Using neuroimaging to infer mental states: A guided tour through the minefield

Russell Poldrack

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Can neuroimaging tell us anything about the mind?

Can neuroimaging tell us anything about the mind?



"No amount of knowledge about the hardware of a computer will tell you anything serious about the nature of the software that the computer runs. In the same way, no facts about the activity of the brain could be used to confirm or refute some information-processing model of cognition." (Coltheart, 2004, p. 22)

Max Coltheart

OP-ED CONTRIBUTORS This Is Your Brain on Politics

The New York Times

Published: November 11, 2007

This article was written by Marco Iacoboni, Joshua Freedman and Jonas Kaplan of the University of California, Los Angeles, Semel Institute for Neuroscience; Kathleen Hall Jamieson of the Annenberg Public Policy Center at the University of Pennsylvania; and Tom Freedman, Bill Knapp and Kathryn Fitzgerald of FKF Applied Research.

Multimedia



This Is Your Brain on Politics

IN anticipation of the 2008 presidential election, we used functional magnetic resonance imaging to watch the brains of a group of swing voters as they responded to the leading presidential candidates. Our results reveal some voter impressions on which this election may well turn.

Our 20 subjects — registered voters who stated that they were open to choosing a candidate from either party next November — included 10 men and 10 women. In late summer, we asked them to answer a list of questions about their political preferences, then observed their brain activity

for nearly an hour in the scanner at the Ahmanson Lovelace Brain Mapping Center at the University of California, Los Angeles. Afterward, each subject filled out a second questionnaire.



"In response to images of Democratic candidates, men exhibited activity in the medial orbital prefrontal cortex, indicating emotional connection and positive feelings."

"Images of Fred Thompson led to increased activity in the inferior frontal cortex, a brain structure associated with empathy."

"Subjects who had an unfavorable view of John Edwards responded to pictures of him with feelings of disgust, evidenced by increased activity in the insula, a brain area associated with negative emotions."

Do you really love your iPhone?

The New York Times

The Opinion Pages

OP-ED CONTRIBUTOR You Love Your iPhone. Literally.

By MARTIN LINDSTROM Published: September 30, 2011



MARTIN LINDSTROM Foreword by Paco Underhill

"Earlier this year, I carried out an fMRI experiment to find out whether iPhones were really, truly addictive, no less so than alcohol, cocaine, shopping or video games. In conjunction with the San Diego-based firm MindSign Neuromarketing, I enlisted eight men and eight women between the ages of 18 and 25. Our 16 subjects were exposed separately to audio and to video of a ringing and vibrating iPhone...most striking of all was the flurry of activation in the insular cortex of the brain, which is associated with feelings of love and compassion. The subjects' brains responded to the sound of their phones as they would respond to the presence or proximity of a girlfriend, boyfriend or family member. In short, the subjects didn't demonstrate the classic brain-based signs of addiction. Instead, they loved their iPhones.

To the Editor:

"You Love Your iPhone. Literally," by Martin Lindstrom (Op-Ed, Oct. 1), purports to show, using brain imaging, that our attachment to digital devices reflects not addiction but instead the same kind of emotion that we feel for human loved ones.

However, the evidence the writer presents does not show this.

The brain region that he points to as being "associated with feelings of love and compassion" (the insular cortex) is active in as many as one-third of all brain imaging studies.

Further, in studies of decision making the insular cortex is more often associated with negative than positive emotions.

The kind of reasoning that Mr. Lindstrom uses is well known to be flawed, because there is rarely a one-to-one mapping between any brain region and a single mental state; insular cortex activity could reflect one or more of several psychological processes.

We find it surprising that The Times would publish claims like this that lack scientific validity.

RUSSELL POLDRACK Austin, Tex., Oct. 3, 2011

The writer is a professor of psychology and neurobiology at the University of Texas at Austin. His letter was signed by 44 other neuroscientists.













