Predicting Typicality Effect from Brain Activation Patterns in Healthy Adults and Individuals with Aphasia: a Multi-Voxel Pattern Analysis

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Introduction

Semantics: relationships between words and the signified knowledge.

Semantic representation in healthy adults:

- left-lateralized in frontal, temporal parietal, and prefrontal regions[1].
- *Controlled semantic cognition* (CSC)[2] : ATL, PFC, pMTG, IPS, pre-SMA, ACC/mPFC.
- Multiple-demand network[3].

Semantic representation in individuals with aphasia (PWA): distributed network involved in access to or executive control of language[4].

Category-specific representation: anatomically distinct account[5]; distributed account[6]; continuous account[7].

Feature-specific representation: semantic typicality

- Faster and more accurate access to *typical* than *atypical* exemplars in healthy adults[8]; Inconsistent behavioral performance in PWA[9].
- Hierarchical theory of object processing: early visual regions and higher temporal regions in healthy adults[10].
- *Prediction in PWA*: different neural representation of typicality than healthy adults.

Multi-voxel pattern analysis[18] (MVPA): machine learning algorithms (e.g., LSVM) extract information from brain activity patterns, and predict corresponding condition of interest in fMRI task.

- *Searchlight-based MVPA[11]*: reduce overfitting; no *a priori* region specification is needed
- *Linear classifier:* $f(x) = g\,(w_1x_1 + w_2x_2 \ldots w_yx_y)$

Objectives

1. Which brain regions show neural encoding of semantic typicality associated with behavioral performance in healthy adults?

- *Hypothesis:* faster and more accurate responses in typical than in atypical exemplars; above-the-chance (%50) classification accuracy in the visual and temporal regions.

2. Which brain regions show neural encoding of semantic typicality associated with behavioral performance in PWA?

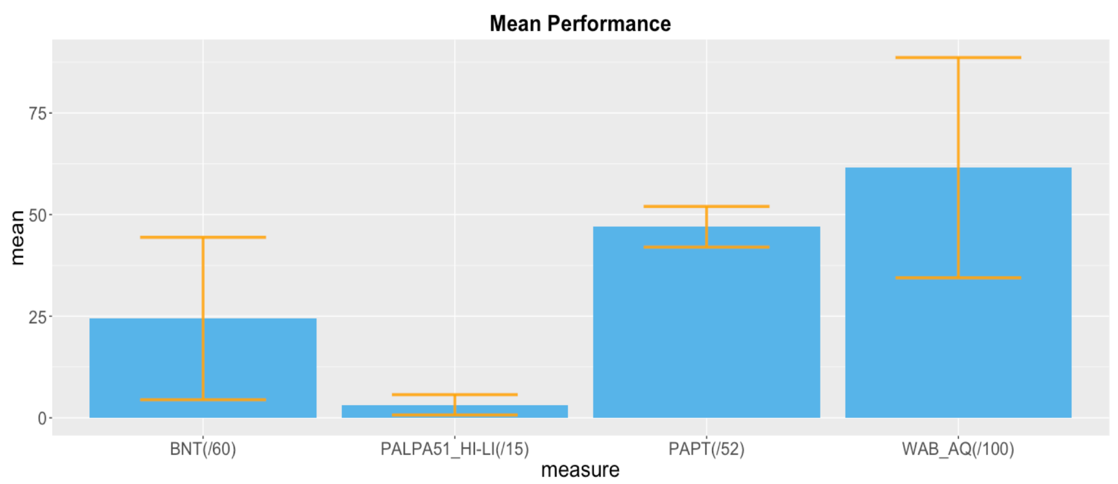
- *Hypothesis*: behavioral typicality effect would vary from healthy adults; different brain regions differentiating between typical and atypical exemplars. Above-the-chance (%50) classification accuracy in these brain regions.

