Understanding pain and emotions using MVPA

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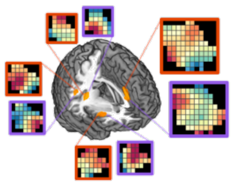
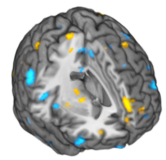
Roadmap

Physical pain
vs. social rejection



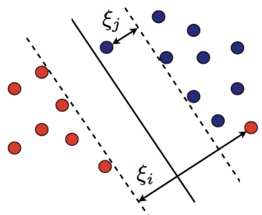
Somatic vs.
vicarious pain



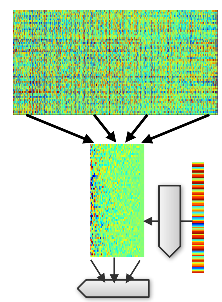
CANLab
MatLab Tools

CANLab

SVMs

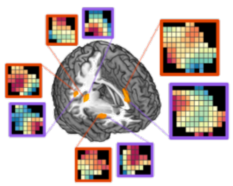


LASSO-PCR

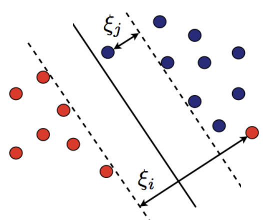


Roadmap

Physical pain vs. social rejection



SVMs



Does rejection hurt?

Shared psychological correlates between social rejection and physical pain

- “I am hurt”
- “broken hearted”
- “emotionally scarred”…

Macdonald & Leary, 2005, *Psychological Bulletin*

Does rejection hurt?

Shared psychological correlates between social rejection and physical pain

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- “broken hearte
- “emotionally sc

Table 1
International Terms for Hurt Feelings

Language	Native term	English translation
German	verletzt sein	hurt or wounded
French	blessé	hurt
Dutch	gekwetst	hurt
Spanish	sentirse herido	feel injured or harmed
Italian	ferito	hurt
Greek	pligomenos	hurt
Hebrew	he pag’ah baregashot shelo	she hit/damaged his feelings
Hungarian	megsertoedni	being hurt
Armenian	zkatsoumnires tsavtsoutsir	you hurt my feelings
Mandarin	shang liao kan ching	hurt feelings
Cantonese	siong sum	hurt heart
Tibetan	snying la phog	hit the heart
Bhutanese	sems lu phog	hit the mind
Inuktitut	anniqtuq	hurt by harsh words
Korean	상처받다	hurt, wounded

Macdonald & Leary, 2005, *Psychological Bulletin*

Does rejection hurt?

In terms of language, *yes*.

But is this more than a *metaphor*?

Does rejection literally hurt?

Does Rejection Hurt? An fMRI Study of Social Exclusion

Naomi I. Eisenberger,[1]* Matthew D. Lieberman,[1] Kipling D. Williams[2]

A neuroimaging study examined the neural correlates of social exclusion and tested the hypothesis that the brain bases of social pain are similar to those of physical pain. Participants were scanned while playing a virtual ball-tossing game in which they were ultimately excluded. Paralleling results from physical pain studies, the anterior cingulate cortex (ACC) was more active during exclusion than during inclusion and correlated positively with self-reported distress. Right ventral prefrontal cortex (RVPFC) was active during exclusion and correlated negatively with self-reported distress. ACC changes mediated the RVPFC-distress correlation, suggesting that RVPFC regulates the distress of social exclusion by disrupting ACC activity.

It is a basic feature of human experience to feel soothed in the presence of close others and to feel distressed when left behind. Many languages reflect this experience in the assignment of physical pain words ("hurt feelings") to describe experiences of social separation (*1*). However, the notion that the pain associated with losing someone is similar to the pain experienced upon physical injury seems more metaphorical than real. Nonetheless, evidence suggests that some of the same neural machinery recruited in the experience of physical pain may also be involved in the experience of pain associated with social separation or

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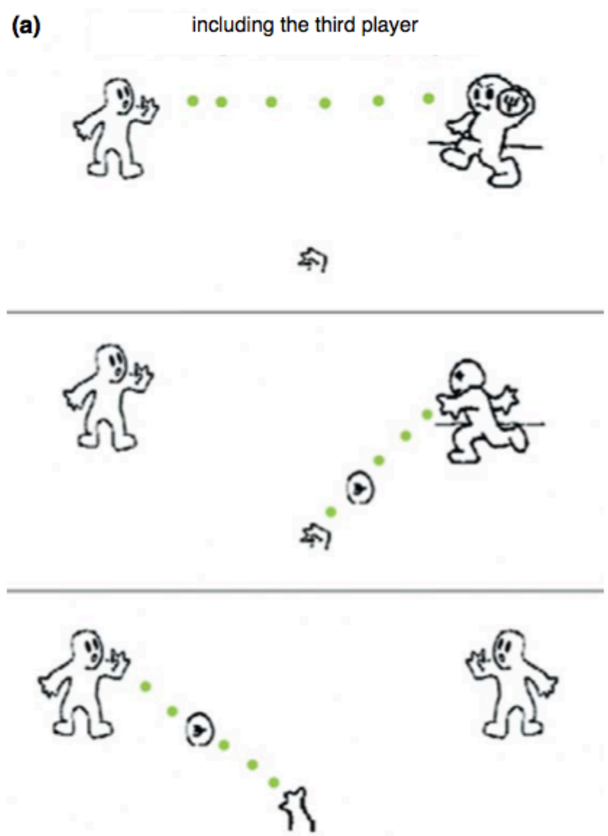
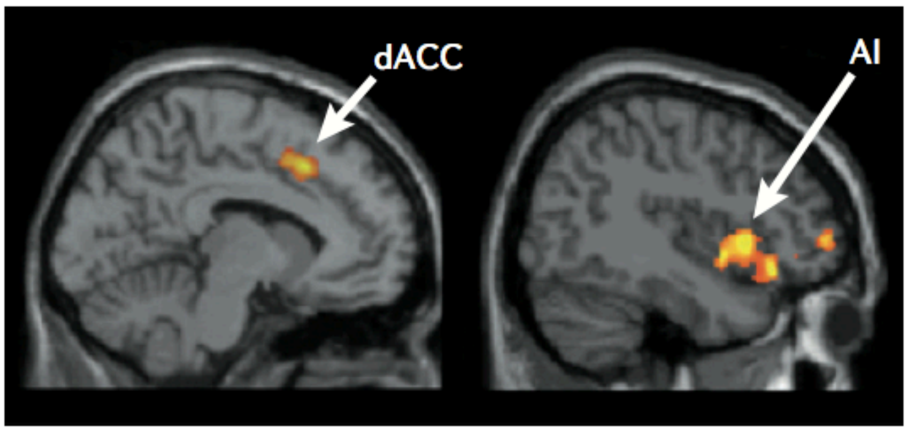
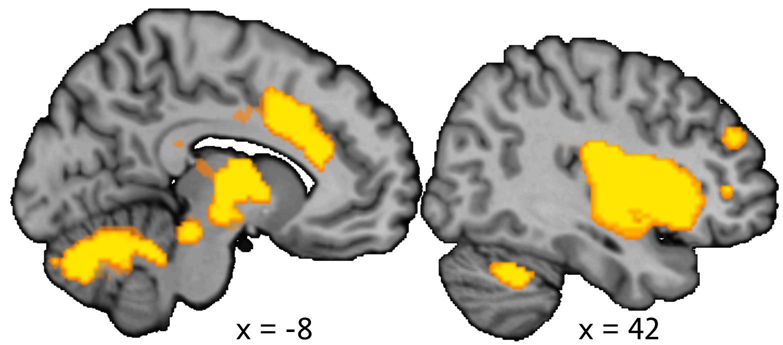


Eisenberger et al., 2003, *Science*



x = -8 x = 42

Pain-processing regions (thermal pain)



Wager lab, N = 115 p < .05 FWE corrected

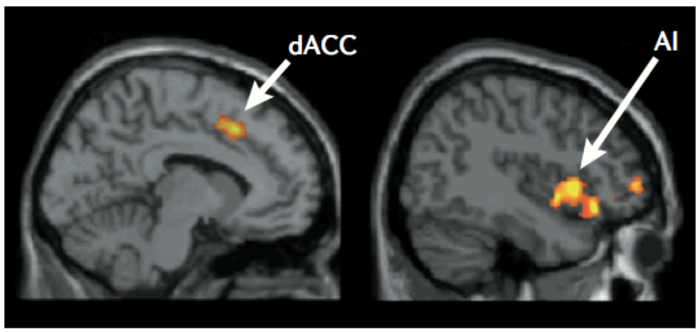
"Common-coding interpretation"

Shared neural representations between social and physical pain

Eisenberger et al., 2003, *Science*

Summary of neural activations in social pain studies

Among 24 studies,
67% reported **dACC** and **AI** activation



Task	dACC	AI	subACC	Thal	S1	S2	PI	PAG	Refs
Adult samples									
Cyberball	↑	↑	-	-	-	-	-	-	7
Cyberball	↑	↑	-	-	-	-	-	-	66
Cyberball	↑	↑	-	-	-	-	-	-	67
Cyberball	↑	↑	↑	-	-	-	↑	-	68
Cyberball	↑	-	-	-	-	-	-	-	69
Cyberball	-	↑	-	-	-	-	-	-	70
Cyberball	↑	-	↑	-	-	-	↑	-	71
Cyberball	-	-	-	-	-	-	↑	-	76
Negative evaluation	-	↑	↓	-	-	-	-	-	84
Negative evaluation	↑	-	-	-	-	-	-	-	88
Evaluative threat	↑	-	-	-	-	-	-	-	86
Evaluative threat	-	↓	-	-	-	-	-	-	139
Rejection images	↑	↑	-	-	-	-	-	-	89
Disapproving faces	-	-	-	-	-	-	-	-	90
Romantic rejection	↑	↑	-	-	-	-	↑	-	91
Romantic rejection	↑	↑	-	↑	-	↑	↑	-	92
Bereavement	↑	↑	-	-	-	-	-	-	93
Bereavement	↑	↑	-	-	-	-	-	↑	94
Bereavement	↑	↑	-	↑	-	-	-	↑	95
Samples that included adolescents									
Cyberball	↑	↑	↑	↑	-	-	-	-	72*
Cyberball	-	-	↑	-	-	-	-	-	83*
Cyberball	-	↑	↑	-	-	-	-	-	73‡
Cyberball	↑	↑	↑	-	-	-	-	-	74‡
Cyberball	-	↑	↑	-	-	-	↑	-	75‡

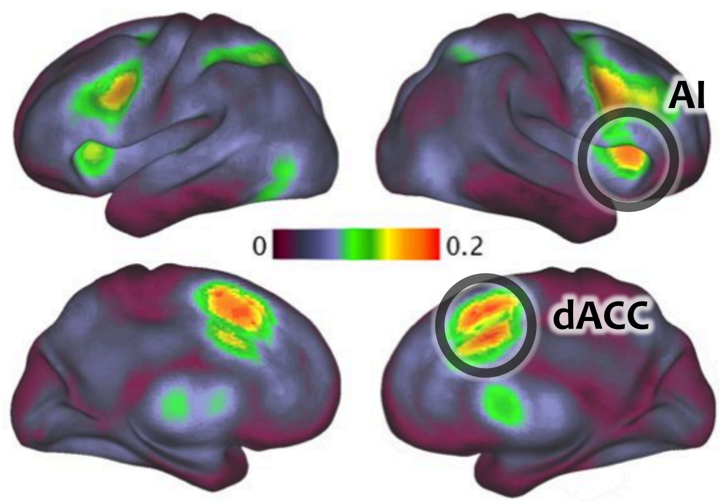
Eisenberger, 2012, *Nat Rev Neurosci*

Issues with specificity

AI and **dACC** are among the most frequently activated brain areas in fMRI studies across all task types (Yarkoni et al., 2012).

Does this mean these regions are ***non-specific***?

Base rate of activations, **P(activation)** across 3489 neuroimaging studies



Issues with specificity

AI and **dACC** are among the most frequently activated brain areas in fMRI studies across all task types (Yarkoni et al., 2012).

