Integrating MVPA and Connectivity in a Multiple Constraint Network to Bootstrap Brain Models

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Highlights

- We introduce a data-driven method for bootstrapping biologically plausible models
- Mutually-constraining analyses find models that best fit all available evidence
- Functional connectivity constraints improved MVPA accuracy
- Models simulated lesion-site appropriate impairment
- Models support direct tests of causation between connectivity and representation

A presentation of this poster can also be found in the CNS2020 Data Blitz, Session 3, Talk 6.

Background

Models of Cognitive Processing in a Dynamic Brain

- Contemporary models assume cognitive processing occurs in dynamic brain networks
- Some regions appear to be functionally specialized by virtue of signals they process
  - Determined by how they are connected
  - E.g., populations receiving visual input will be involved in visual processing
- Brain-based models are aimed at identifying and explaining interactions among these functional networks

How are Brain-Based Cognitive Models Generated?

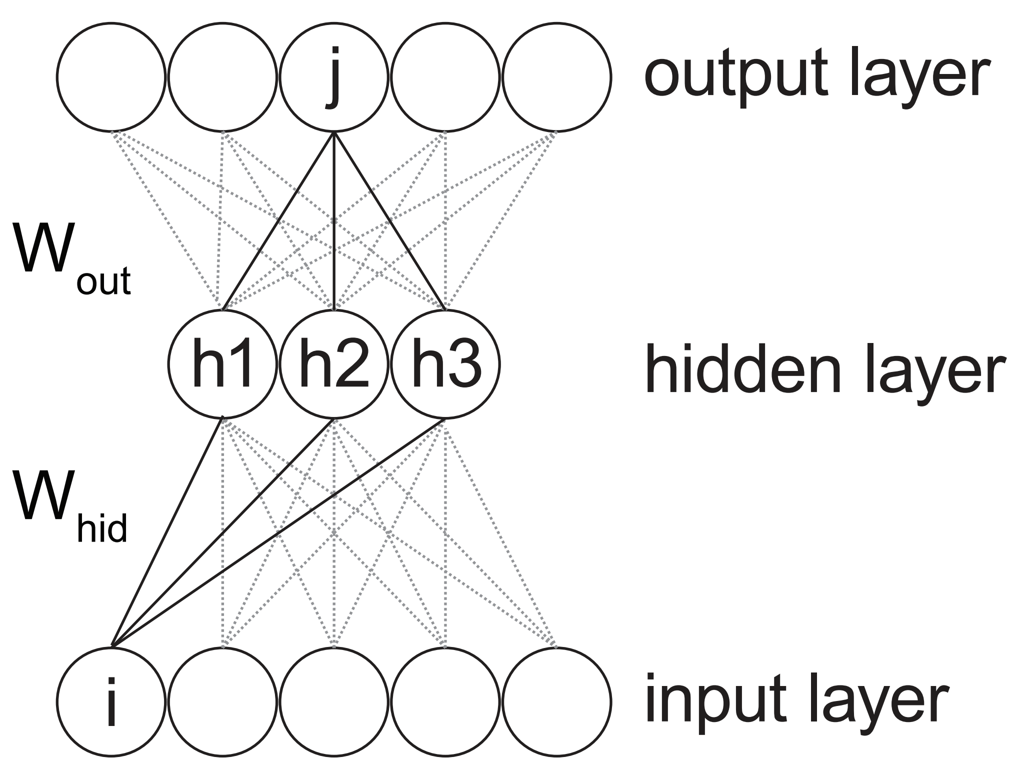
- Brain-based models are largely informed by traditional univariate methods (e.g. SPM)
  - Compare observed voxel time courses in isolation to canonical HRF; measure fit
- Univariate models ignore potentially informative relationships with other regions
  - If a region is only conditionally involved in a task, it will have poor fit using univariate GLM; weak test statistic fails to detect involvement in task
- MVPA accounts for holistic patterns not accounted for in GLM
  - MVPA typically only performed within ROIs informed by univariate analyses
- Neither GLM nor MVPA analyze data as a network
- Connectivity studies (e.g., fc-rsMRI) analyze data as a network but network elements are identified using univariate methods