Insula activation is weakly selective



Some voxels active in more than 20% of studies

Yarkoni et al., 2011

Reverse inference

 Informal reverse inference provides relatively weak evidence £ 1

TRENDS in Cognitive Sciences Vol.10 No.2 February 2006

ACTION OF DEVICE TY WAS DEPENDED

Can cognitive processes be inferred from neuroimaging data?

Russell A. Poldrack

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There is much interest currently in using functional neuroimaging techniques to understand better the nature of cognition. One particular practice that has become common is 'reverse inference', by which the engagement of a particular cognitive process is inferred from the activation of a particular brain region. Such inferences are not deductively valid, but can still provide some information. Using a Bayesian analysis of the BrainMap neuroimaging database, I characterize the amount of additional evidence in favor of the engagement of a cognitive process that can be offered by a reverse inference. Its usefulness is particularly limited by the selectivity of activation in the region of interest. I argue that cognitive neuroscientists should be circumspect in the use of reverse inference, particularly when selectivity of the region in question cannot be established or is known to be weak.

Introduction

Functional neuroimaging techniques such as functional magnetic resonance imaging (fMRI) provide a measure of local brain activity in response to cognitive tasks undertaken during scanning. These data allow the cognitive neuroscientist to infer something about the role of particular brain regions in cognitive function. However, there is increasing use of neuroimaging data to make the opposite inference; that is, to infer the engagement of particular cognitive functions based on activation in particular brain regions. My goal here is to analyze this practice, known as 'reverse inference', and to characterize some limitations on the effectiveness of this strategy. The companion paper in this issue by Henson [1] discusses a complementary strategy for using neuroimaging to distinguish competing cognitive theories.

The goal of cognitive psychology is to understand the underlying mental architecture that supports cognitive functions. To this end, cognitive psychologists examine the effects of task manipulations on behavioral variables, such as response time or accuracy, and use these data to test models of cognitive function. However, it is often not possible to determine on the basis of behavioral variables alone whether a particular cognitive process is engaged, or whether a particular theory of cognitive architecture is correct; for example, there are well-known examples of theoretical indeterminacy based on behavioral data [2]. If

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TICS, 2006

neuroimaging were able to provide information regarding what cognitive processes were engaged in performance of a particular task, cognitive psychologists would have gained a powerful new tool. Researchers outside cognitive psychology are also sometimes interested in using neuroimaging to determine the engagement of particular cognitive processes. For example, philosophers might wish to know the degree to which emotion versus deliberative reasoning plays a role in moral judgments [3].

Inference in neuroimaging

The usual kind of inference that is drawn from neuroimaging data is of the form 'if cognitive process X is engaged, then brain area Z is active'. Perusal of the discussion sections of a few fMRI articles will quickly reveal, however, an epidemic of reasoning taking the following form:

- In the present study, when task comparison A was presented, brain area Z was active.
- (2) In other studies, when cognitive process X was putatively engaged, then brain area Z was active.
- (3) Thus, the activity of area Z in the present study demonstrates engagement of cognitive process X by task comparison A.

This is a 'reverse inference', in that it reasons backwards from the presence of brain activation to the engagement of a particular cognitive function.

In many cases the use of reverse inference is informal; the presence of unexpected activation in a particular region is explained by reference to other studies that found activation in the same region. However, in some studies the reverse inference is a central feature. In one study [4], subjects were scanned using PET while they performed an economic exchange task in which they had the chance to punish those who defected. Activation was observed in the dorsal striatum when participants subjected defectors to effective punishment; this activation was inferred to reflect the rewarding properties of altruistic punishment. Similarly, a study using fMRI in rats [5] compared activity during pup suckling versus cocaine administration. Greater activity in the dorsal and ventral striatum during suckling compared with cocaine administration led the authors to conclude that 'pup suckling is more rewarding than cocaine' (p. 149). In each of these studies, a cognitive process ('reward') was inferred from activation in a particular brain system (the striatum). Nearly every

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Formalizing reverse inference