Methods

Subjects

- 35 PWA due to left MCA infarct[1], 14 excluded (N = 21, 7F, mean age = 60.76 ± 10.64 y, mean months post onset = 65.71 + 102.13); mean lesion volume (SD) = 104,647 ± 69,682.17 mm^3
- 21 neurologically healthy adults, 3 excluded (N = 18, 8F, mean age = 59.86 ± 10.50 y)

Standardized Language Assessments

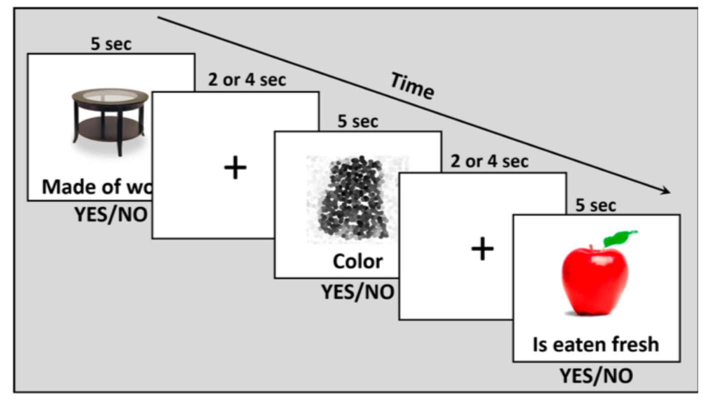


WAB AQ: Western Aphasia Battery Aphasia Quotient; PPT: Pyramids and Palm Trees; PALPA: Psycholinguistic Assessment of Language Processing in Aphasia; HI: Hight Imageability; LI: Low Imageability.

fMRI Task Stimuli and Procedure

Picture stimuli: 36 color photos (half typical and half atypical) of real items from each of five semantic categories: birds, vegetables, furniture, clothing, fruits; 36 scrambled pictures; split across two runs

- Balanced for: familiarity, length, lexical frequency, concreteness[12]
- Each subject viewed fruits + two other categories (counterbalanced across subjects)
- *Semantic features:* Core, prototypical, and distinctive; controlled for type of information conveyed, and whether defining or characteristic of the category



[1]This data is part of The Center for the Neurobiology of Language Recovery (CNLR) funded by NIH/NIDCD.

Methods

fMRI Data Acquisition and Preprocessing

- 3.0 T Siemens Trio Tim using 20-channel head + neck coil
- *T1:* TR = 2300 ms, TE = 2.91 ms, 176 sagittal slices, 1 x 1 x 1 mm voxels, 256 x 256 matrix, FOV = 256 mm, flip angle = 9º, fold-over direction = AP
- *T2*-weighted EPI:* TR = 2570ms, TE = 30ms, 40 axial slices, 3mm slices interleaved with 2 x 2 x 3 mm voxels, 80 x 78 matrix, FOV = 220 x 220 mm, 40 axial, flip angle = 90º

Data Analysis

Percentage of spared tissue: volume of the spared tissue ROIs divided by the total volume of the region from AAL Atlas in the MarsBAR for SPM (Brett et al., 2002)

Behavioral analysis: linear mixed-effects model (accurate RTs) and generalized mixed-effects model (accuracy; 1 = accurate, 0 = inaccurate)

- *Fixed factors:* typicality, group, category, typicality-by-group; *random intercept:* subject

Preprocessing (SPM12[13])

1) Slice timing
2) Spatial realignment with 4th degree B-spline
3) Coregistration
4) Structural segmentation
5) Spatial and functional normalization to the MNI space; high-pass filter with a cutoff of 1/128 s
6) *Spatial smoothing with 4mm Gaussian kernel (for univariate analysis)

fMRI Univariate Analysis (SPM12)

1) 1st-level GLM: typical, atypical, scrambled
   - Typical > Atypical
   - Atypical > Typical

