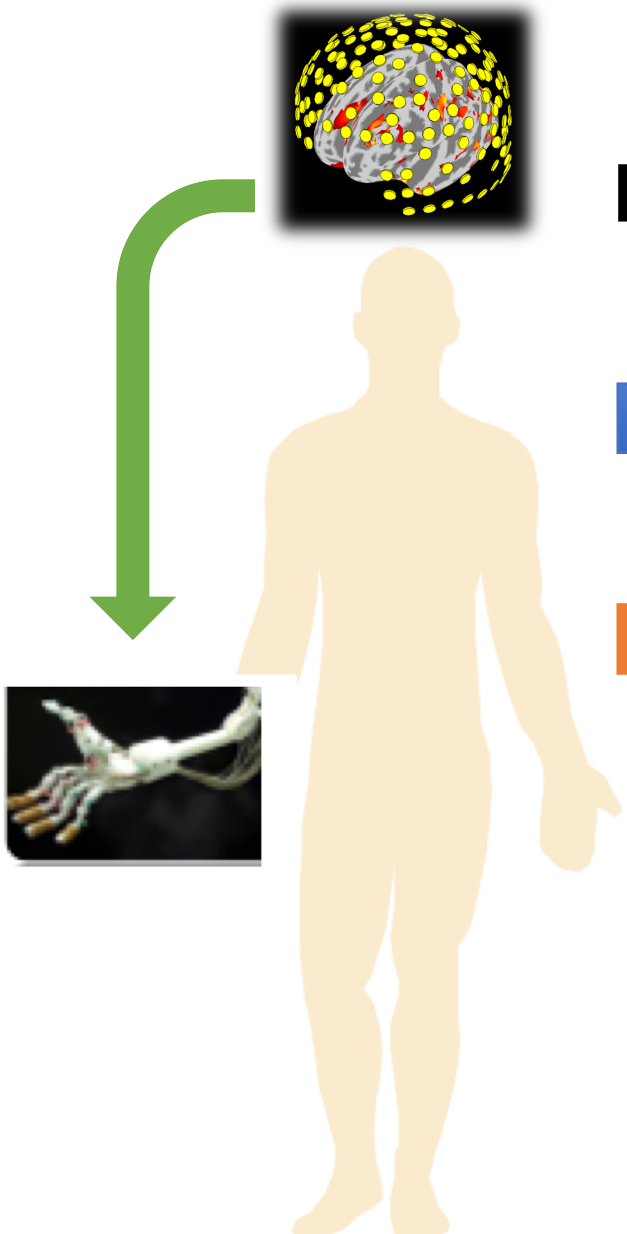
Strong pain



Weak pain

T.Makin et al., Nature communications 2012

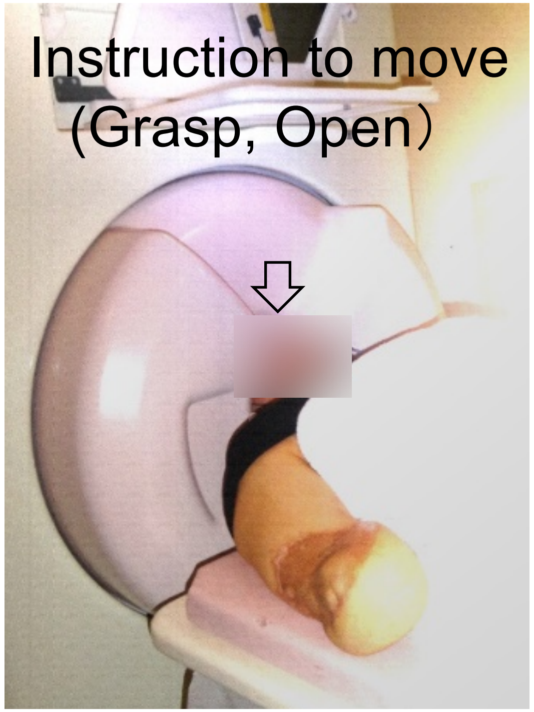
Modulation of pain by BMI



Brain-Machine Interface (BMI)

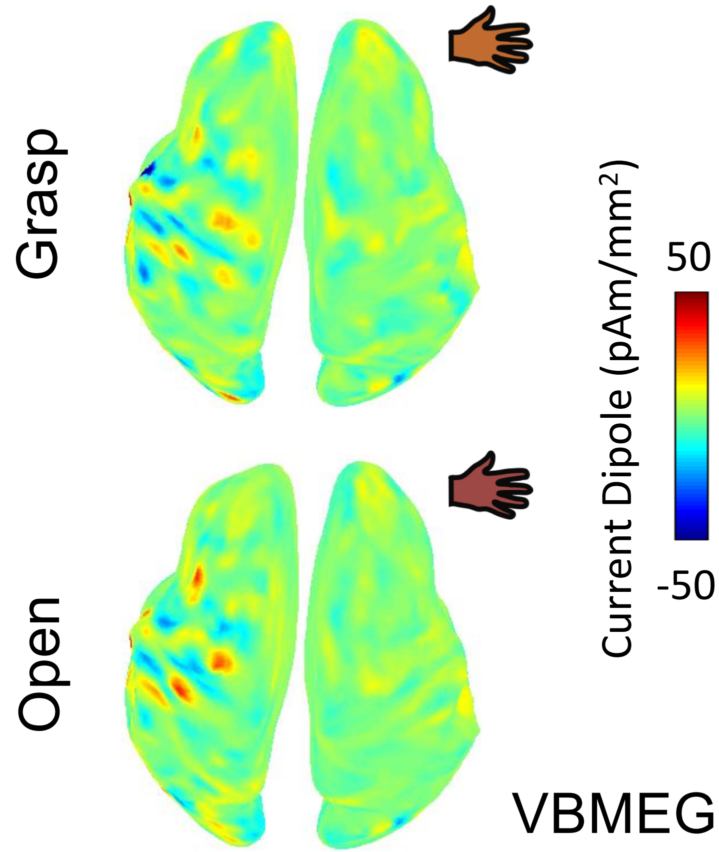
- Induce plastic changes in sensorimotor representation
- Pain?