Does this mean these regions are ***non-specific***? **Maybe not.**

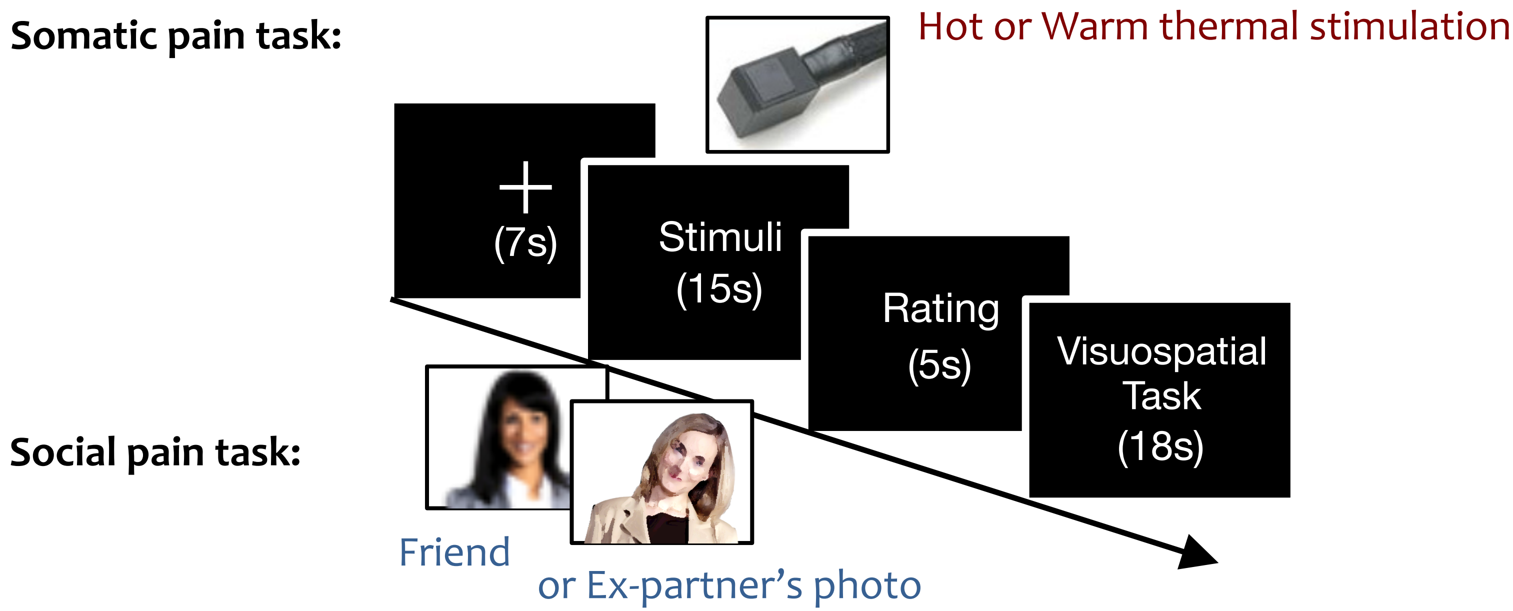
Animal single-neuron studies showed that the **ACC** contains neuronal sets that *specifically* encode nociceptive signal (e.g., Shyu et al., 2010).

This discrepancy may be due to the *information loss* when fMRI signal is spatially averaged over relatively large anatomical regions, because the neural representation is highly distributed (e.g., Haxby et al, 2001; *population codes*).

Therefore, **multivariate pattern analysis** (MVPA) approach might be able to identify specific fMRI patterns for pain and/or rejection within these regions.

Study1: Methods

- We analyzed a dataset from an fMRI experiment (*N* = 60) using somatic and social pain tasks.
- All 60 individuals (31 females, M_{age} = 20.8, SD_{age} = 3.0) recently experienced an unwanted break-up with their romantic partners and felt intensely rejected.



Woo et al., 2014, *Nature Communications*

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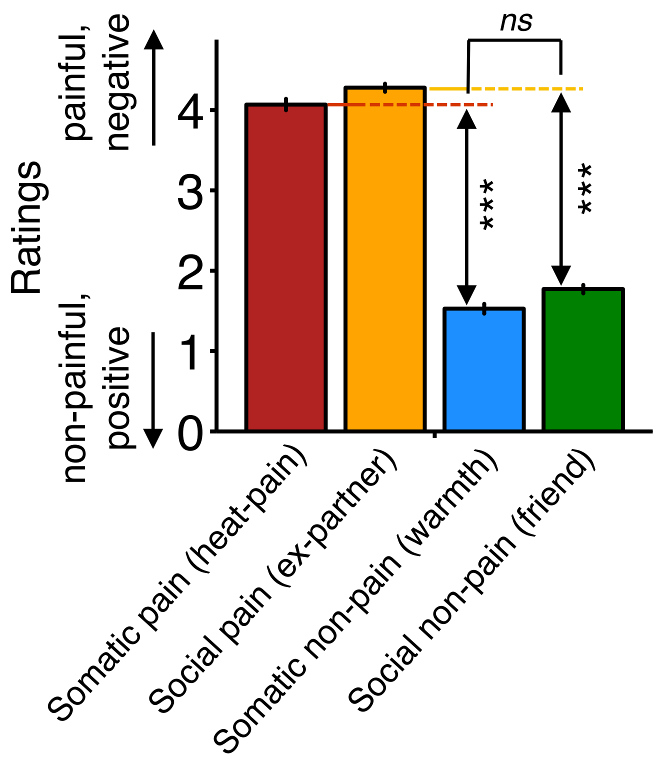
- The somatic and social pain tasks consisted of two consecutive runs (one for pain, another for no pain) of eight trials (i.e., 16 total trials). The order of the two tasks was counterbalanced across participants.

- After each trial, participants rated the pain intensity that they experienced for the somatic pain task and the intensity of negative emotion for the social pain task.

- After the fMRI scanning, participants described their stream of thoughts that they had while they were viewing ex-partner's photo in the scanner.

Woo et al., 2014, *Nature Communications*

Behavioral data I : ratings

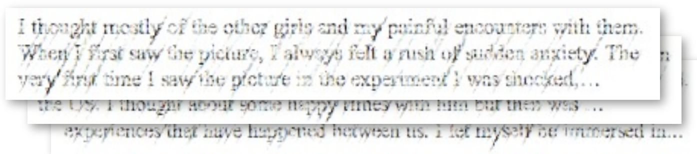


Both the “Ex-partner” and “Heat-pain” conditions elicited statistically equivalent levels of self-reported negative emotion and painful sensation compared to the “Friend” and “Warmth” conditions

Woo et al., 2014, *Nature Communications*

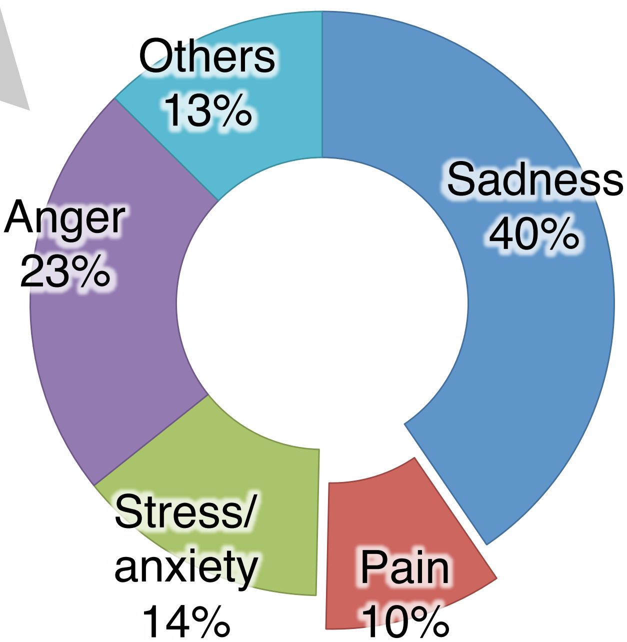
Behavioral data II : post-scan description of thoughts

Post-scan description of the stream of thoughts during the Ex-partner trial


I thought mostly of the other girls and my painful encounters with them. When I first saw the picture, I always felt a rush of sudden anxiety. The very first time I saw the picture in the experiment I was shocked,…
the US. I thought about some happy times with him but then was …
experiences that have happened between us. I let myself be immersed in…

Filtered with negative emotion words in LIWC dictionary

Calculated word frequency for each negative emotion category



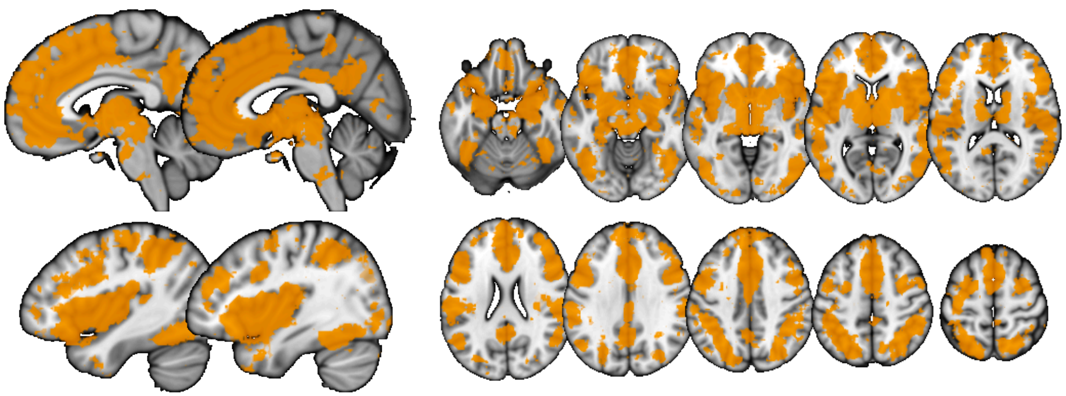
10% of negative emotion words used were pain-related (e.g., painful, hurt, hurtful), and 23% of participants (14 out of 60) used at least one pain-related word.

Woo et al., 2014, *Nature Communications*

MVPA analysis

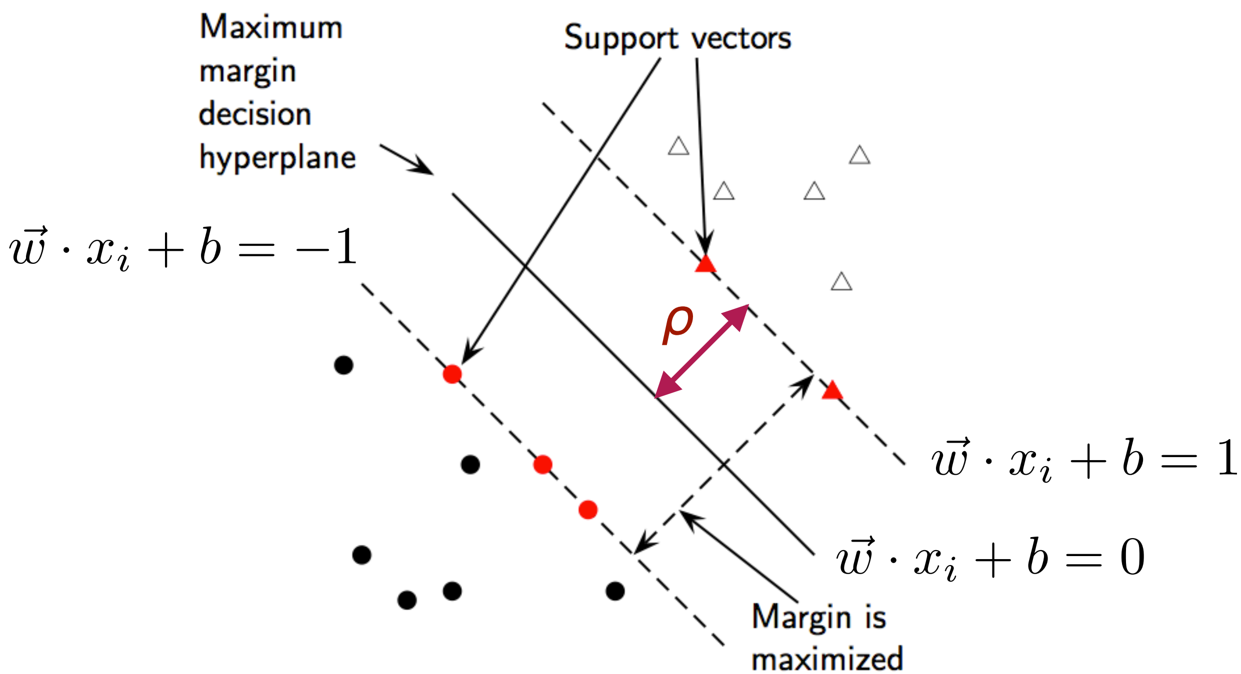
- We trained linear **support vector machines** (SVMs) to separately discriminate "Heat-pain" and "Ex-partner" vs. control conditions (using both one-vs-all and one-vs-one approach)
- For **feature selection**, we used *a priori* mask associated with 'pain', 'emotion', and 'social', based on a large-scale meta-analysis database (neurosynth.org; Yarkoni et al., 2012).
- We used a **leave-one-subject-out cross-validation** procedure to estimate classification accuracy.

