Module 30:
MVPA Example

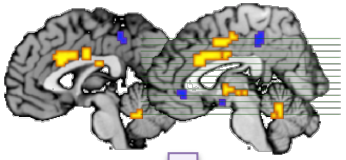
Pain Biomarkers

- Pain is an important health problem affecting the quality of life in a large segment of the population.
  - It is usually measured using self-reports.

- The goal is to define robust and meaningful fMRI-based biomarkers for physical pain that can augment reported pain as outcome measures.

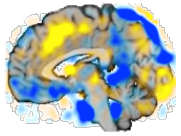
Illustration

Biomarker Pattern



$\underline{w} = (w_1, \ldots . w_V)$

Brain Activity



Cross-product

Biomarker Response

5.3

$\underline{x} = (x_1, \ldots . x_V)$

$y = \underline{w}^T \underline{x}$

Statistical Learning

- We develop the biomarker using data from a study of thermal pain (n=20).
  - Statistical learning techniques are used to identify spatial patterns of fMRI activity that accurately and specifically predict physical pain at the individual level.

- The development of this method entails:
  - defining appropriate features;
  - choosing a classifier;
  - training and testing the classifier; and
  - validating results on new data sets.

Example

- Participants (n=20) received a series of thermal stimulations for 12 trials at each of four intensities: innocuous warmth and three levels of increasingly painful heat.
  - Each trial consisted of separate periods of anticipation, thermal pain and pain recall.
  - The outcome measure was a trail-specific pain rating reported on a continuous visual analogue scale.

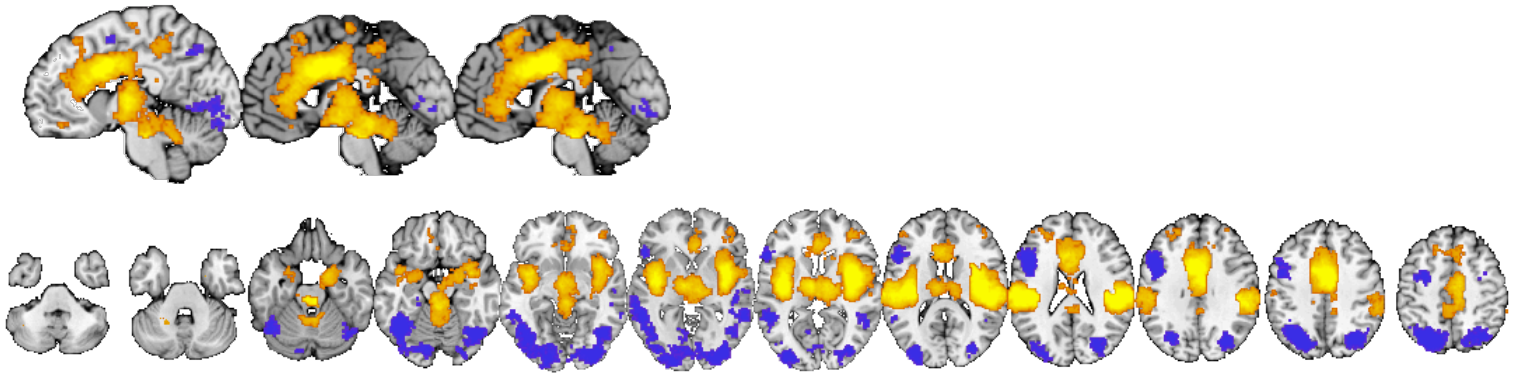
Cue	Pain	ISI 1	Rating	ISI2
8 s	10 s	14 s	4 s	10 s

Performing MVPA

- The process of performing MVPA follows a series of steps:
  - Defining features and classes
  - Feature selection
  - Choosing a classifier
  - Training and testing the classifer
  - Examining results

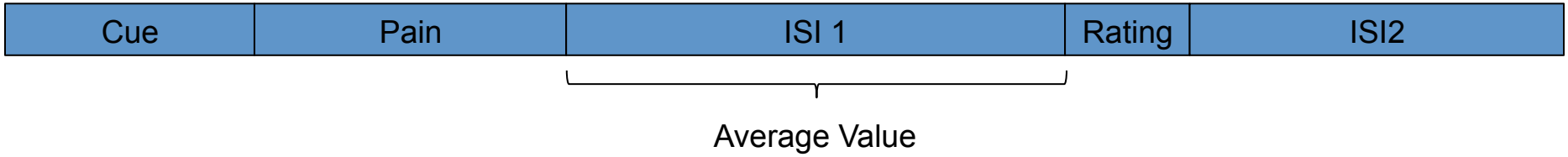
Feature Selection

- Voxels within pain-related brain regions were selected based on prior literature.
  - Performed a meta-analysis of 224 previous studies to select ~16,000 voxels associated with pain.