MEG during phantom hand movements

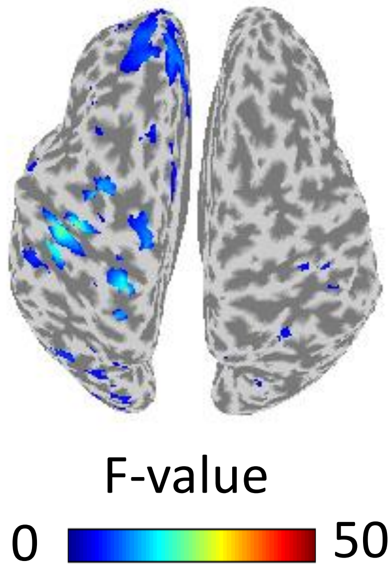


160ch MEG (Richo)

time-averaged cortical currents (0-500ms)



VBMEG

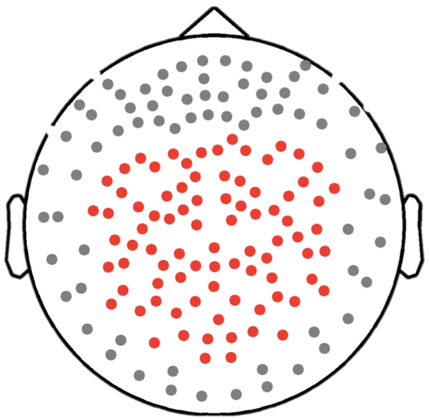


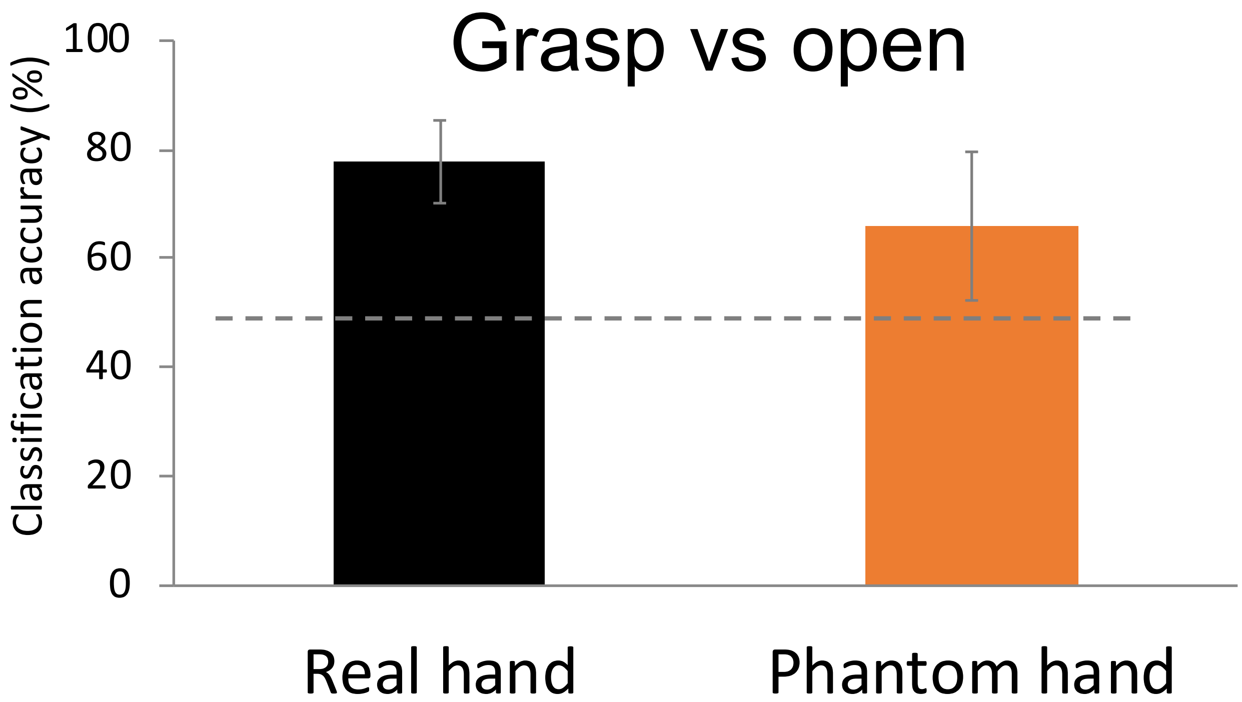
F-value of ANOVA was evaluated among two types of movements (F-values with $p<0.01$ were shown)

The patients moved their phantom hands to be grasping or opening according to the instructions, while the MEG signals were recorded.