***A priori* Neurosynth mask**



Woo et al., 2014, *Nature Communications*

Support vector machines (SVMs)



Distance of a point to hyperplane: $\dfrac{|\vec{w} \cdot x_i + b|}{\|\vec{w}\|}$

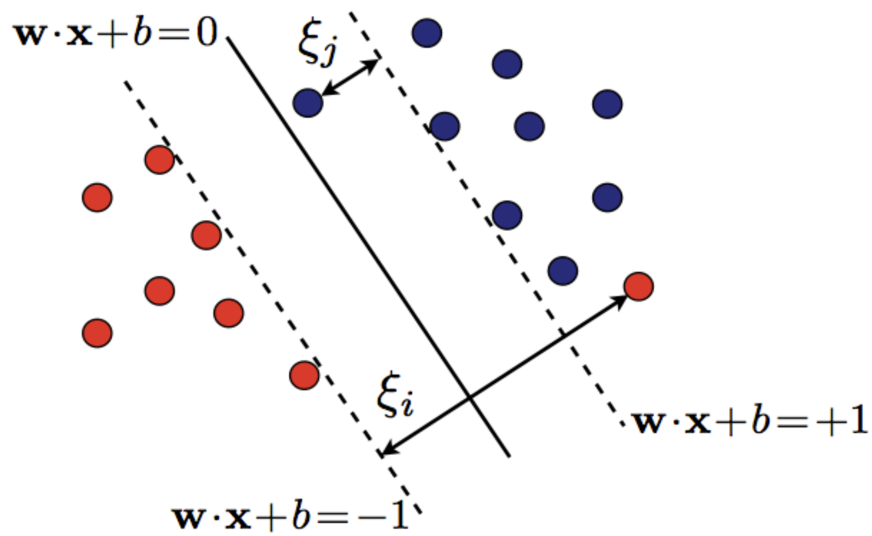
Margin: $\rho \equiv \min\limits_{x \in s} \dfrac{|\vec{w} \cdot x_i + b|}{\|\vec{w}\|} = \dfrac{1}{\|\vec{w}\|}$

Optimization: $\min\limits_{\vec{w},b} \dfrac{1}{2}\|\vec{w}\|^2$ subject to $y_i(\vec{w} \cdot x_i + b) \geq 1, \forall i \in [1, m]$

Mohri, 2012, *Foundations of Machine Learning*

Support vector machines (SVMs)

Non-separable case (slack SVMs)



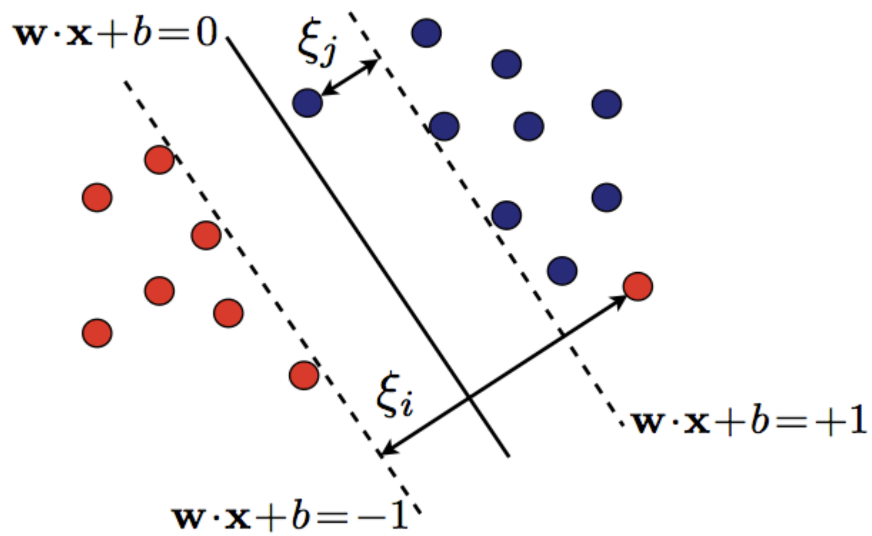
Optimization: $\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C\sum_{i=1} \xi_i^p$

subject to $y_i(\vec{w}\cdot x_i + b) \geq 1 - \xi_i, \xi_i \geq 0, i \in [1, m]$

Mohri, 2012, *Foundations of Machine Learning*

Support vector machines (SVMs)

Non-separable case (slack SVMs)



Optimization: $\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C\sum_{i=1}\xi_i^p$

subject to $y_i(\vec{w}\cdot x_i + b) \geq 1 - \xi_i, \xi_i \geq 0, i \in [1, m]$

- Standard margin

Mohri, 2012, *Foundations of Machine Learning*

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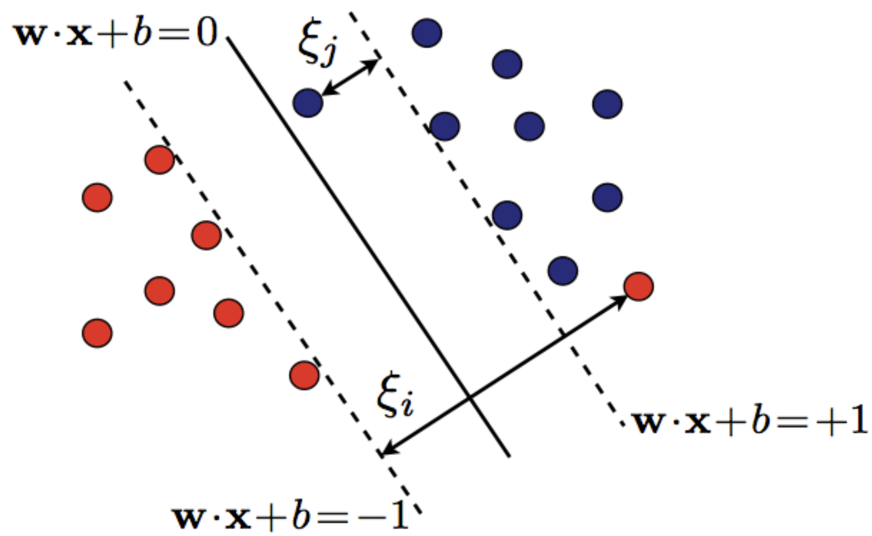
Non-separable case (slack SVMs)



Optimization: $\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C\sum_{i=1} {\xi_i}^p$

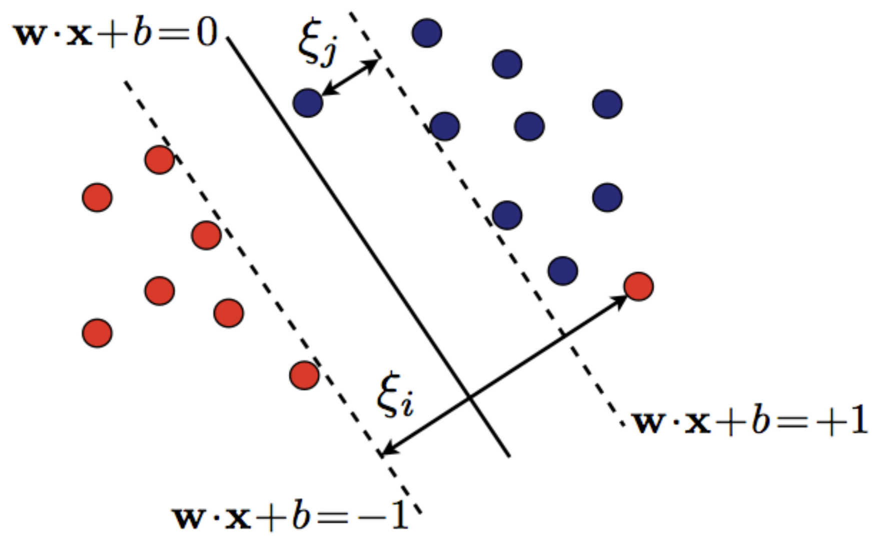
subject to $y_i(\vec{w}\cdot x_i + b) \geq 1 - \xi_i, \xi_i \geq 0, i \in [1, m]$

- Standard margin
- How wrong a point is (slack variables)

Mohri, 2012, *Foundations of Machine Learning*

Support vector machines (SVMs)

Non-separable case (slack SVMs)



Optimization: $\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C \sum_{i=1} \xi_i^p$

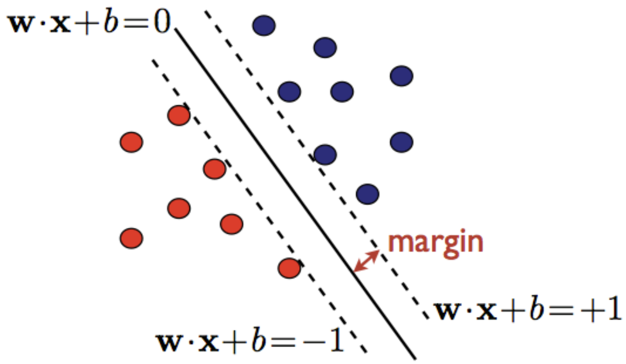
subject to $y_i(\vec{w} \cdot x_i + b) \geq 1 - \xi_i, \xi_i \geq 0, i \in [1, m]$

- Standard margin
- How wrong a point is (slack variables)
- Tradeoff between margin and slack variables

Mohri, 2012, *Foundations of Machine Learning*

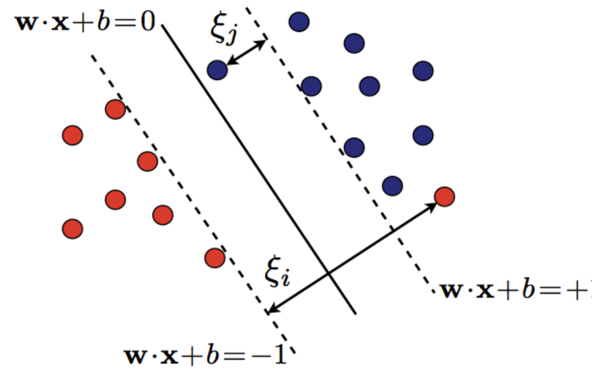
Support vector machines (SVMs)

Separable case



$$\min_{\vec{w},b} \frac{1}{2}\|\vec{w}\|^2$$

Non-Separable case



$$\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C\sum_{i=1}\xi_i^p$$

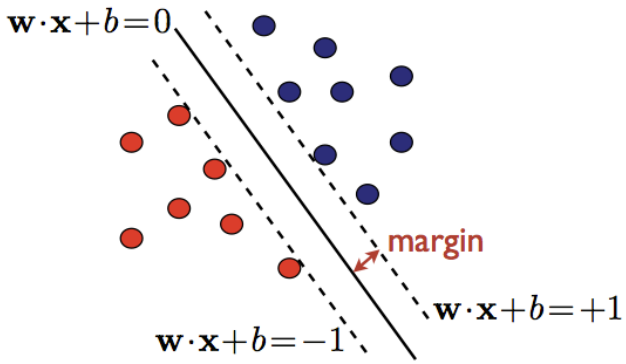
$$\mathcal{L} = \sum_{i=1}^{m}\alpha_i - \frac{1}{2}\sum_{i,j=1}^{m}\alpha_i\alpha_j y_i y_j(\mathbf{x_i}\cdot\mathbf{x_j})$$