- How can we more formally test the predictive ability of fMRI?
- Answer: statistical methods for prediction
 - Machine learning/statistical learning/pattern recognition



Decoding mental states using machine learning





96% correct classification



Haxby et al., 2001, Science



Train on 7 runs, test on 8th



Haynes et al., 2007, *Current Biology*

Mind-reading machine knows what you see

15:26 25 April 2005 NewScientist.com news service

SCIENTIFIC AMERICAN.com

April 25, 2005

Brain Scans Helps Scientists "Read" Minds



"60 Minutes", January 4, 2009



"60 Minutes", January 4, 2009



"60 Minutes", January 4, 2009



"It's tough to make predictions, especially about the future." - Yogi Berra

Predicting mental states across people

- Existing work has primarily examined ability to predict mental states using a classifier trained on data from the same person
- For many applications of interest, such training data would not exist for the individual being tested
- Can we accurately generalize to new individuals?

Predicting risky decisions



Balloon Analog Risk Task (BART)

Helfinstein et al, 2014, PNAS

Crossvalidation across subjects



Randomly assign to folds 50 times and average results

Helfinstein et al, 2014, PNAS

Classification accuracy for risk-taking

Searchlight classification accuracy



Whole-brain classification: 72% p<0.002 under null hypothesis (by randomization)

Helfinstein et al, 2014, PNAS

Classifying based on activity balance



Blue: Pre-Pump > Pre-Cashout Red: Pre-Cashout > Pre-Pump

Helfinstein et al, 2014, PNAS

Decoding different mental states

- Can we predict what task a subject was performing, using a classifier trained on other people?
 - 8 tasks, 130 subjects total

Task #	Task description	# subjects	Design type		
1	Risky decision making (Balloon analog risk task) (Stover et al., in preparation)	16	Event-related		
2	Probabilistic classification (no feedback) (Aron et al., unpublished)	20	Event-related		
3	Rhyme judgments on pseudowords (Xue et al., unpublished)	13	Event-related		
4	Working memory (tone counting) (Foerde et al., 2006)	17	Event-related		
5	50/50 gain-loss gamble decisions (Tom et al., 2007)	16	Blocked		
6	Living/nonliving decision on mirror-reversed words (Poldrack et al., unpublished)	14	Blocked		
7	Reading pseudowords aloud (Xue et al., submitted)	19	Event-related		
8	Response inhibition (successful stopping) (Aron & Poldrack, 2006)	15	Event-related		

Analysis	Crossvalidated accuracy	# of voxels included	
Union of all in-mask voxels across subjects (one-vs-one)	74%	417,231	
Intersection of in-mask voxels across subjects (one-vs-many)	80.8%	214,940	
Positively activated voxels only (across all 130 subjects, t > 3, p<. 002) (one-vs-many)	74.6%	83,825	
Deactivated voxels only (t < -3, p<.002) (one-vs-many)	50.8%	23,736	



lion

	Task chosen by classfier										
		Task 1	Task 2	Task 3	Task 4	Task 5	Task 6	Task 7	Task 8		
True task	Task 1	87.5	6.0	0.0	0.0	6.0	0.0	0.0	0.0		
	Task 2	0.0	90.0	0.0	0.0	0.0	0.0	5.0	5.0		
	Task 3	8.0	23.0	61.5	0.0	0.0	8.0	0.0	0.0		
	Task 4	0.0	0.0	0.0	82.4	0.0	0.0	0.0	18.0		
	Task 5	0.0	38.0	0.0	0.0	43.8	18.2	0.0	0.0		
	Task 6	0.0	28.0	0.0	0.0	0.0	71.4	0.0	0.0		
	Task 7	0.0	11.0	0.0	0.0	0.0	0.0	84.0	5.0		
	Task 8	0.0	0.0	7.0	0.0	0.0	0.0	27.0	63.0		