Movement type classification using MEG sensor signals

Sensors used for decoding





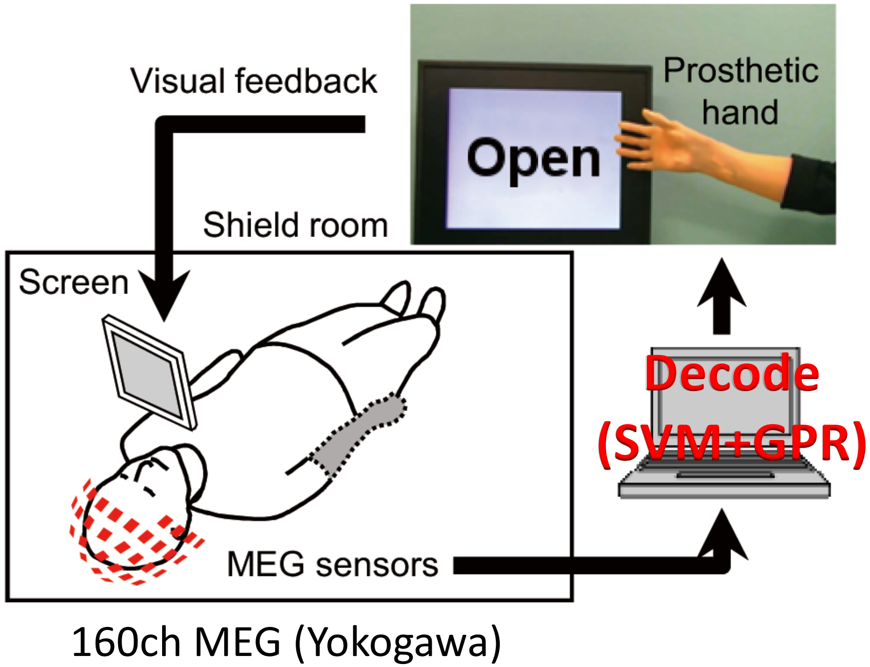
Real hand decoder

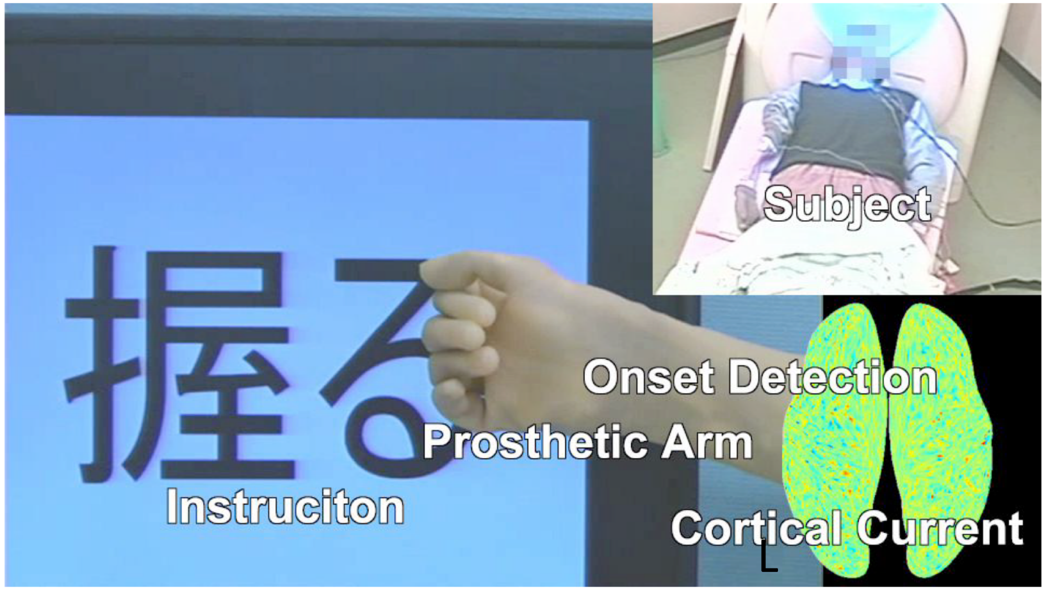
Phantom decoder

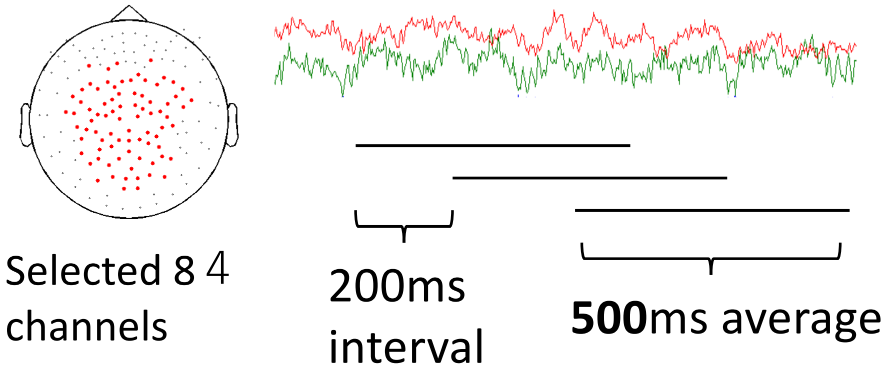
Time-averaged signals (500ms)
Support vector machine (SVM)
Nested 10 fold cross-validation

mean±95%CI, *n*=10

MEG-based BMI robotic hand



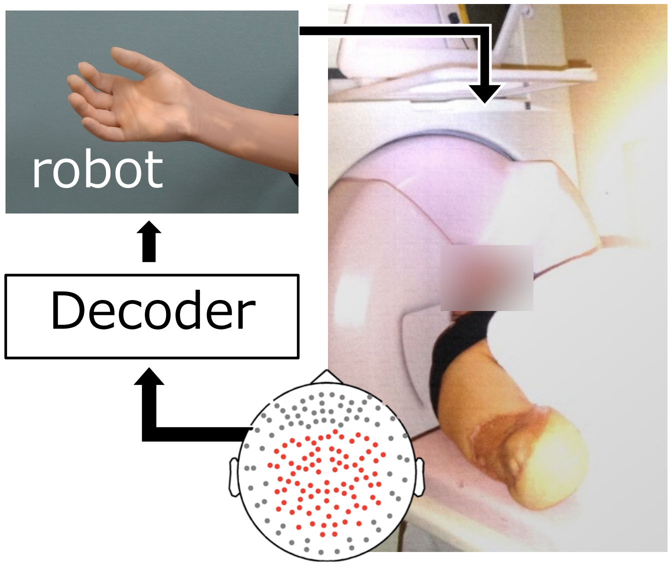




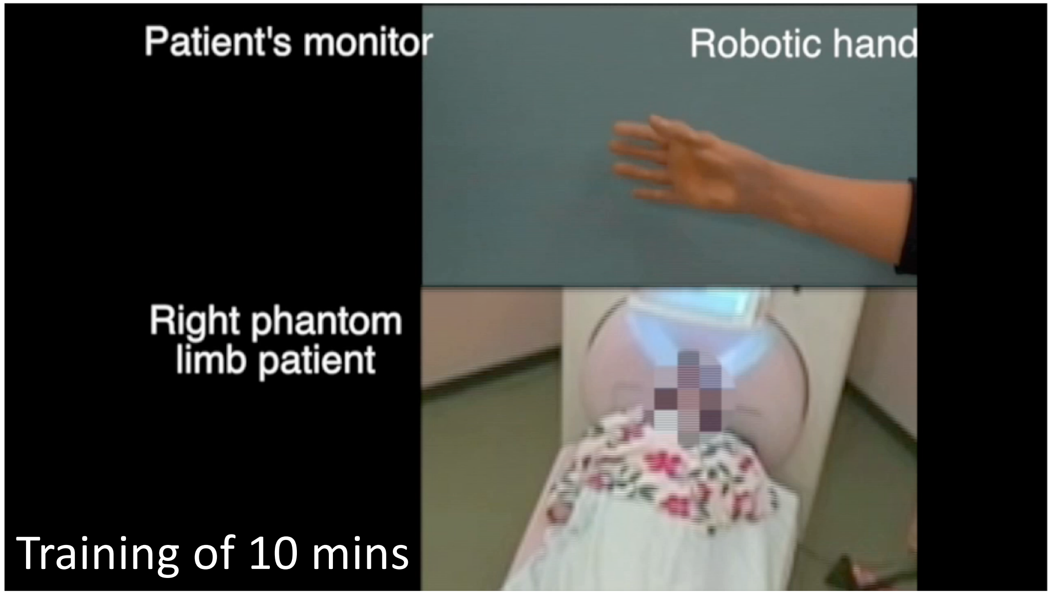
R. Fukuma et al, PLoS One, 2015
R. Fukuma et al, Scientific Reports, 2016

BMI training to control robot

Patients watched the movement of robot through the monitor

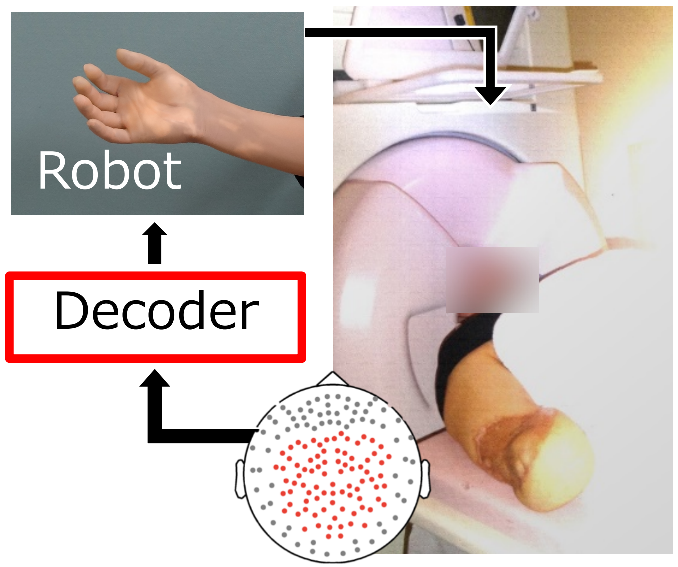


Patients controlled the prosthetic hand by moving phantom hands



2016/10/27 NHK News

Experimental condition



Offline phantom hand task (pre-BMI)