Same objective function in the form of dual optimization problem

Mohri, 2012, *Foundations of Machine Learning*

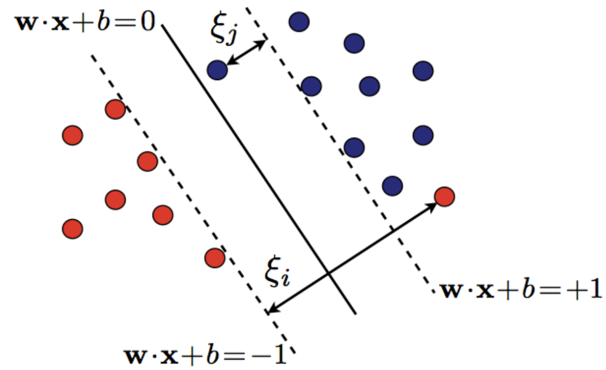
Support vector machines (SVMs)

Separable case



$$\min_{\vec{w},b} \frac{1}{2}\|\vec{w}\|^2$$

Non-Separable case



$$\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C\sum_{i=1} \xi_i^p$$

$$\mathcal{L} = \sum_{i=1}^{m} \alpha_i - \frac{1}{2}\sum_{i,j=1}^{m} \alpha_i\alpha_j y_i y_j (\mathbf{x_i}\cdot\mathbf{x_j})$$

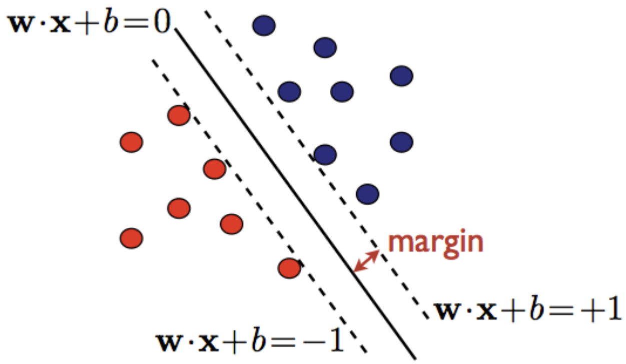
Same objective function in the form of dual optimization problem

This dot product is the basis for the Kernel method: $K : \mathcal{X}\times\mathcal{X}\to\mathbb{R}$

Mohri, 2012, *Foundations of Machine Learning*

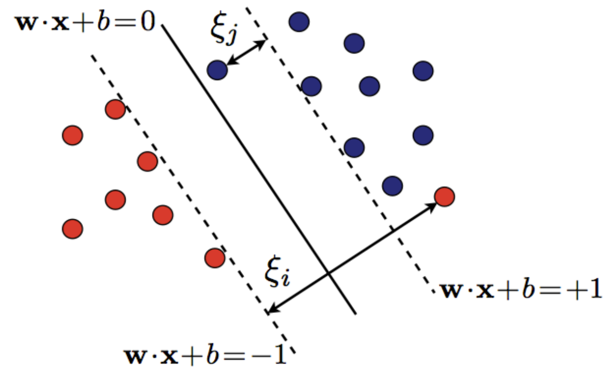
Support vector machines (SVMs)

Separable case



$$\min_{\vec{w},b} \frac{1}{2}\|\vec{w}\|^2$$

Non-Separable case



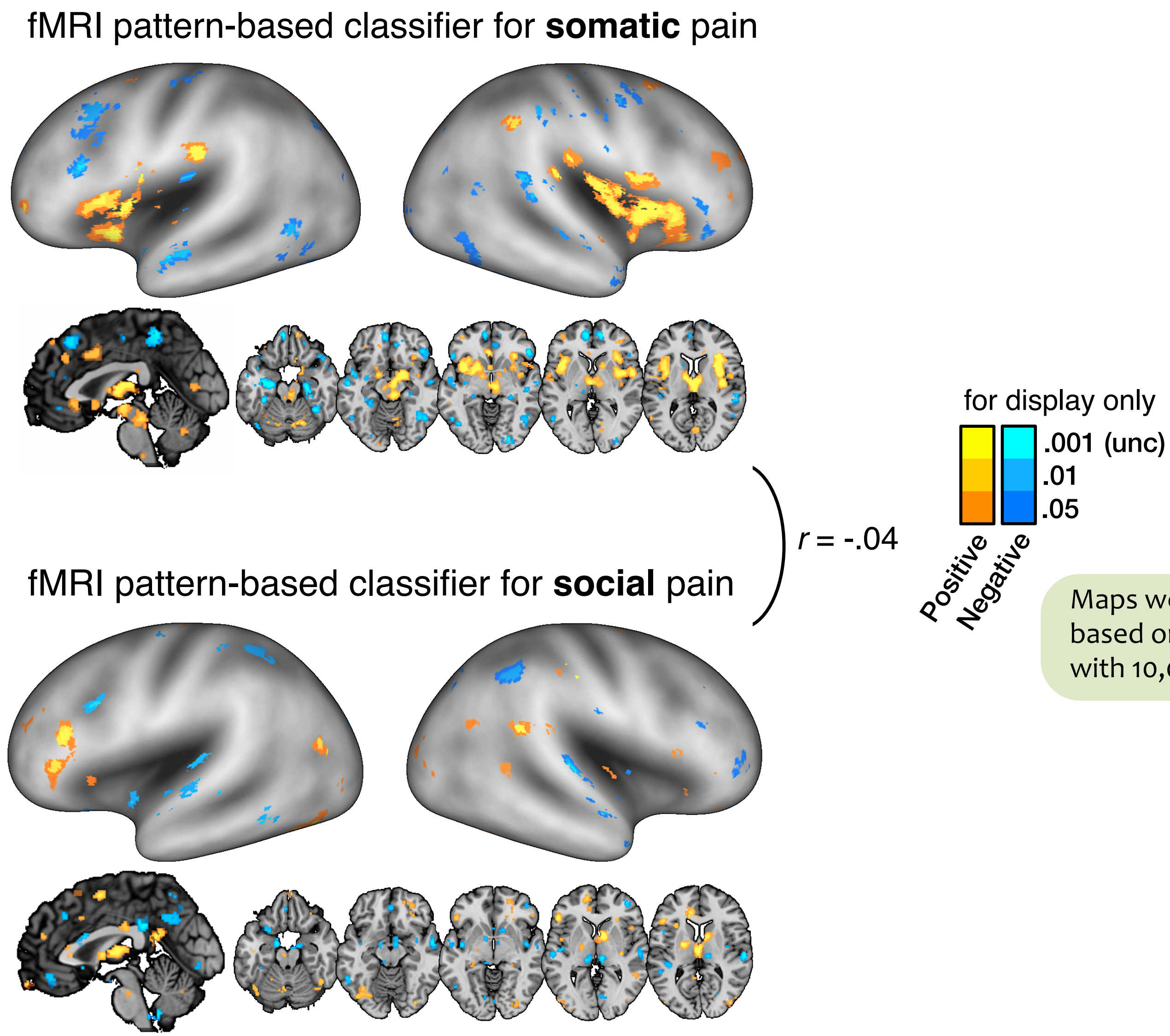
$$\min_{\vec{w},b,\xi} \frac{1}{2}\|\vec{w}\|^2 + C\sum_{i=1} \xi_i^p$$

Generalization error bound: $R(h) \leq \hat{R}_\rho(h) + 2\sqrt{\frac{r^2\Lambda^2/\rho^2}{m}} + \sqrt{\frac{\log\frac{1}{\delta}}{2m}}$

- does not depend directly on *the dimension of the feature space*, but *only on the margin*.
- Therefore, **SVMs** has a *theoretical guarantee* of bypassing the *curse of dimensionality*, and works well in practice.

Mohri, 2012, *Foundations of Machine Learning*

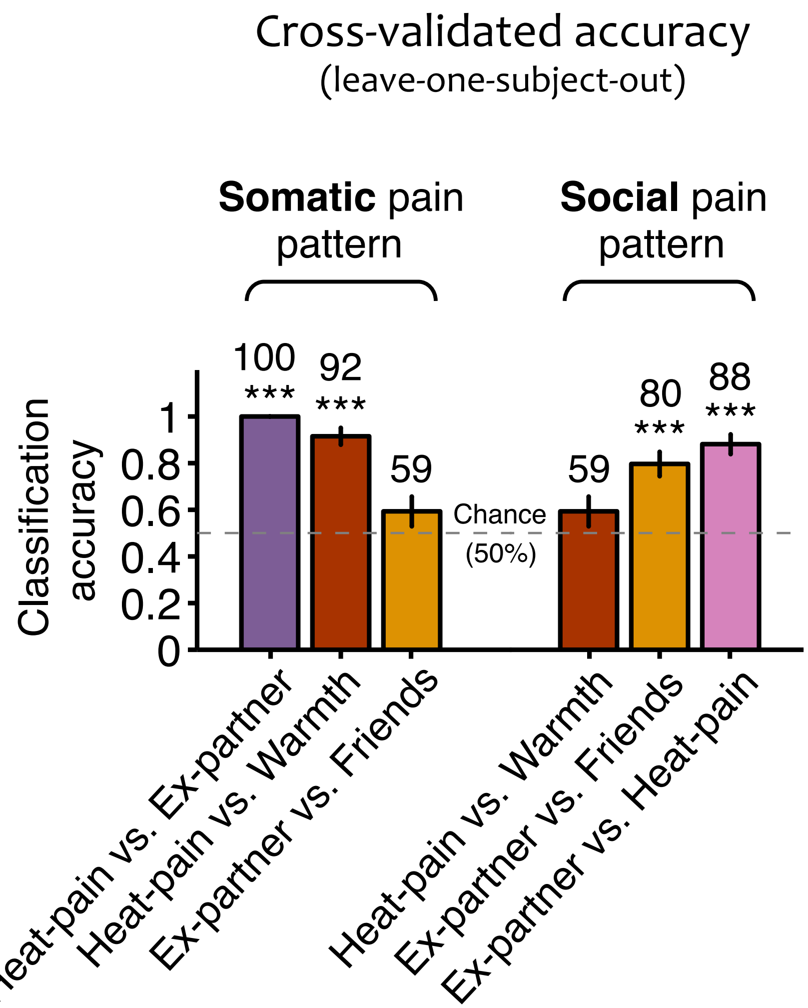
MVPA results I: Whole-brain SVMs



Maps were thresholded based on bootstrap tests with 10,000 iterations.