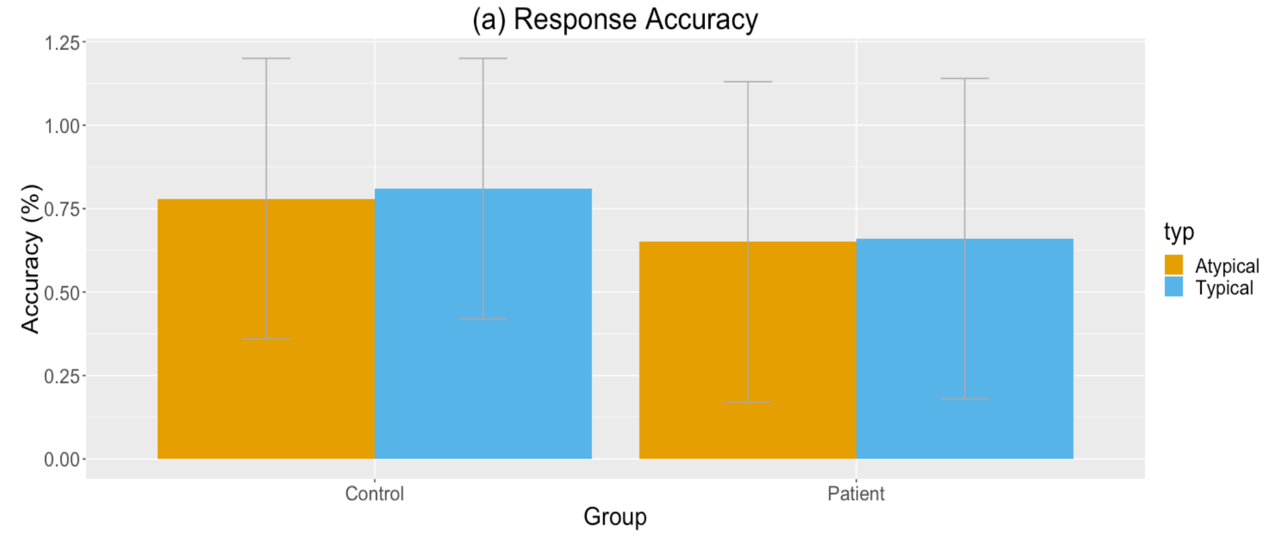
   Onsets and durations convolved with the canonical HRF and its temporal derivative
2) 2nd-level: one-sample *t* test ($p < .001$); corrected for multiple comparison (FDR at $p < .05$)

Searchlight MVPA

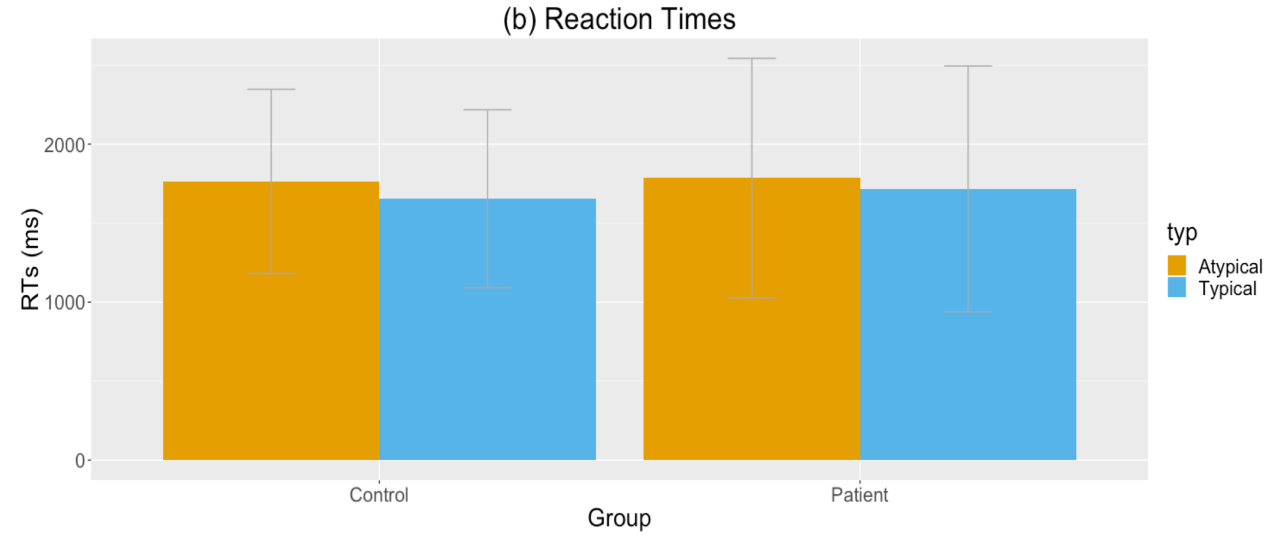
The Decoding Toolbox (TDT[14]); Radius = 9mm
Input: beta values from 1st-level univariate analysis (unsmoothed)
Classifier: LSVM with leave-one-run-out cross validation
Output: individual's accuracy map (-50 to 50)
Group-level: smoothing with 6mm FWHM; one-sample *t* test ($p < .001$), corrected for multiple comparisons (FWE at $p < .05$)