Poldrack, Halchenko, & Hanson, 2009, *Psychological Science*

Larger-scale decoding



26 tasks, 482 images from 338 subjects

Classification results



Poldrack et al., 2013, Frontiers in Neuroinformatics

Predicting individual differences from fMRI

- In neuroscience, correlations are often colloquially described as "prediction", but true prediction requires generalization to new samples
- The ability to predict quantitative variables for new individuals can be tested using crossvalidation



Leave-one-out crossvalidation



full-sample $R^2 = 0.694$

Leave-one-out crossvalidation



full-sample $R^2 = 0.694$
Leave-one-out crossvalidation



full-sample $R^2 = 0.694$

LOO CV $R^2 = 0.586$ mean new sample $R^2 = 0.591$

Correlation ≠ Prediction



- I datapoints sampled from normal distribution (no correlation)
 one outlier
 full-sample R² =0.785
- •LOO CV $R^2 = 0.025$

•Highlights importance of examining the raw data!



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Neuroprediction of future rearrest
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Eyal Aharoni^{a,b,1,2}, Gina M. Vincent^c, Carla L. Harenski^a, Vince D. Calhoun^{a,d}, Walter Sinnott-Armstrong^e, Michael S. Gazzaniga^f, and Kent A. Kiehl^{a,b,2}

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PNAS

EARLY EDITION

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"The present analysis shows that hemodynamic activity within the brain prospectively predicted rearrest in an offender sample."



Fig. 1. Cox survival function showing proportional rearrest survival rates of high (solid green) vs. low (dashed red) ACC response groups for any crime over a 4-y period. Results of this median split analysis were equivalent to that of the parametric model: bootstrapped B = 0.96; SE = 0.40; P < 0.01; 95% CI, 0.29–1.84. The mean survival times to rearrest for the low and high ACC activity groups were 25.27 (2.80) mo and 32.42 (2.73) mo, respectively. The overall probabilities of rearrest were 60% for the low ACC group and 46% for the high ACC group.

Aharoni et al., 2013

Prediction error using crossvalidation



Predicting individual differences from fMRI



p<.05 (by randomization)

Variables tested: Age: subject's age SSRT: stop signal reaction time GoRT: go reaction time SDRT: std. dev. of go reaction time

Cohen et al., 2010, *Frontiers in Human Neuroscience*

- All of the results to this point were based on fMRI data from individual subjects
- Can we push this even further?
 - Can we use meta-analytic data from papers?

Activation locations

Brain activity is reported in (somewhat) standardized format



Table 1 Regions that showed a condition × time interaction in the ANOVA analysis

No.	Region	Hemisphere	BA	х	у	z	mm ³
1	Middle/superior temporal gyrus	L	21/22/37	- 52	-54	9	13257
2	Inferior frontal gyrus	L	45/46/9	- 49	26	6	2781
3	Posterior cerebellum	L		- 19	-79	-38	2214
4	Dorsomedial PFC	L	9/8	-11	42	47	3051
5	Left anterior PFC	L	10	-37	49	15	2025
6	Inferior parietal cortex	L	40/7	-42	-58	47	3132
7	Dorsal premotor cortex	L	6	-43	0	50	1485
8	Lingual gyrus	L	17	-10	-95	-2	378
9	Middle /superior temporal gyrus	R	21/22/37	52	-40	5	16470
10	Inferior frontal gyrus	R	45/46	51	28	6	2241
11	Posterior cerebellum	R		23	-78	-34	2808
12	Dorsomedial PFC	R	9	5	53	29	405
13	Right anterior PFC	R	10	38	42	21	5022
14	Inferior parietal cortex	R	40/7	42	-53	48	9963
15	Superior frontal gyrus	R	6/8	10	28	60	297
16	Anterior cingulate cortex	M	32	0	26	35	5076
17	Posterior cingulate cortex	M	23/31/7	0	-35	31	9612
18	Precuneus	М	7/19	1	-76	36	10044