There is a disconnect between the belief that cognitive processes entail interacting brain networks, and contemporary analytic methods that ignore or fail to take full advantage of global network dynamics

Multiple Constraint Network

Our solution is to leverage whole-brain MVPA and Connectivity in a single analytic approach

- Previous work [1] showed autoencoders can be used to encode functional connectivity
  - Autoencoders capture correlations among encoded features
  - Compression of pattern encodings performs a nonlinear Principle Components Analysis
- Implementations of autoencoders can be extended to include additional functionality
- Multivariate pattern analyses (MVPA) often employ PCA as a data reduction technique
- Suggests a single model containing both an autoencoder and MVPA classifier
  - Autoencoder component encodes functional connectivity from activity patterns
  - MVPA classifier learns categories associated with activity patterns
  - Both category and functional connectivity encoded in the same model
- MVPA classifications will depend on the weights that also encode functional connectivity
- Model performance improves with training that updates weights
  - Weight updates that affect classification accuracy also affect functional connectivity and vice versa



An autoencoder is a network that learns the set of weights {W_{hid}, W_{out}} that allow it to reproduce a pattern in the input layer among the corresponding units in the output layer

The task is made challenging by the fact that the input pattern must be transmitted through a much smaller hidden layer, forcing the network to learn a compressed encoding of the input

These networks consequently learn a PCA representation of the data

The predictive relationship (i.e., partial correlation) between elements **i** *and* **j** *can be estimated from the summed path weights between the corresponding input and output units, as in the figure above*

Functional Neuroimaging Procedures

Multisensory Imagery Task

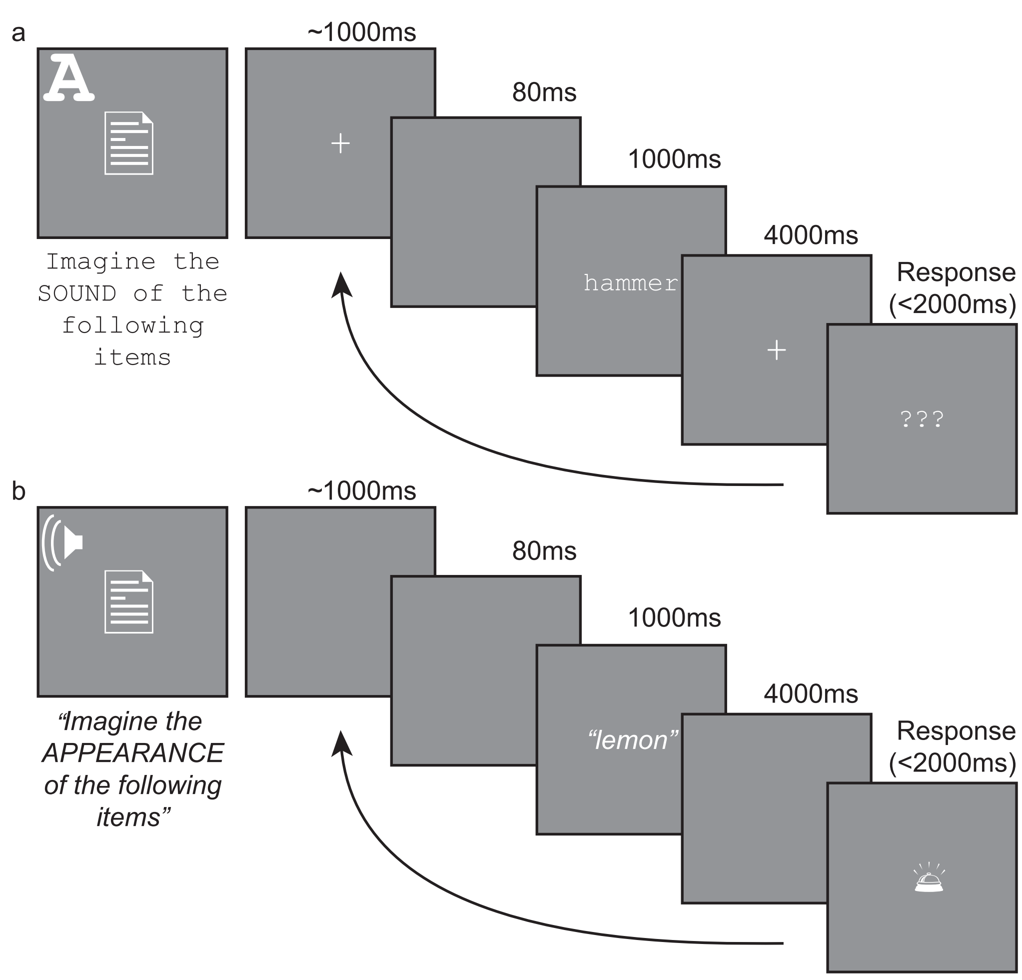
- 11 participants imagined concepts from three manipulable object categories
  - Handheld Tools, Musical Instruments, Fruits & Vegetables
  - Imagery was with respect to each of the 5 senses, fully crossed
- Blocked design: 6 runs x 5 blocks/run x 8 trials/block