Data Averaging I

- Time courses immediately following the end of heat application were included in the analysis;
  - Averaged brain activity at each temperature for each participant over a 14s post-stimulus window.
  - At each temperature we obtained 12 maps and 12 responses for each subject.



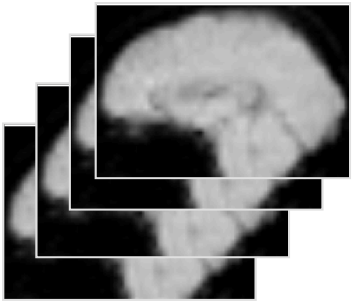
Data Averaging II

- Data were averaged over repeated trials at each intensity level.
  - Averaged the 12 repetitions at each temperature for each participant to yield 4 unique maps per subject.
  - Averaged pain response for each participant in each condition.

Maps

Responses

Subject *i*

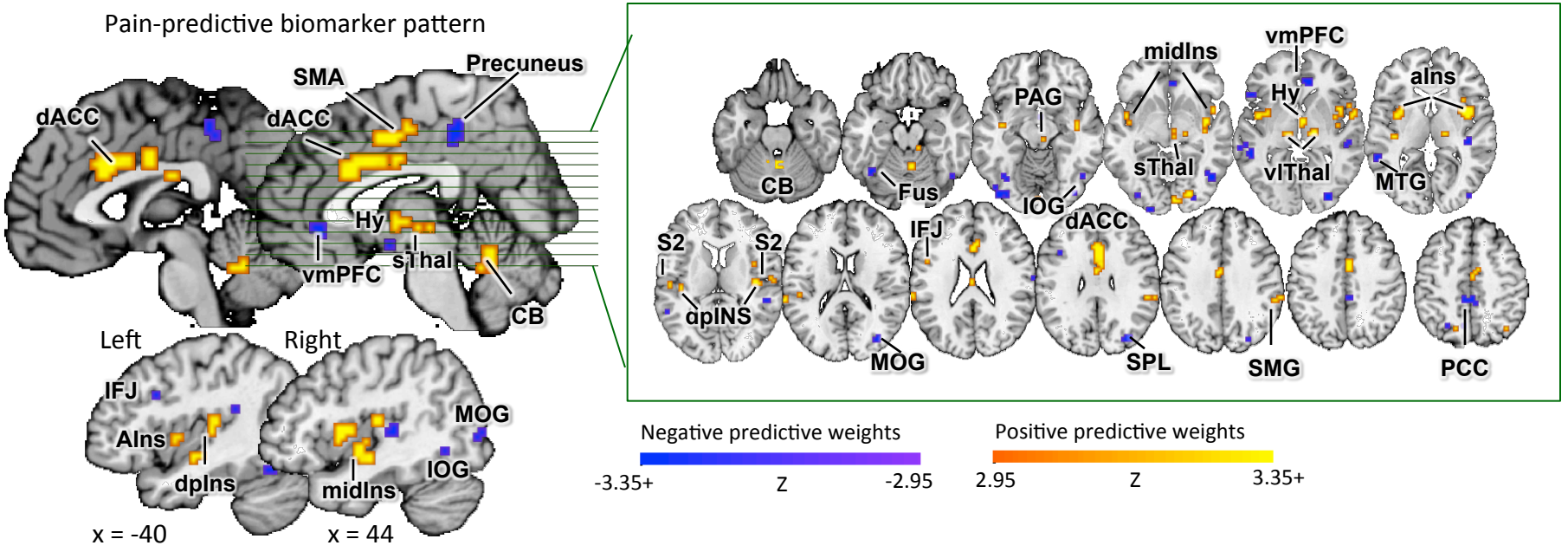


Machine Learning

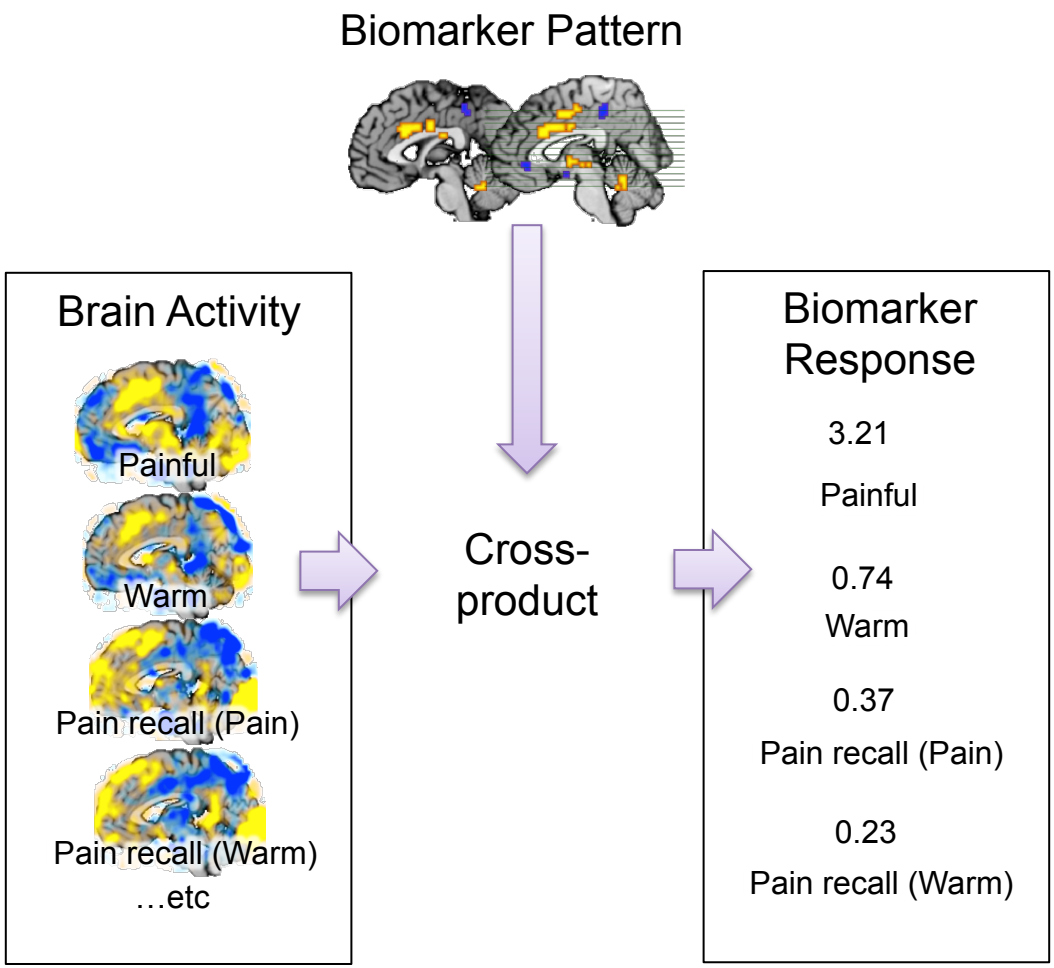
- Classifier:
  - LASSO-PCR
  - Other classifier techniques gave comparable results.

- Training and testing:
  - Used leave-one-subject out cross-validation.

Weight Maps

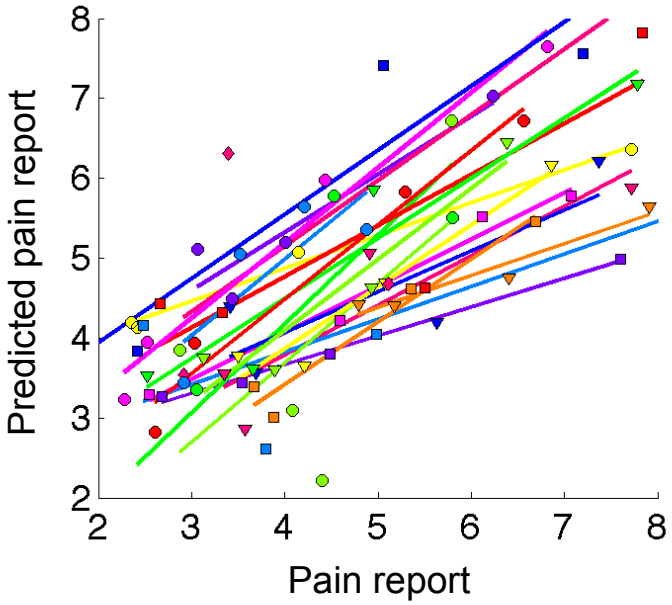

Pain-predictive biomarker pattern
dACC
SMA
Precuneus
dACC
Hy
sThal
vmPFC
CB
Left
Right
IFJ
AIns
dpIns
midIns
MOG
lOG
x = -40
x = 44
CB
Fus
PAG
midIns
vmPFC
Hy
aIns
sThal
vlThal
MTG
lOG
dACC
S2
S2
IFJ
dpINS
MOG
SPL
SMG
PCC
Negative predictive weights
-3.35+
Z
-2.95
Positive predictive weights
2.95
Z
3.35+