Creating meta-analytic brain maps

- Automated Coordinate Extraction (Yarkoni et al, 2011, *Nature Methods*)
 - Automatically extracts activation tables from fMRI papers for 17 journals
 - Current database has 4,393 papers (with full text)
 - Good accuracy
 - 84% sensitivity, 97% specificity against SumsDB manual database
- Meta-analytic maps created for each paper
 - 10mm sphere placed at each focus

Automated	<u>Z</u>	Y	X
coordinate	-6	57	12
extraction	15	21	33
	60	15	24
	51	6	42
	57	-3	24



Neurosynth.org

neurosynth.org beta										
Home	Images	Data	Resources	Blog	FAQ					
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y = +4

V

Automated meta-analysis



Automated meta-analysis



Yarkoni et al., 2011, *Nature Methods*

Classification of cognitive states

- Given 2+ terms, can determine which is most likely given the data
- Naive Bayes classifier: assumes that all features (voxels) are independent; selects the most probable class
- Can apply this to any activation map—studies, individual subjects, etc.



Yarkoni et al, 2011, Nature Methods

Classification of new studies

- Cross-validated classification of all studies in database
- Select 25 high-frequency terms
- Pairwise classification: how well can we distinguish between each pair of terms?

Yarkoni et al, 2011, Nature Methods



Yarkoni et al, 2011, *Nature Methods*

Using classification to understand mental structure

WM: working memory TS: Task switching RS: Response selection RI: Response inhibition CC: Cognitive control BI: Bilingual language A' (k=3)



Lenartowicz et al, 2010, *Topics in Cognitive Science*

What about individual subjects?

- Can we identify cognitive states in individual (new) subjects?
- Difficult, because:
 - No opportunity for training
 - Data is of a fundamentally different type
- Tested in samples of subjects from working memory, emotion, and pain studies
 - Can we predict source study type?

Yarkoni et al, 2011, Nature Methods

Classifying individual subjects



Yarkoni et al, 2011, *Nature Methods*

Automating reverse inference



Neurovault + Neurosynth = automated reverse inference





Feature loadings

To compare the decoded image against a term, click on an arrow below.



Showing 1 to 10 of 92 entries

Previous Next

Gorgolewski et al., submitted

Summary: Decoding mental states

- We can decode mental states across individuals
- This can provide insights into the similarity space of mental processes
 - And ultimately inform our ontology of mental processes

Decoding representational structure using fMRI

Psychological theories rarely make clear predictions about activation
But they often make predictions about similarity relations between stimuli

We can test those against neuroimaging data
In principle we don't even have to care where the effects happen in the brain

Representational similarity analysis



Davis & Poldrack, 2013

Representational analysis using fMRI



Kriegeskorte et al., 2008

Typicality

• Some birds are "birdier" than others











Typicality

Dimension 2: Predacity



Dimension 1: Size

After Smith, Shoben, & Rips (1974) Photos via <u>http://www.birdphotography.com/</u>

Typicality is highly unconstrained

- May reflect:
 - Average similarity to other category members
 - Similarity to idealized members
 - Caricature effects

 Can we find a neural signature that is related to psychological typicality?



Davis & Poldrack, 2013, Cerebral Cortex



Davis & Poldrack, 2013, Cerebral Cortex



DISTANCE IS DEFINED AS THE CORRELATION DISTANCE BETWEEN TWO BETA-SERIES ACTIVATION PATTERNS

$$d_{ij} = \left[1 - corr(\beta_i, \beta_j)\right]/2$$

Davis & Poldrack, 2013, *Cerebral Cortex*



DISTANCE IS DEFINED AS THE CORRELATION DISTANCE BETWEEN TWO BETA-SERIES ACTIVATION PATTERNS

$$d_{ij} = \left[1 - corr(\beta_i, \beta_j)\right]/2$$

SIMILARITY IS AN EXPONENTIAL FUNCTION OF THE DISTANCE BETWEEN TWO REPRESENTATIONS

$$s_{ij} = \exp(-d_{ij})$$

Davis & Poldrack, 2013, Cerebral Cortex



DISTANCE IS DEFINED AS THE CORRELATION DISTANCE BETWEEN TWO BETA-SERIES ACTIVATION PATTERNS

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SIMILARITY IS AN EXPONENTIAL FUNCTION OF THE DISTANCE BETWEEN TWO REPRESENTATIONS