- Each block directed participants to imagine items from one of the three categories with respect to one of the five senses
  - The same category did not appear twice in a row within a run
  - All five sensorimotor imagery modalities were used exactly once per run
  - Instructions and stimuli presented either visually or auditorily (eyes closed)
    - Fully-crossed ***except*** visual imagery ***always*** presented auditorily and vice versa

Participants imagined a series of items from a single category (e.g., TOOLS) with respect to a single modality (e.g., SOUND). Instructions and stimuli were presented either visually (a) or auditorily (b)

Sound imagery always used visual presentation and visual imagery always used auditory presentation.

This was to minimize interference of e.g., visual perception on visual imagery



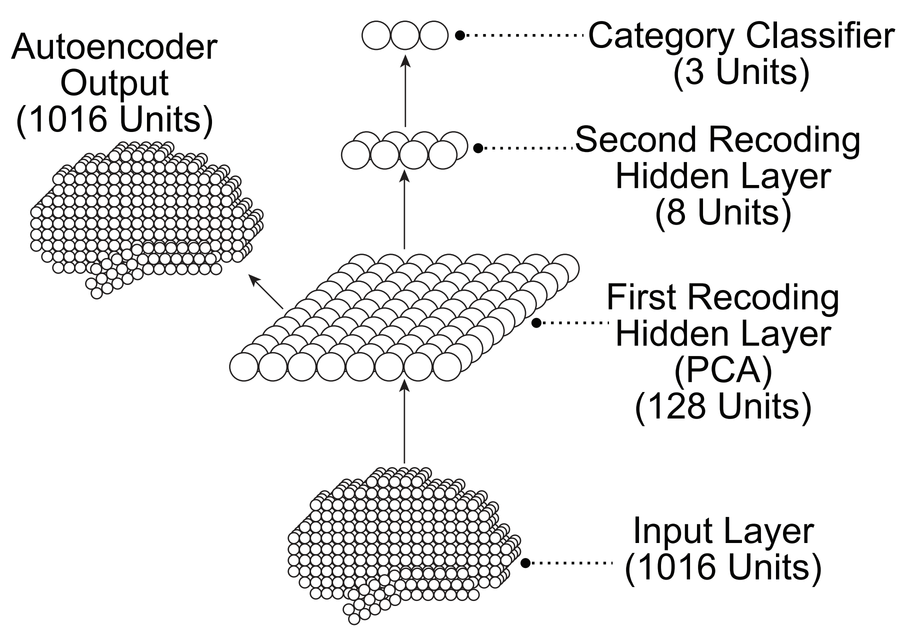
Machine Learning Procedures

Data Preparation

- BOLD time series coregistered to anatomical volumes processed in FreeSurfer
- T1w volume parcellated into 1000 cortical surface plus 16 subcortical volume ROIs
- Time series averaged over all functional voxels in each ROI
- Computed median signal in 6-second window following each trial onset within each ROI
  - Median signal across all ROIs used as the whole-brain activity pattern for that trial
  - 240 (trials) x 1016 (ROI) matrix of BOLD patterns per session
  - Each pattern tagged with respect to category (Tool, Instrument, Fruit)