Pain evaluation (Visual analogue scale, VAS)

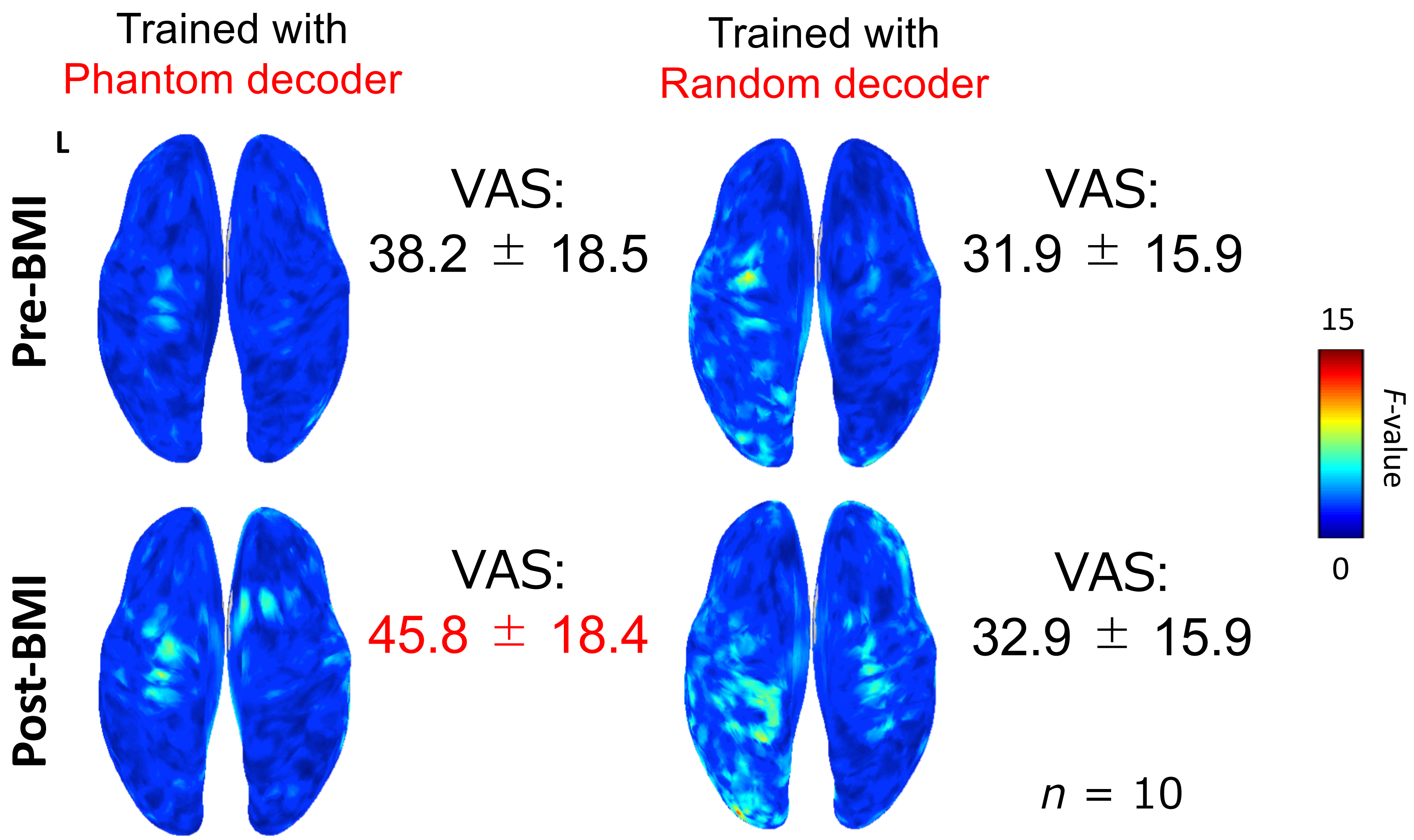
BMI training (10mins) with:
1) Phantom, 2) Random 3) Real decoder

Pain evaluation (VAS)

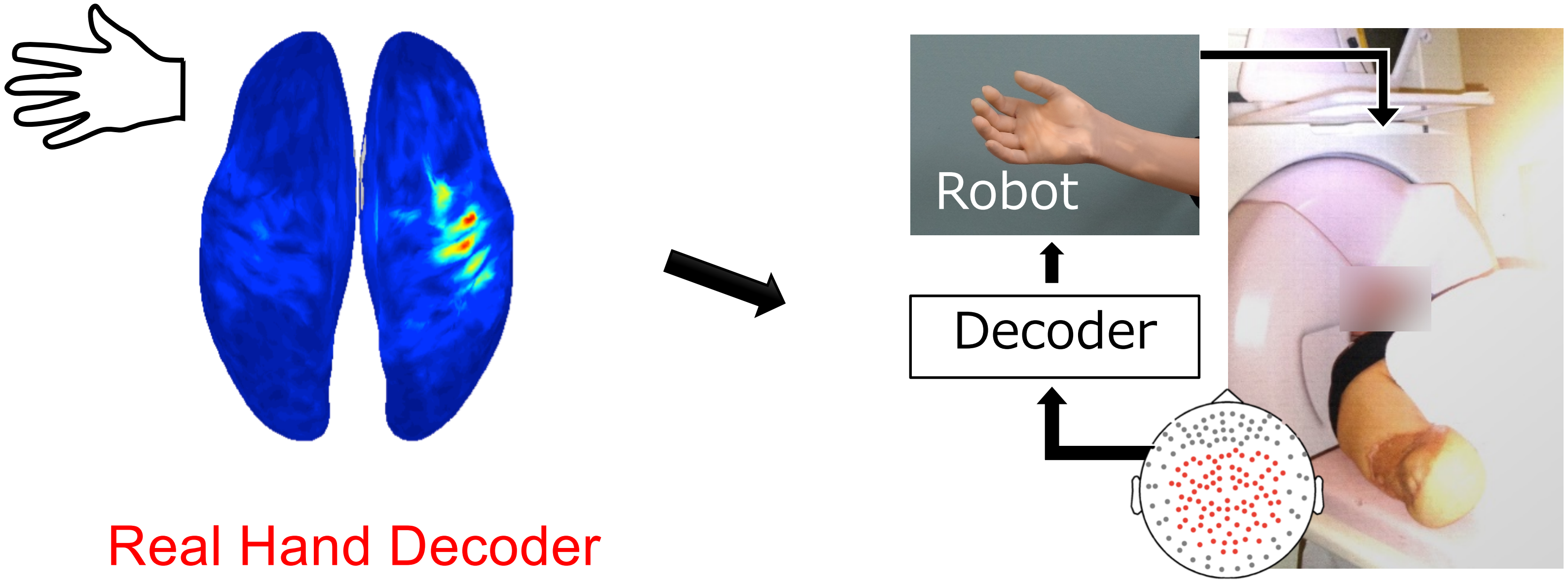
Offline phantom hand task (post-BMI)