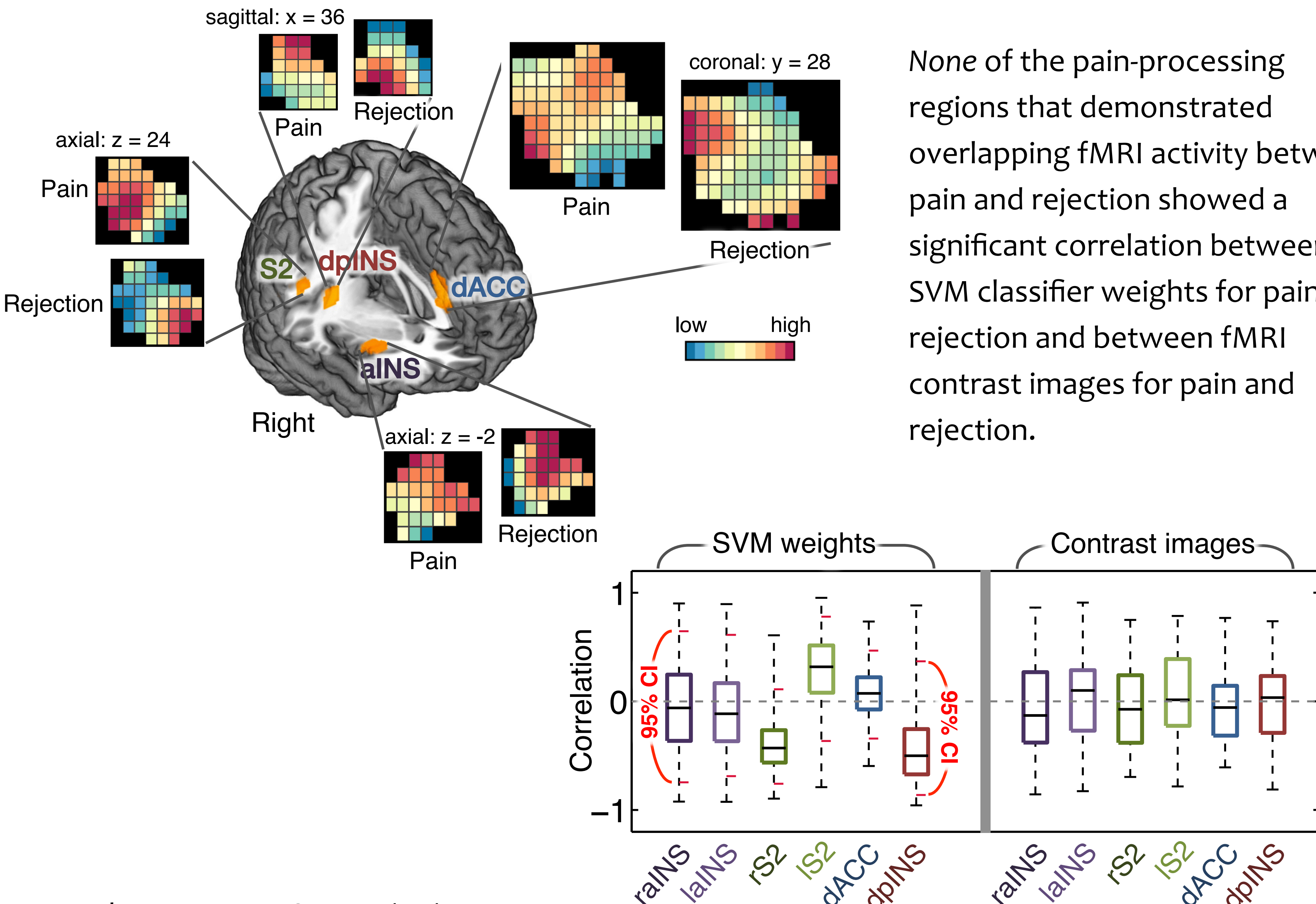
Woo et al., 2014, *Nature Communications*

MVPA results I: Whole-brain SVMs



Woo et al., 2014, *Nature Communications*

MVPA results II: pattern similarity

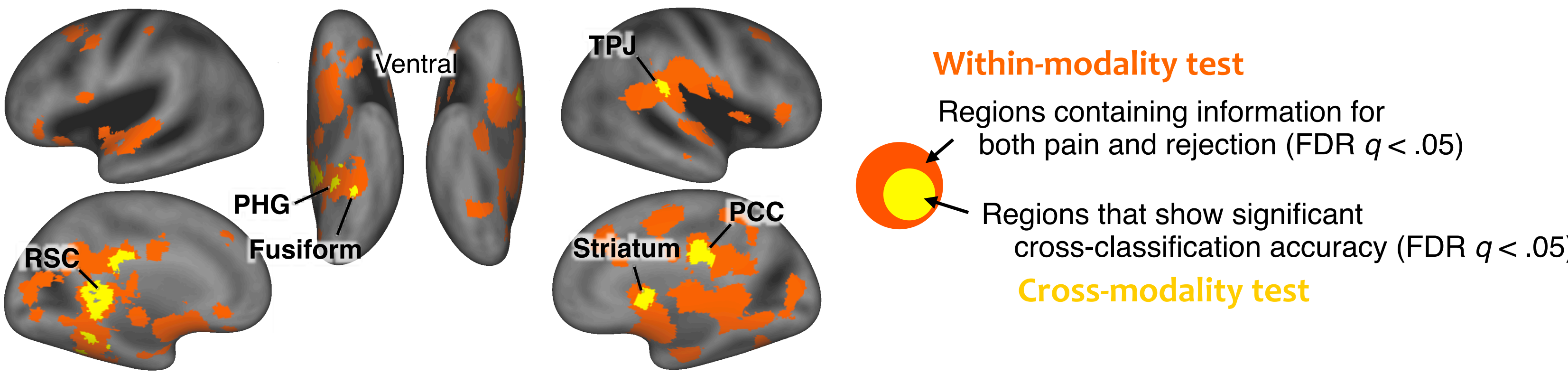


None of the pain-processing regions that demonstrated overlapping fMRI activity between pain and rejection showed a significant correlation between SVM classifier weights for pain and rejection and between fMRI contrast images for pain and rejection.

Woo et al., 2014, *Nature Communications*

MVPA results III: cross-prediction using searchlight

Results with 6-mm radius spherical searchlights around center voxels



None of the regions that showed significant cross-classification (pain -> rejection, rejection -> pain) between pain and rejection (colored *yellow*) were primary targets for nociceptive afferents.

Woo et al., 2014, *Nature Communications*

Study1: Conclusion

1. These findings demonstrate separate representations for pain and rejection, despite common fMRI activity at the gross anatomical level.

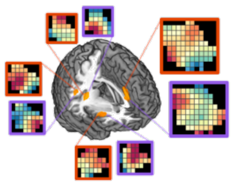
2. These findings directly challenge the shared-representation theory between physical and social pain.

3. Rather than co-opting pain circuitry, rejection involves distinct neural processes that can be identified and targeted in human.

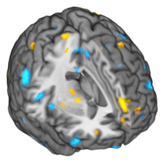
Woo et al., 2014, *Nature Communications*

Roadmap

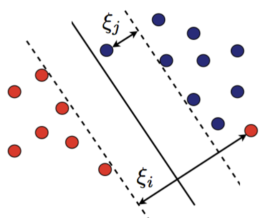
Physical pain
vs. social rejection



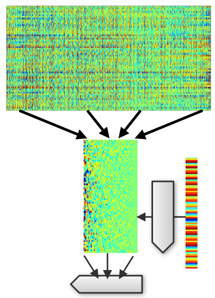
**Somatic vs.
vicarious pain**



SVMs



LASSO-PCR



Useful grouping in machine learning

	discrete	*continuous*
supervised	**classification**	**regression**
unsupervised	**clustering**	**dimensionality reduction**

Useful grouping in machine learning

	discrete	*continuous*
supervised	**classification**	**regression**
unsupervised	**clustering**	**dimensionality reduction**

Classification

SVM, naïve Bayes, logistic regression, boosting

- Two-class, multiclass emotion classification (pain vs. rejection)

Slides adapted from *Jordan Boyd-Graber*

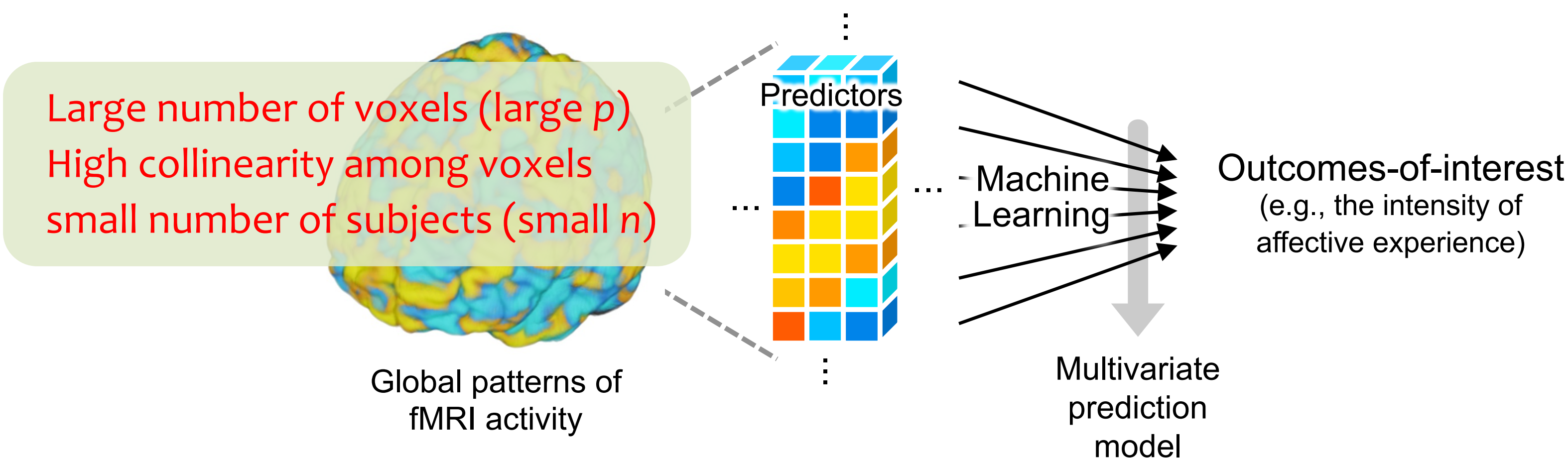
Useful grouping in machine learning

	discrete	*continuous*
supervised	**classification**	**regression**
unsupervised	**clustering**	**dimensionality reduction**

Regression

Linear Regression, Ridge Regression, Lasso

e.g., predicting the intensity of affective experience



Slides adapted from *Jordan Boyd-Graber*

Useful grouping in machine learning

	discrete	*continuous*
supervised	**classification**	**regression**
unsupervised	**clustering**	**dimensionality reduction**

Dimensionality Reduction

PCA, ICA, ...

Slides adapted from *Jordan Boyd-Graber*

Useful grouping in machine learning

	discrete	*continuous*
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unsupervised	**clustering**	**dimensionality reduction**

LASSO-PCR
= PCA + lasso regression

Two-step efforts to obtain stable predictive weights and reduce *variance* of the model performance

1. Dimension reduction (PCA)
2. Penalized regression (Lasso)

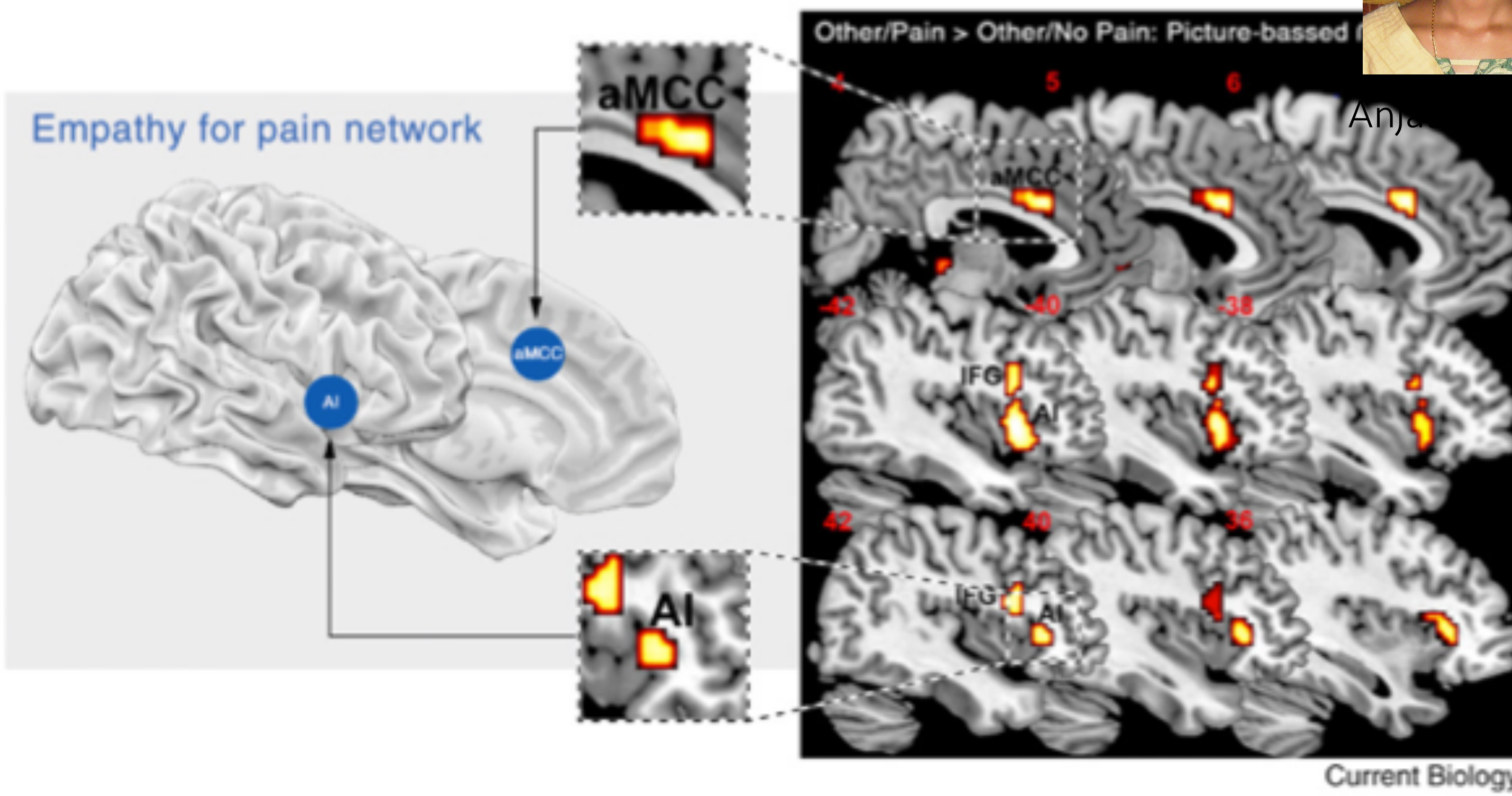
in Wager et al., 2011, *J Neuro*; Wager et al., 2013, *NEJM*