Analysis

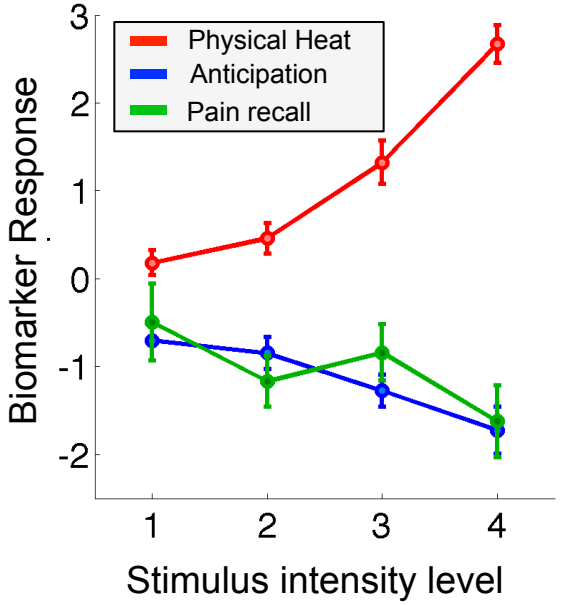

Biomarker Pattern
Brain Activity
Painful
Warm
Pain recall (Pain)
Pain recall (Warm)
…etc
Cross-product
Biomarker Response
3.21
Painful
0.74
Warm
0.37
Pain recall (Pain)
0.23
Pain recall (Warm)

Results

Cross-validated prediction of pain



Pain vs. other affective events



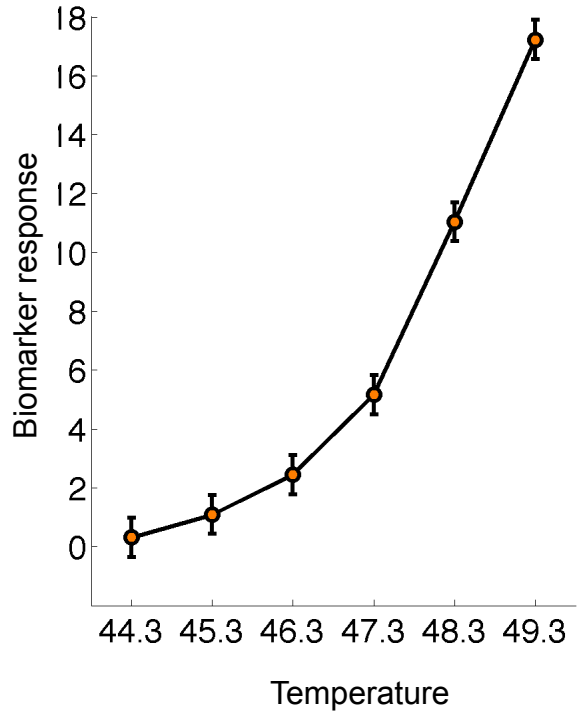
Study II

- Participants (n=33) received a series of 75 thermal stimulations across six different temperatures.

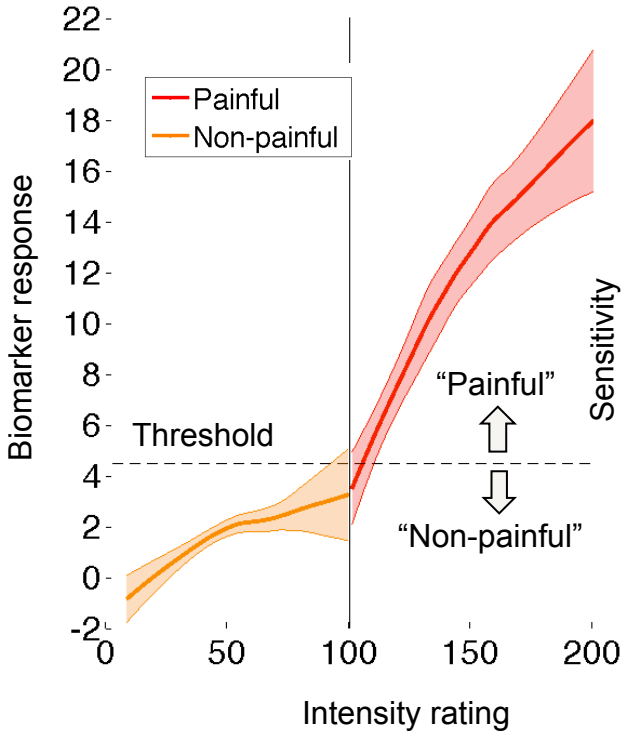
- After each stimulus, participants rated whether it was painful or not.
  - If non-painful, intensity was rated on a 100-point scale ranging from “no sensation at all” to “very warm but not yet painful.”
  - If painful, intensity was rated on a 100-point scale ranging from “no pain” to “worst imaginable pain.”

Results – Study II

Biomarker response by condition



Response by reported intensity



An fMRI-Based Neurologic Signature of Physical Pain

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End of Module

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