$$s_{ij} = \exp(-d_{ij})$$

TYPICALITY IS BASED ON THE SUM OF SIMILARITIES BETWEEN REPRESENTATIONS OF AN OBJECT AND OTHER CATEGORY MEMBERS

Davis & Poldrack, 2013, Cerebral Cortex

$$typ(i \mid J) = \sum_{j \in J} S_{ij}$$

Is neural typicality associated with subjective typicality ratings?

• Used a task in which subjective typicality and physical feature resemblance are dissociated

Category Structure (Davis & Love, 2010)



Davis & Poldrack, 2013, Cerebral Cortex

Task: Learning phase







Davis & Poldrack, 2013, Cerebral Cortex

Task: Categorization judgment





performed while scanning

Davis & Poldrack, 2013, Cerebral Cortex
Task: Typicality judgment





performed outside scanner

Davis & Poldrack, 2013, Cerebral Cortex

Single-trial fMRI response estimation



beta-series

LS-single (Mumford et al., 2012)

Design matrices for single-trial estimation

Idealized stimuli are judged most typical



GAM fit to typicality ratings



Davis & Poldrack, 2013, Cerebral Cortex

Alternative Predictions

 Neural similarity space will reflect subjective typicality



Obtained from behavior

 Neural similarity space will reflect physical typicality (likelihood given category)



Obtained using GCM

Davis & Poldrack, 2013, Cerebral Cortex

Applying the neural typicality measure

 Correlate neural typicality with psychological and physical predictions



Neural typicality

Regions in which neural typicality and psychological typicality are correlated



Davis & Poldrack, 2013, Cerebral Cortex

Univariate typicality effect



Regions in which univariate activation and psychological typicality are correlated



Davis & Poldrack, 2013, Cerebral Cortex

Physical similarity

- Physical similarity predictions obtained using GCM
 - Examined across multiple levels of variance
- There were no regions in which neural typicality or activation reflected physical typicality/



Davis & Poldrack, 2013, Cerebral Cortex

- Activation patterns are isomorphic to mental representations
- Subjective typicality reflected in neural typicality
 - Univariate analysis would have told a very different story

How does MVPA compare to univariate analysis?



Demeaned pattern

Decoding continuous variables



Tom et al., 2007, Science



The opportunistic nature of MVPA



Jimura & Poldrack, 2011, Neuropsychologia

Differential sensitivity of MVPA



Jimura & Poldrack, 2011, Neuropsychologia

MVPA is sensitive to univariate patterns



Davis, Laroque et al., 2014, Neuroimage



Davis, Laroque et al., 2014, *Neuroimage*

MVPA is less sensitive to between-subject variability



Davis, Laroque et al., 2014, Neuroimage

Some things we have learned

- If classification results look too good, you have most likely done something wrong
- Always confirm results by randomizing data from the very beginning
 - run many times to get null distribution, make sure it's actually at chance
- Crossvalidation with regression is very tricky (don't use LOO)
- Differences between univariate and multivariate analyses can't be easily interpreted (Davis et al., 2014, *Neuroimage*)
- Trials orders must be separately randomized for each subject (Mumford et al., 2014, *Neuroimage*)

Conclusions

- Neuroimaging data CAN provide evidence relevant to psychological questions
 - But informal reverse inference is not the way!
- Machine learning methods provide the means to decode and predict mental states from neuroimaging data
- Multivariate analyses can establish isomorphisms between neural and mental representations

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James S. McDonnell Foundation



Data sets and code will be made available at <u>www.openfmri.org</u>