Shared neural representations between somatic vs. vicarious pain

Empathy for pain tasks

- **picture-based:** e.g., Pictures of hands/feet in painful vs. non-painful situations
- **cue-based:** e.g., Painful and non-painful electric stimulation of self and other

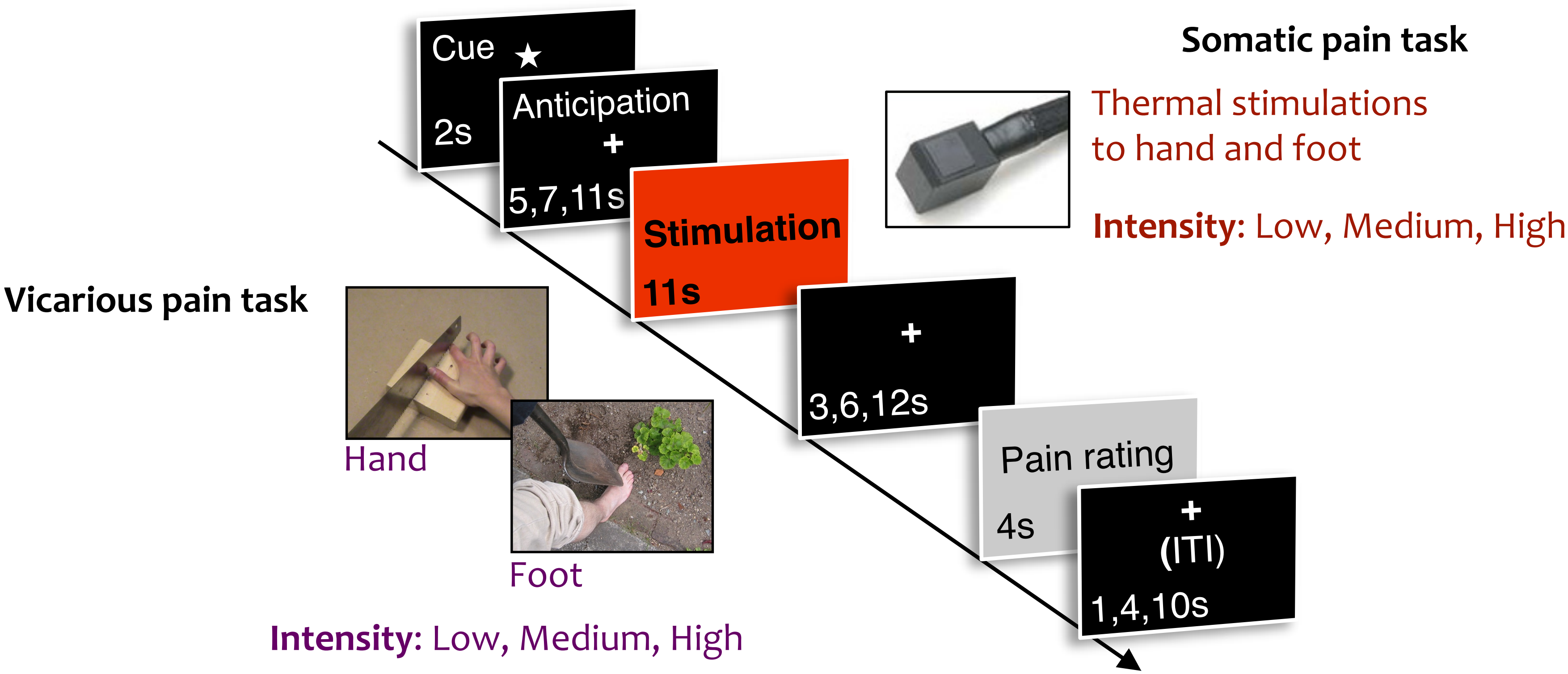
Anja hnan



Singer & Klimecki, 2014, *Current Biology*

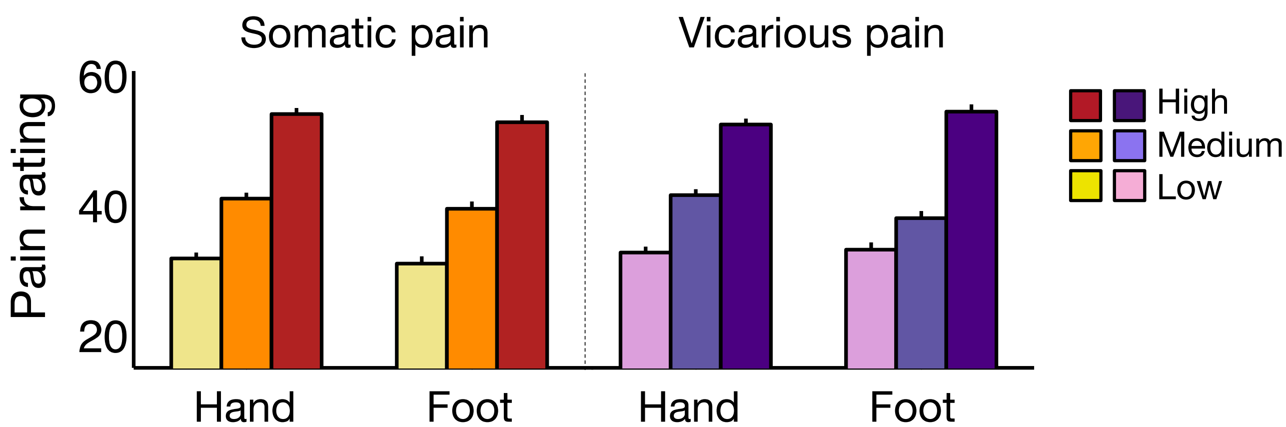
Study2: Methods

- We conducted an fMRI experiment (N = 30) with somatic and vicarious pain tasks.
- In the somatic pain task, we administered thermal stimulations to hand and foot with low (46°C), medium (47°C), and high (48°C) temperatures.
- In the vicarious pain task, we showed pictures that contain painful events (low, medium, and high intensity normed by independent 20 participants) on hands and feet.

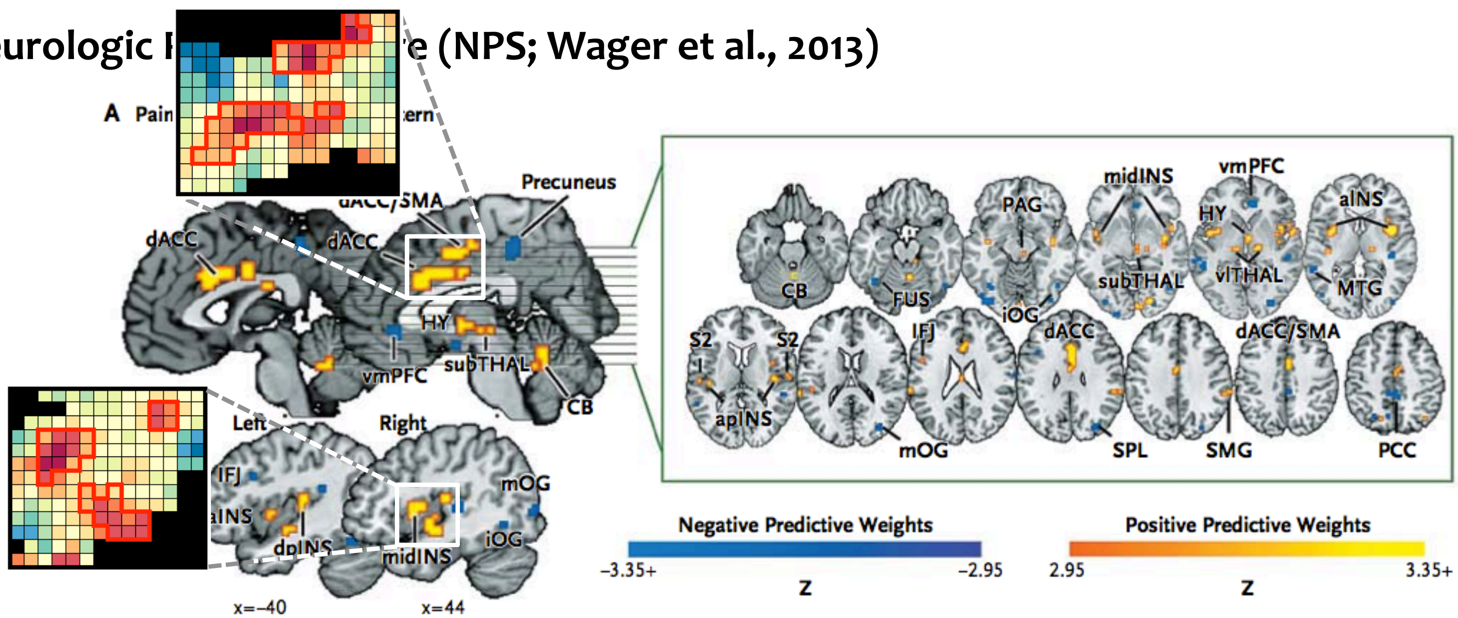


Krishnan, Woo et al., submitted

Results1: Behavioral ratings and NPS response



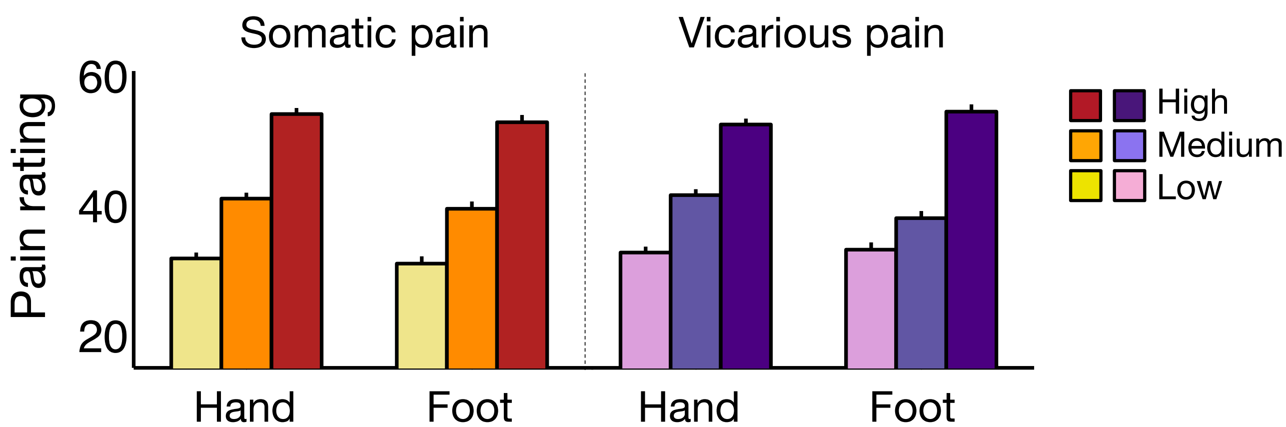
Neurologic P… …e (NPS; Wager et al., 2013)