1. Phantom decoder was constructed using the MEG signals during the phantom hand movements
2. Random decoder was constructed using the MEG signals during the phantom hand movement with randomly relabeled classes
3. Real hand Decoder was constructed using the MEG signals during the intact hand movements

Enhanced phantom hand representation with pain increase



Real hand decoder



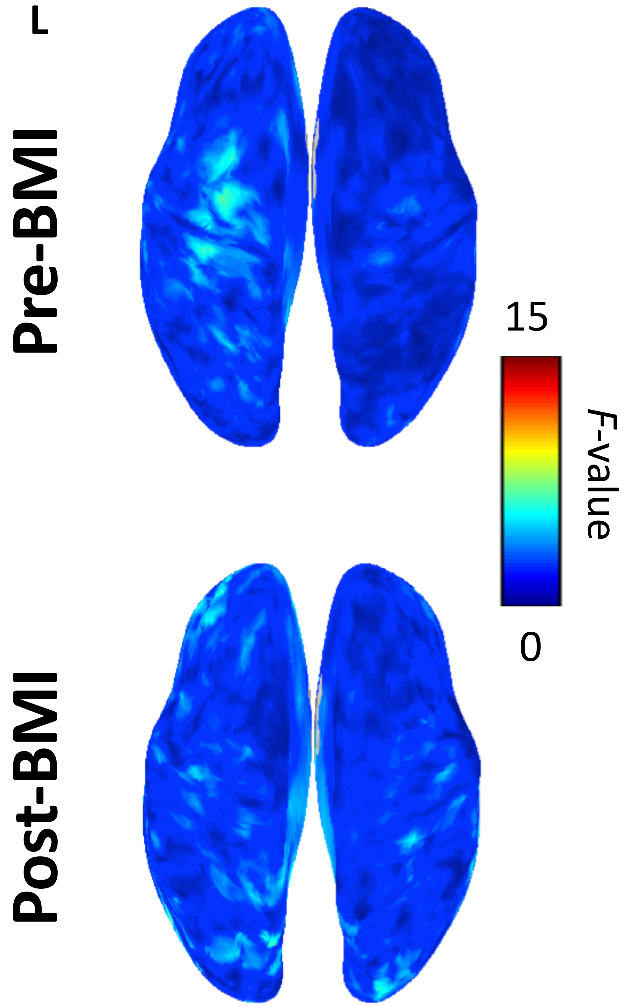
Real Hand Decoder
was constructed using the MEG signals during intact hand movements

Patients controlled the prosthetic hand by moving their phantom hands

The patients unintentionally associate their phantom hand movements with the representation of the intact hand's movement, which were different from the original phantom hand representation. We expected that this BMI training would accelerate the dissociation of the link between the phantom hand and the original cortical representation by creating a link to the new representation.