Results

Behavioral

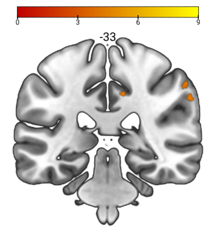
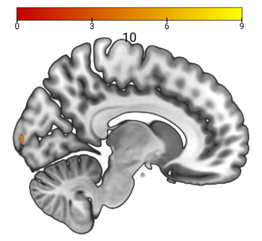
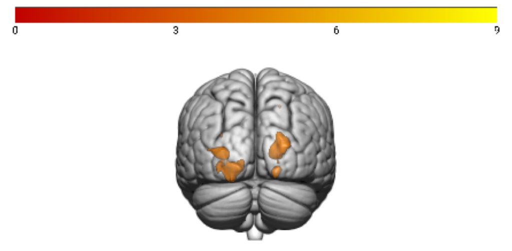
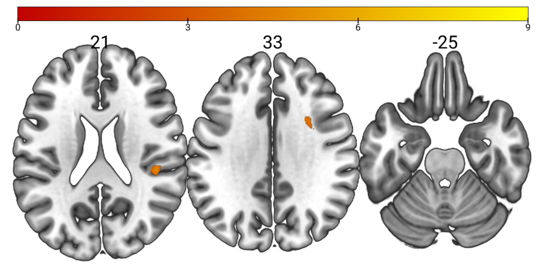


Main effect of typicality (β = -.34, |z| = 2.46, SE = .14, p < .05)
Main effect of group (β = -.98, |z| = 2.45, SE = .40, p < .05)



Main effect of typicality (β = 106.61, |z| = 3.66, SE = 29.11, p < .01)

Results

	Healthy		PWA	
Univariate	uncorrected at $p < .001$ (extent size $k \geq 10$)		uncorrected at $p < .001$ (extent size $k \geq 10$)	
	Typical > Atypical  **1) R Supramarginal 2) R Middle Cingulate**	*Atypical > Typical*  **L Middle Occipital**	*Typical > Atypical* **N.A**	*Atypical > Typical* **N.A**
Searchlight MVPA	cluster-level FWE correction at $p < .05$  **1) LMOG (t = 5.57) extending into L Lingual (t = 5.39) 2) R Calcarine (t = 5.31) extending into R SOG (t = 5.03)**		uncorrected at $p < .001$  **1) R Rolandic Operculum (t = 5.14) 2) L Fusiform (t = 3.74)**	

Post-hoc brain-behavior analysis (PWA):

1) *Spearman's* rank correlation between behavioral language performance (total RTs, accurate RTs, % PAPT, WAB-AQ) and classification accuracies in LMOG and R Calcarine in all PWA (N = 21), Anomic (N = 9), and Broca's (N = 9):
   - **Significant correlation between accurate RTs and classification accuracy in LMOG (ρ = .77, p < .05) in Anomic PWA**
   - ROI classification in PRoNTo 2.1[15], binary LSVM with leave-one-run-out cross validation
2) *Linear mixed-effects model predicting ROI classification from behavioral measures:* main effect of accurate mean RTs (β = .08, |t| = 2.77, SE = .03, p < .05) in the Anomic Group.

Discussions

1. **Which brain regions show neural encoding of semantic typicality associated with behavioral performance in healthy adults?**
   - Neural representation of typicality is built by the visual system at an intermediate processing stage[16].
   - Hierarchical organization of category structure, whose influence on the organization of neural patterns becomes apparent as early as visual regions[23].
   - *LMOG:* shape discrimination of objects[17]; *R Calcarine:* processing certain semantic categories[18].
2. **Which brain regions show neural encoding of semantic typicality associated with behavioral performance in PWA?**
   - Similar behavioral typicality effect as healthy adults, but different neural typicality.
   - Maybe semantic typicality does not directly modulate the neural representation of typical and atypical stimuli in early visual processing due to a damaged semantic network post-stroke, or such effect is not perceived as early as in healthy adults[10].
   - LMOG is still associated with accurate processing of semantic typicality in less severe PWA, but comes at a cost with longer processing time suggesting not as automatic as in healthy adults.

Future studies: functional/structural connectivity between the visual cortex and semantic network in PWA.

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