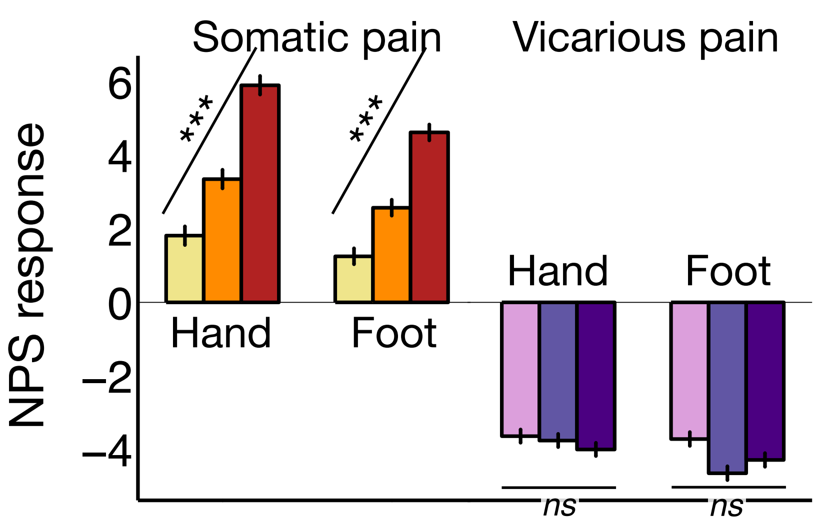


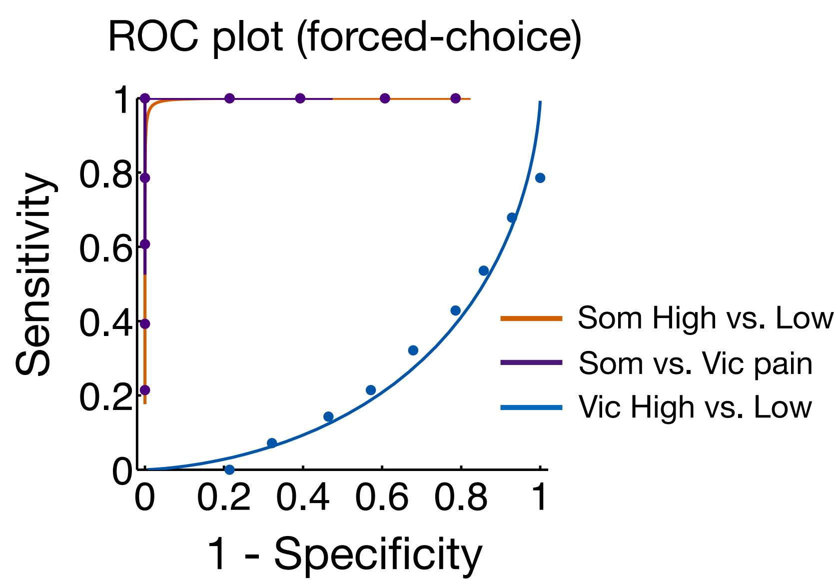
Wager et al., 2013, *NEJM*

Krishnan, Woo et al., submitted

Results1: Behavioral ratings and NPS response



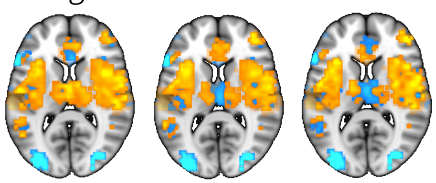




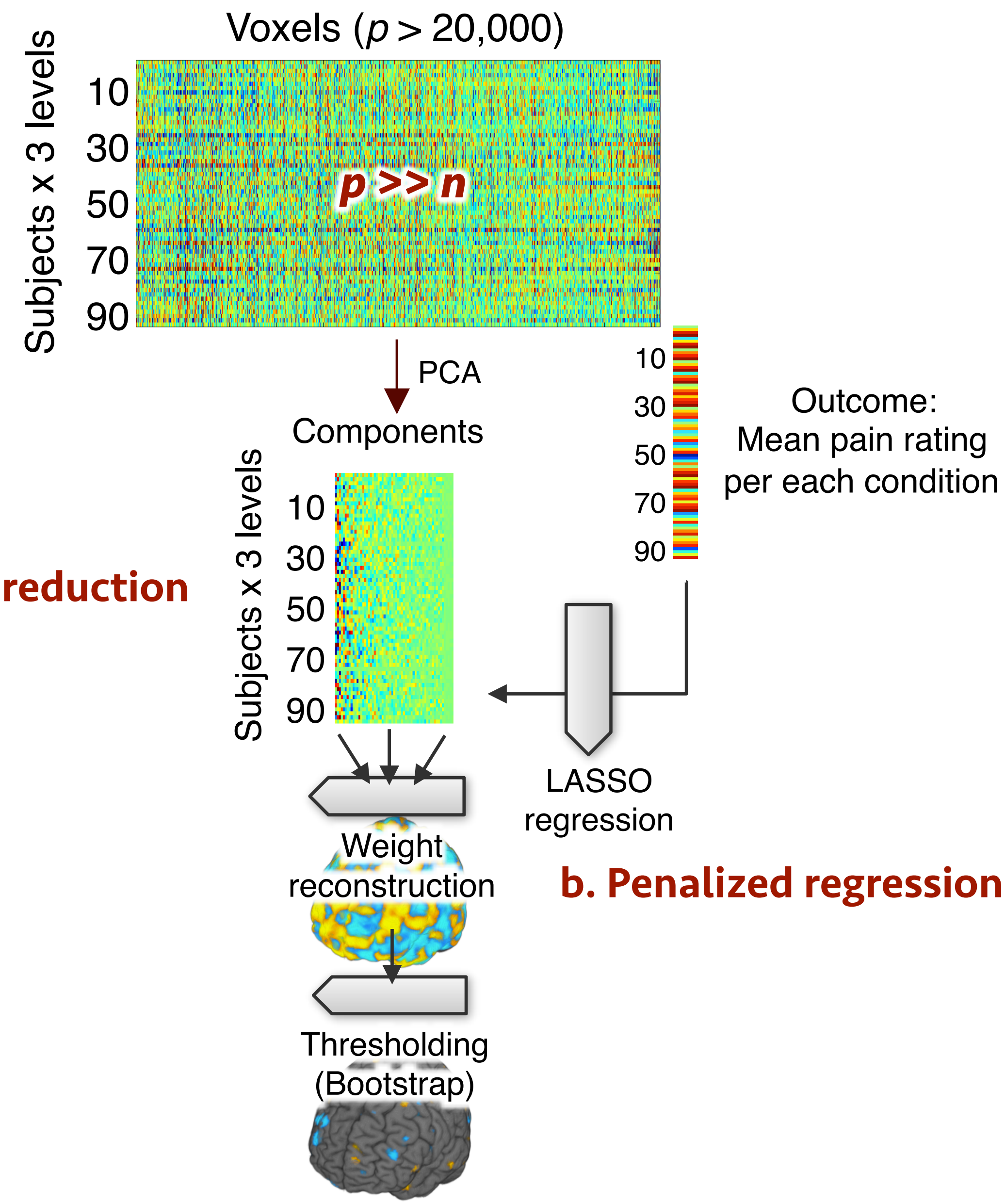
Krishnan, Woo et al., submitted

Results2: Vicarious pain signature (VPS) using LASSO-PCR

Overview of LASSO-PCR algorithm

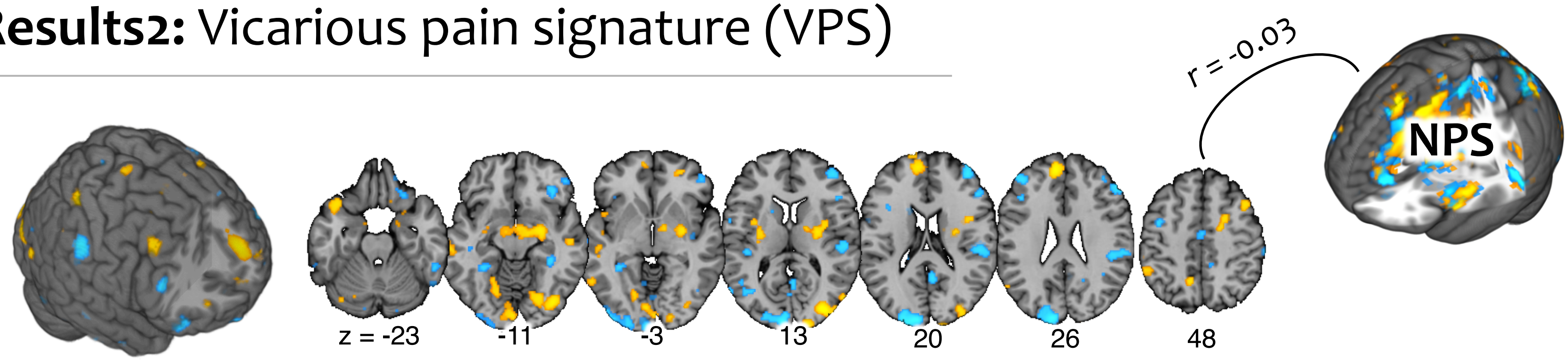


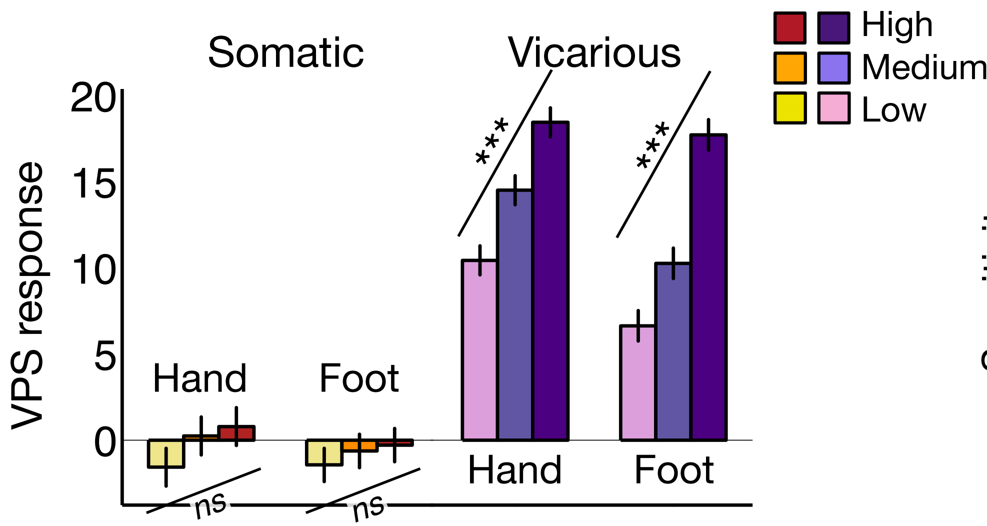
a. Dimension reduction

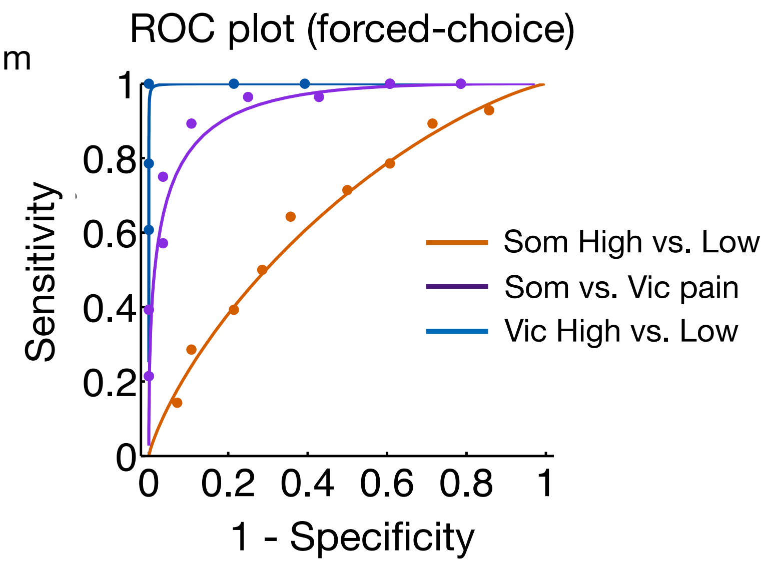


*Obtained unbiased estimates of prediction performance using **leave-one-subject-out cross-validation***