Deteriorated phantom hand representation with pain reduction

Trained with
Real hand decoder

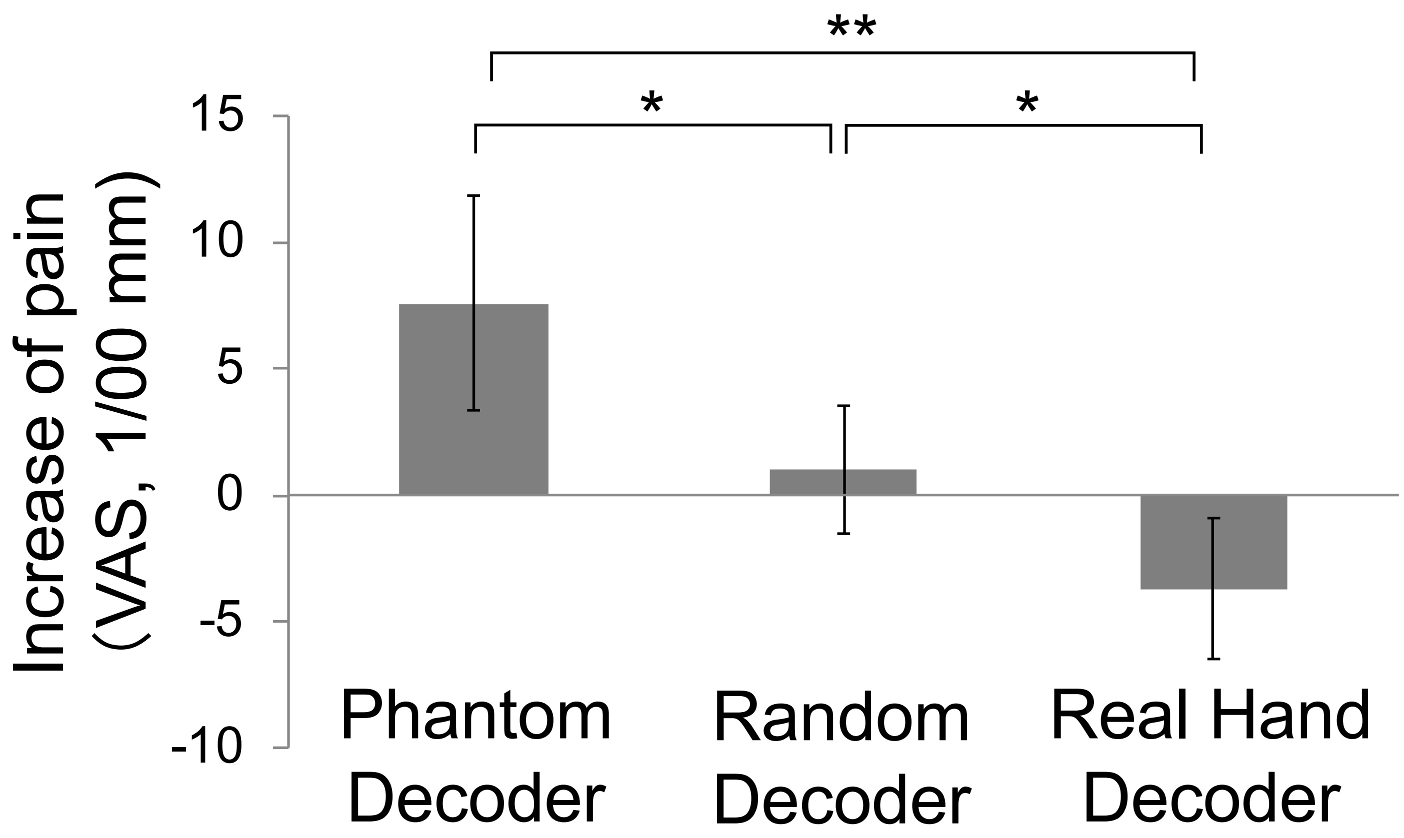


VAS:
38.3 ± 15.5

VAS:
34.6 ± 14.8

n = 10

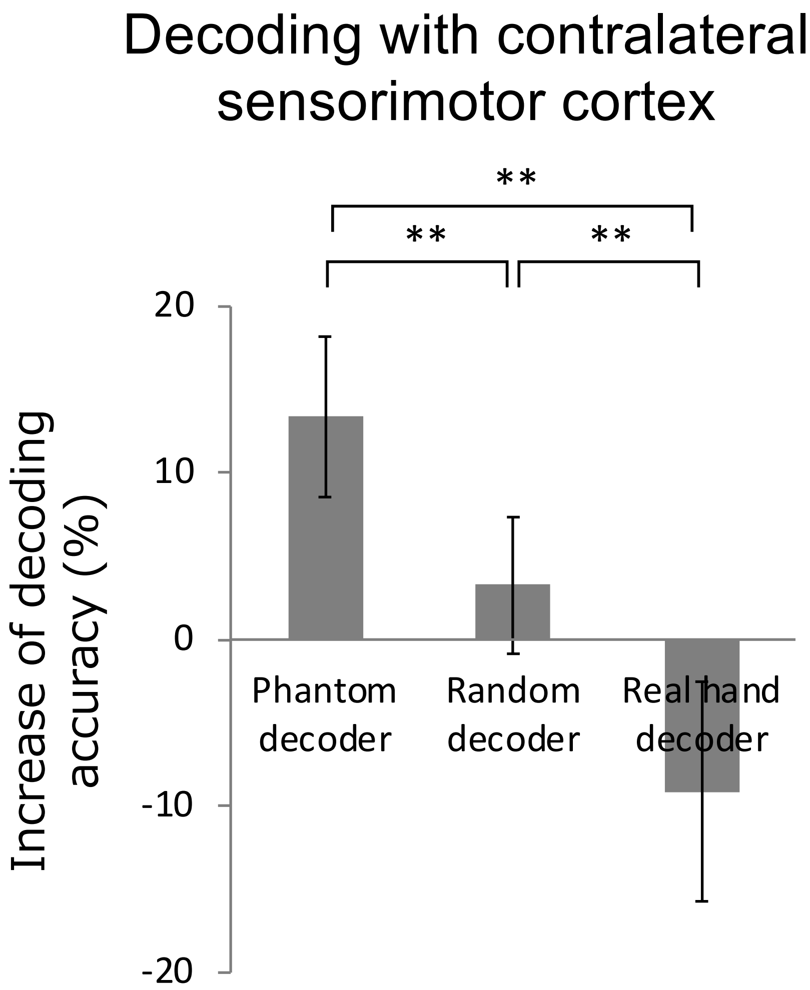
BMI training controlled pain

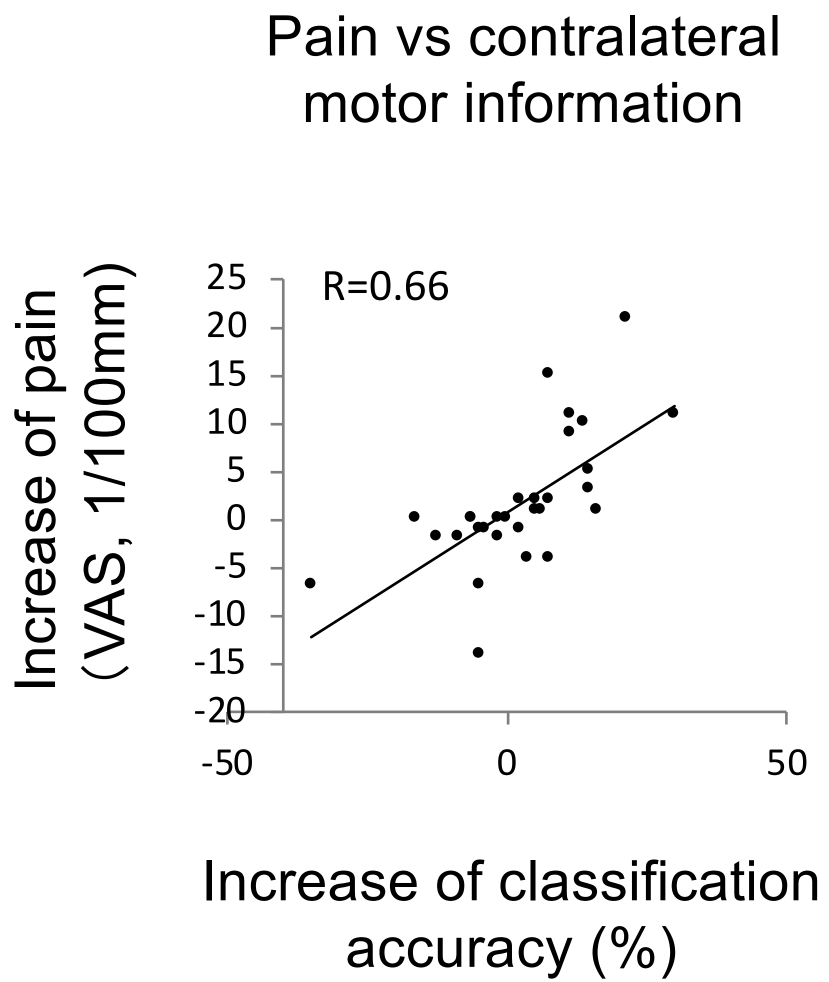


n=10, *p<0.05, **p<0.01, two-tailed Student's *t*-test

T. Yanagisawa et al., Nat Commun, 2016

Pain increased as improved classification accuracies