Multiple Constraint Network Implementation

- Implemented in Python using *TensorFlow/Keras*
- Models comprise two intertwined modules: an Autoencoder and a Classifier
  - Autoencoder and Classifiers have their own output layers
  - Both Autoencoder and Classifiers share a common input layer
    - 1016-unit input layer to represent activity across all ROIs for each trial



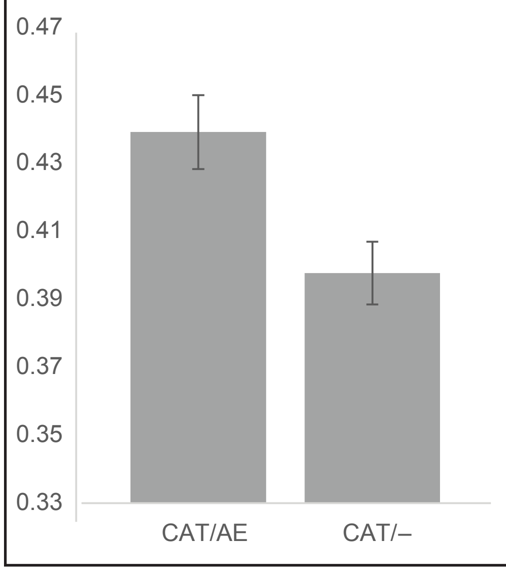
Multiple Constraint Network Training

- K-folds cross-validation
  - Randomly subdivides entire dataset into k folds of training and testing patterns
  - In each fold, some proportion (.8) used as training data and the remainder is witheld
  - At the end of training, test model on witheld validation set patterns
    - Assesses model's ability to generalize to new data
  - Across all K folds, each pattern used as a validation set pattern exactly once
- Each validation fold generates a unique model from random starting parameters and training history
  - R random training replications x K folds generates RK unique models
    - Sample of random models permitting statistical tests on model distributions
- Stochastic iterative training
- For each BOLD pattern:
  - Activate pattern in input layer
  - Attempt to reproduce pattern in Autoencoder output layer
  - Attempt to categorize pattern (Tool, Instrument, Fruit)
  - Difference between obtained and target outputs determines required adjustments
    - Algorithm called ***Stochastic Gradient Descent***
    - Weight adjustments affect all weights to improve ***both*** autoencoder and classifier

Results

Multiple Constraint Model Performance

- Significantly better than chance classification
  - Category identity recovered from coarse-level whole-brain activity
- Autoencoders enhanced classification accuracy in CAT/AE models
  - Compared to otherwise identical CAT/- models without an autoencoder
- Functional connections not well-recovered from category training alone
  - Post-hoc autoencoders generated from yoked-weights in CAT/- (category-only) models did poorly at reproducing input patterns