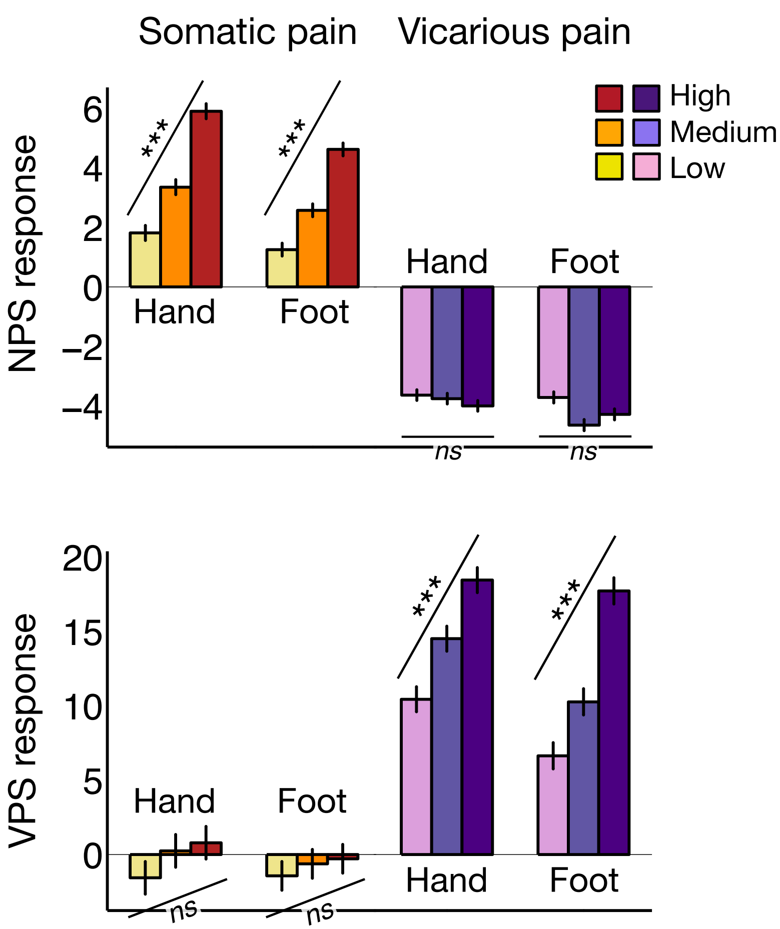
Results2: Vicarious pain signature (VPS)







Study2: Conclusion

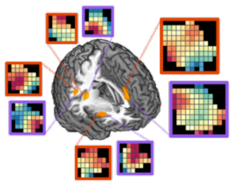


1. We were able to identify dissociable fMRI patterns that accurately track the intensity of first-person and vicarious pain using the LASSO-PCR algorithm.

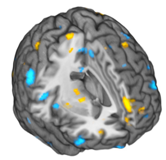
2. These findings challenge the current theory that empathizing with other's pain relies on the first-person, somatic *pain* system in the brain.

Roadmap

Physical pain
vs. social rejection

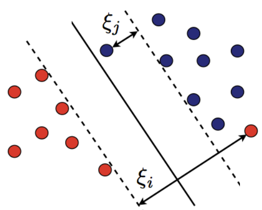


Somatic vs.
vicarious pain

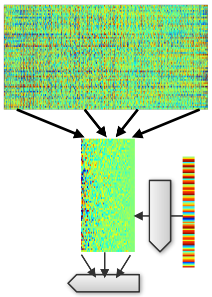


CANLab
MatLab Tools

SVMs

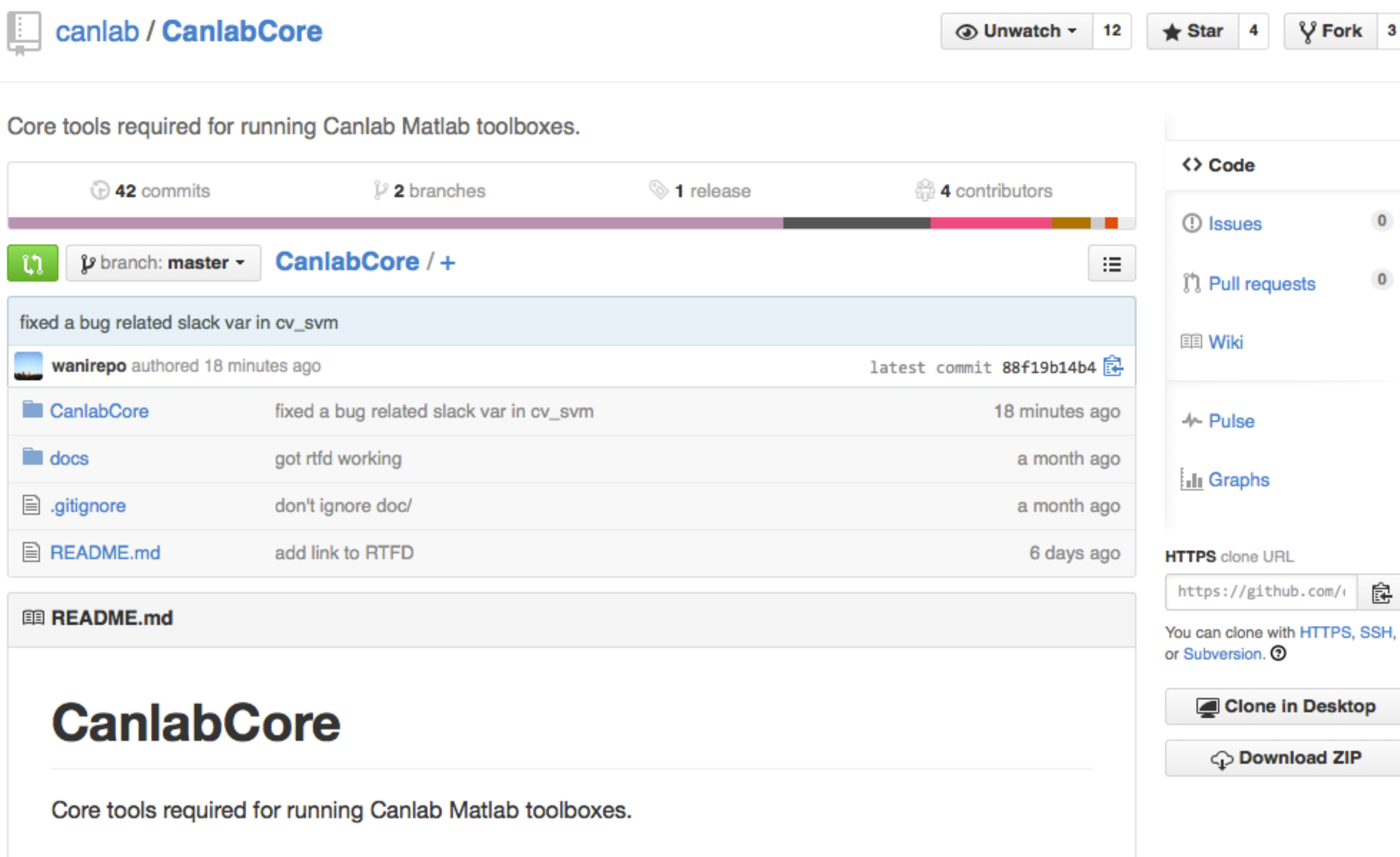


LASSO-PCR



MVPA with CANLab tools

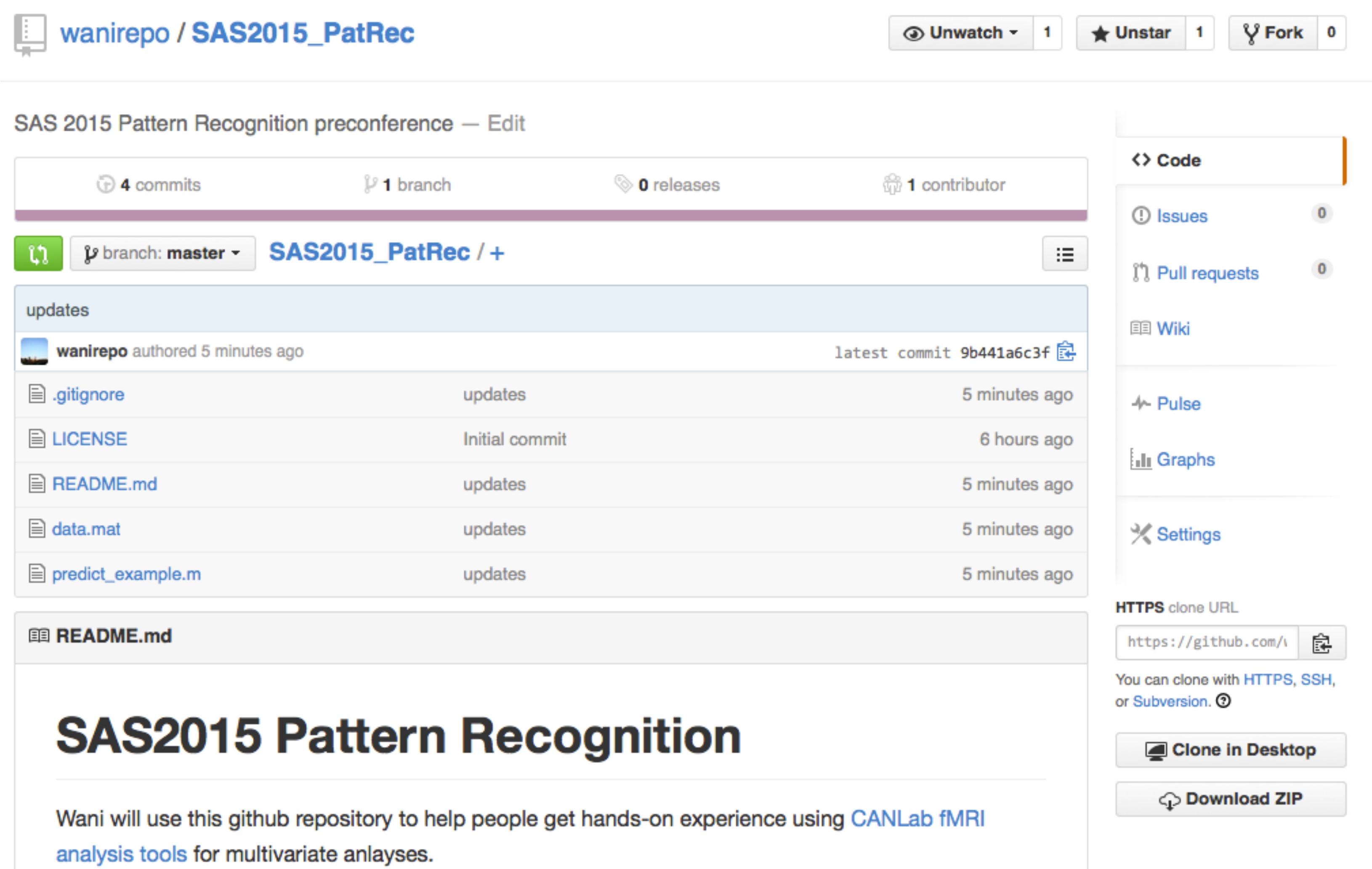
CANLab Github (https://github.com/canlab/CanlabCore)



MVPA with CANLab tools

I made a **Github** and **Hackpad** for this part

- Github: https://github.com/wanirepo/SAS2015_PatRec
- Hackpad: https://hackpad.com/SAS-2015-Pattern-Recognition-nH4ypQDZx1i



Thank you

all for listening!

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Tal Yarkoni