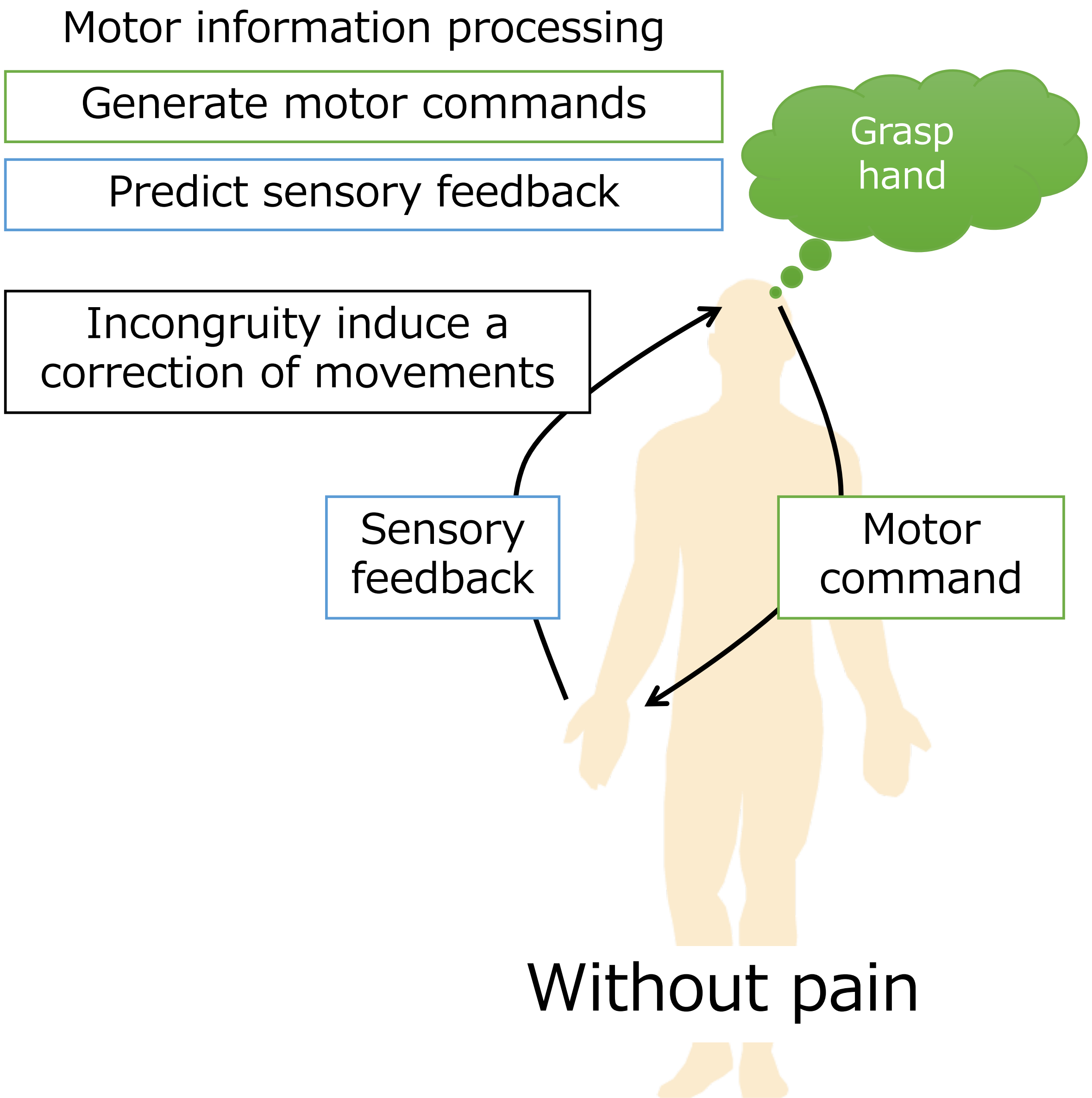
n = 10, $^{**}p$ <0.01, two-tailed Student *t*-test

Interim summary

1. The BMI training significantly **changed the classification accuracy** in the contralateral sensorimotor cortex depending on the decoder type.

2. The classification accuracy was **positively correlated** to the **pain**.

sensory-motor incongruities might cause pain



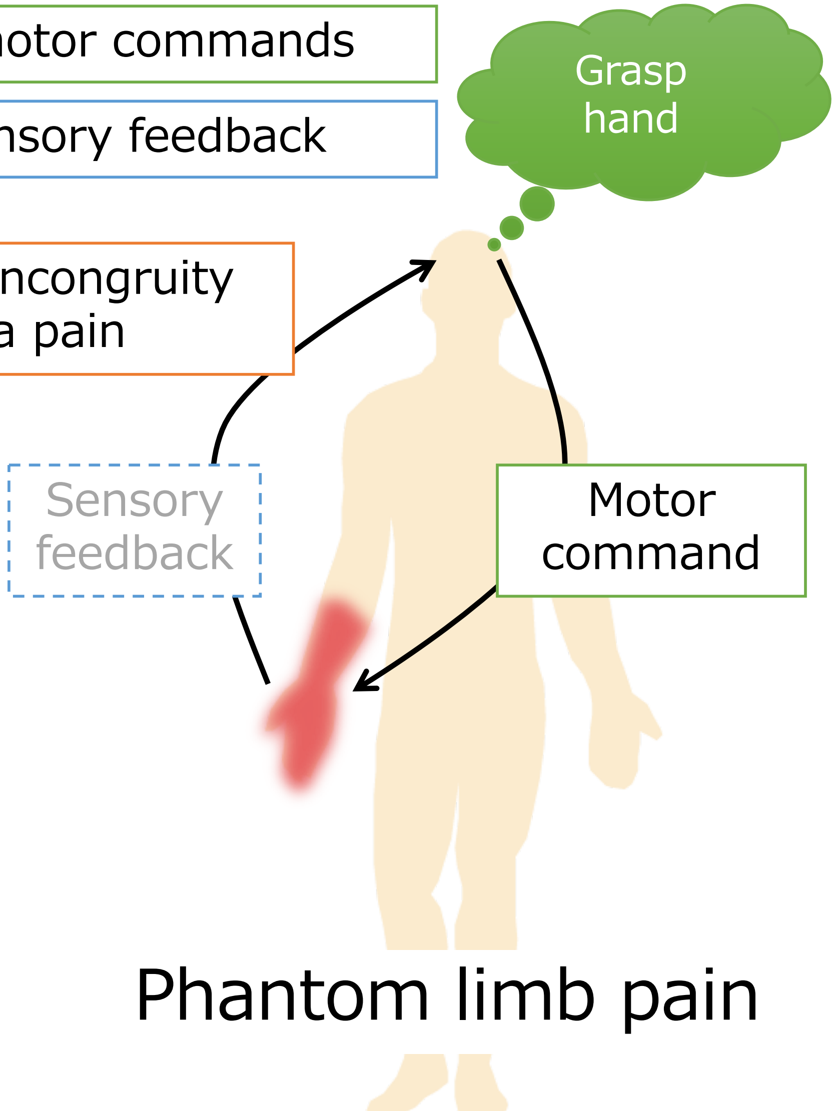
sensory-motor incongruities might cause pain