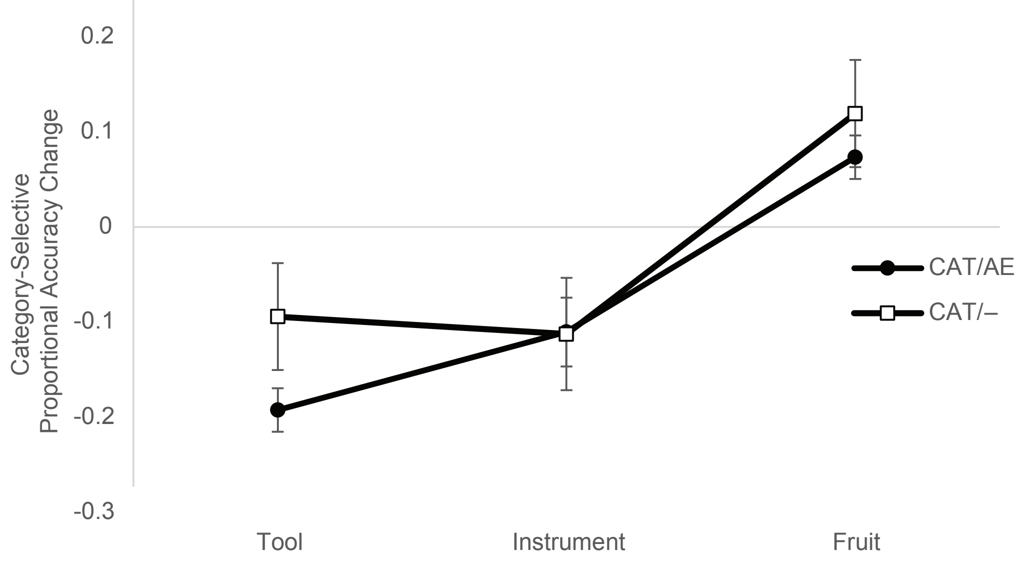


Classification accuracy vs. chance (.33) for classifier networks trained with an autoencoder (CAT/AE) and identical sibling models trained without an autoencoder (CAT/-)

Both types of models classified with significantly better than chance accuracy but CAT/AE models classified with significantly higher accuracy than CAT/- models

Simulating Semantic Memory Impairment

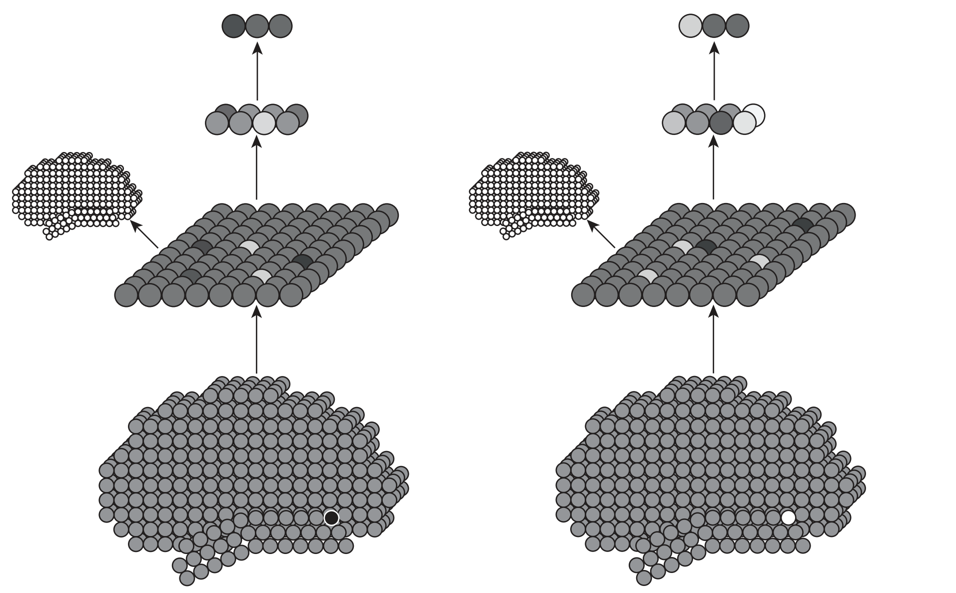
- Hypothesis: Functional connectivity is causally related to categorization in models
- Prediction: Disrupted connectivity should produce plausible categorization impairments
  - Identified lesion sites from clinical literature associated with impairments to tool, musical instrument or fruit/vegetable knowledge
  - Perturbed activity patterns in random subset of lesion sites either consistent or inconsistent with target category; look for a triple dissociation
    - Is a tool-selective impairment induced by lesions to sites associated with tool impairments? Yes, if connectivity is causally related to categorization
    - Is a tool-selective impairment induced by lesions to sites associated with fruit or musical instrument impairments? Not if connectivity is causally related to categorization



- Main effect for network
  - Only Multiple Constraint Networks produced selective impairments
- Triple dissociation: All category-selective impairments were lesion-site appropriate
  - E.g., selective impairments for tools not observed for lesions to sites not associated with impairments of tool knowledge

Multivariate Brain Mapping

- Simulated electrocortical stimulation
- Goal: Identify categorical affiliation of each region
  - Toggle each region while holding activity in all other regions at constant baseline
  - Measure change in activity across category units
  - Toggling categorically affiliated regions should cause a disproportionate change in corresponding categorization units
  - Repeat toggling simulation over a sample of trained models



We can assess whether a region is strongly affiliated with one of the target categories by comparing classifier unit activity when the region is "on" vs. "off"

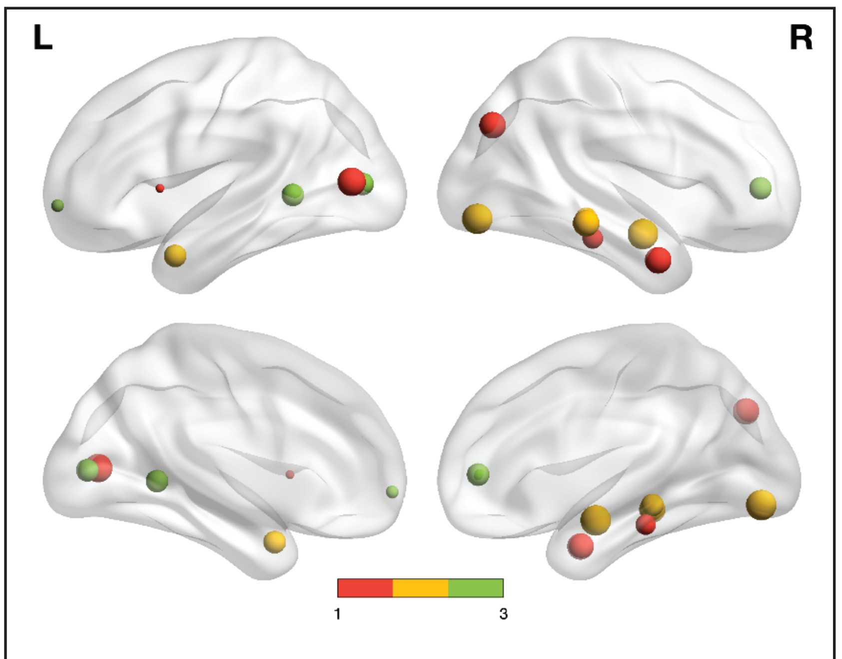
This illustration depicts a hypothetical toggling of a region within the lateral occipitotemporal cortex ("off" = 0, left; "on" = 1, right)

In this example, only the **tool** *classifier unit shows a large difference between the toggled states*

We might infer this region is important for representing tools

Summary of Brain Mapping Findings

- Tool-affiliated regions (red):
  - l. lateral occipitotemporal
    - visuomotor integration [2]
  - r. middle temporal
    - 3rd person action viewing [3]
  - l. pars opercularis
    - tool naming [2]
- Instrument-affiliated regions (yellow)
  - bilateral superior temporal gyrus
    - auditory processing [4]
  - r. middle temporal
    - 3rd person action viewing [3]
- Fruit/Vegetable-affiliated regions (green)
  - l. insula
    - appetitive control; taste evaluation [5]
  - l. visual area V4
    - color discrimination
  - r. superior frontal gyrus
    - discriminating high/low caloric foods [6]



Colored spheres (tool, instrument, fruit) indicate regions where classifier unit change for target category was at least two orders of magnitude greater than for non-target categories combined.

Sphere size is proportional to log-scaled affiliation

Brain mapping test of category affilation identified areas with known or theoretically-relevant ties to the target categories

May be a useful tool for hypothesis generation and testing and discovery

References

[1] McNorgan, C., & Joanisse. M.F. (2014). A connectionist approach to mapping the human connectome permits simulations of neural activity within an artificial brain. *Brain Connectivity, 4 (1),* 40 - 52.

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Acknowledgements

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