Motor information processing

Generate motor commands

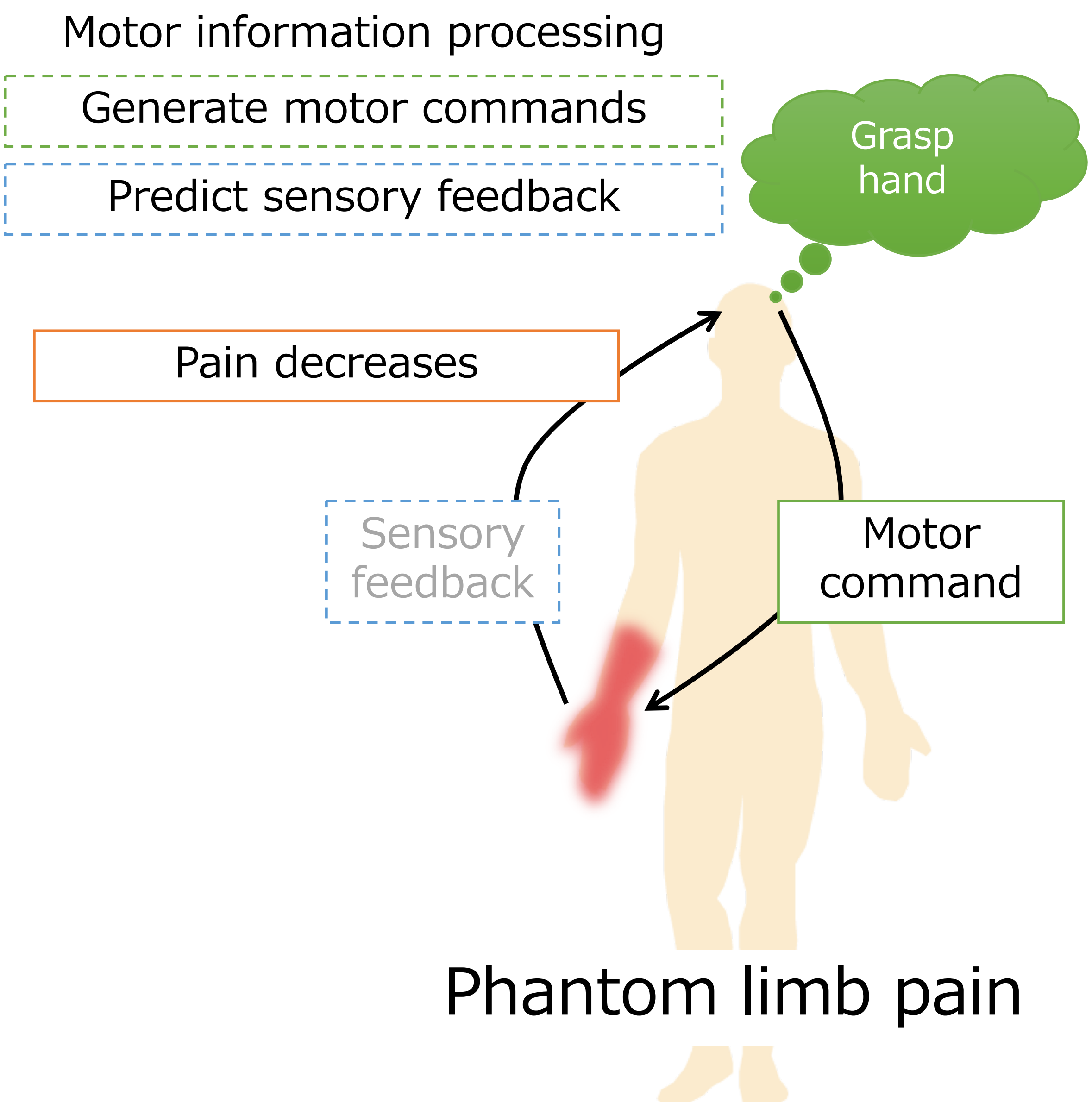
Predict sensory feedback

Continuous incongruity induce a pain



Phantom limb pain

sensory-motor incongruities might cause pain



BMI training disrupt the motor information processing

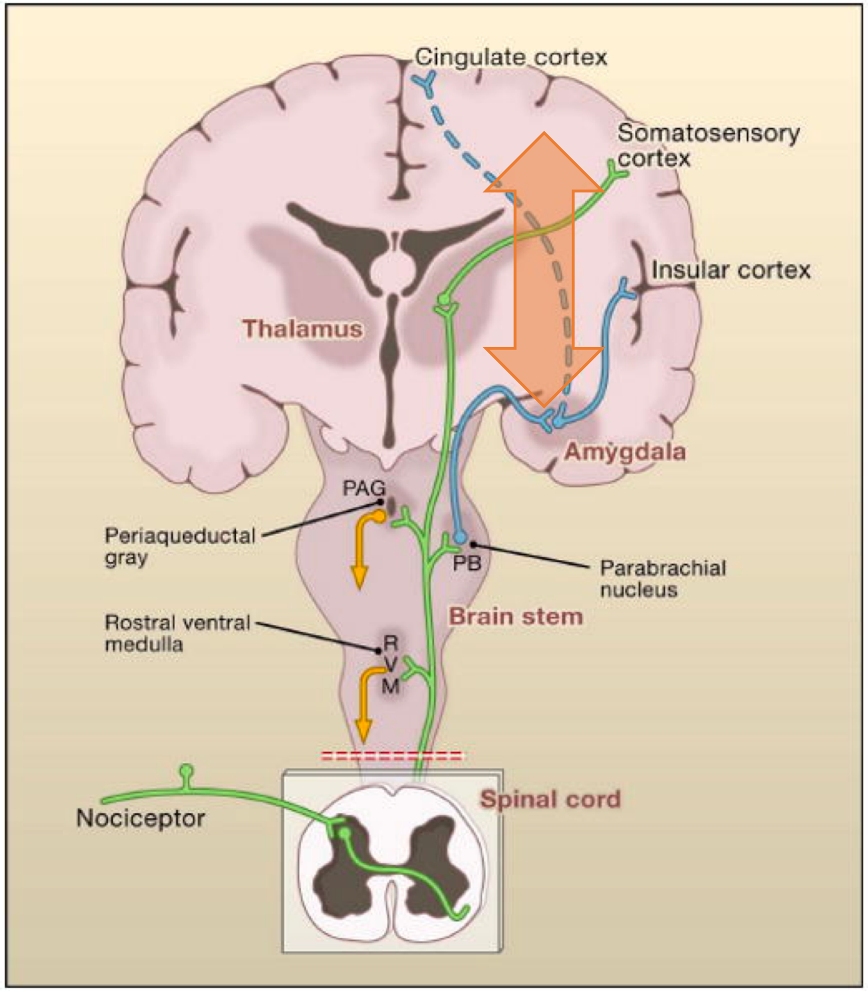
Summary

1. The training to use BMI successfully controlled the motor information of the phantom hand and the pain.

2. The 3-day training significantly reduced the pain for 5 days after the training.

3. **The residual motor information of phantom hand should be weaken to reduce pain**.

Sensorymotor information modulates pain without stimuli



Basbaum et al., Cell, 2009

Pain

The modulation of the sensorimotor information induced changes of chronic pain intensity without somatosensory stimulus.

Conclusion

- Pain is generated in the brain which encodes sensory and affective information, even without somatosensory stimulation.
- We can modulate the brain activities using BMI to control the pain.
- The interaction using BMI will unveil how brain makes haptic affective.

Thank you for your attention

Collaborators:

Yukiyasu Kamitani
(Kyoto U.)

Ben Seymour
(CiNet)

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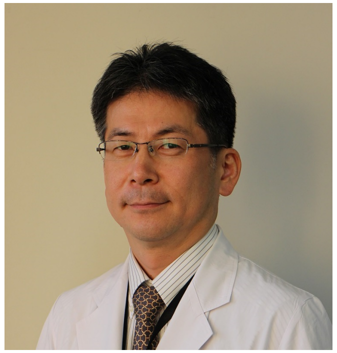
(Osaka Univ.)



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