Frequent, longitudinal sampling reveals learning-related changes in working memory substrates

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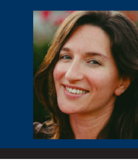


CNS 2020 VIRTUAL

Discrepancies in WM substrates across species and studies

non-human primate (NHP) electrophysiology

- large amount of training (> 10^4 trials)
- single-unit resolution
- PFC activity encodes item-specific information in WM

Leavitt et al., *TiNS*, 2017

Constantinidis et al., *JNeuro*, 2018

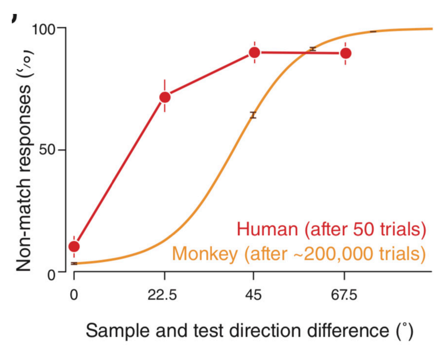
human neuroimaging

- small amount of training (< 10^2 trials)
- voxel-level resolution (2.5 mm, ~LFP)
- distributed, sensory and category-selective regions encode item-specific information in WM

Christophel et al., *TiCS*, 2018 Serences, *Vision Research*, 2016

NHP vs human WM training

Birman & Gardner, *Nature Neuro*, 2016

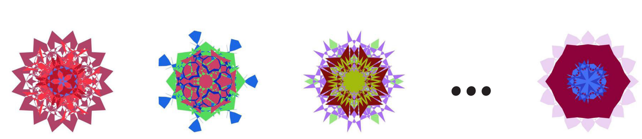


goal: train human participants like NHPs (with extensive behavioral training) to reconcile debate over WM substrates

Longitudinal training of memory representations

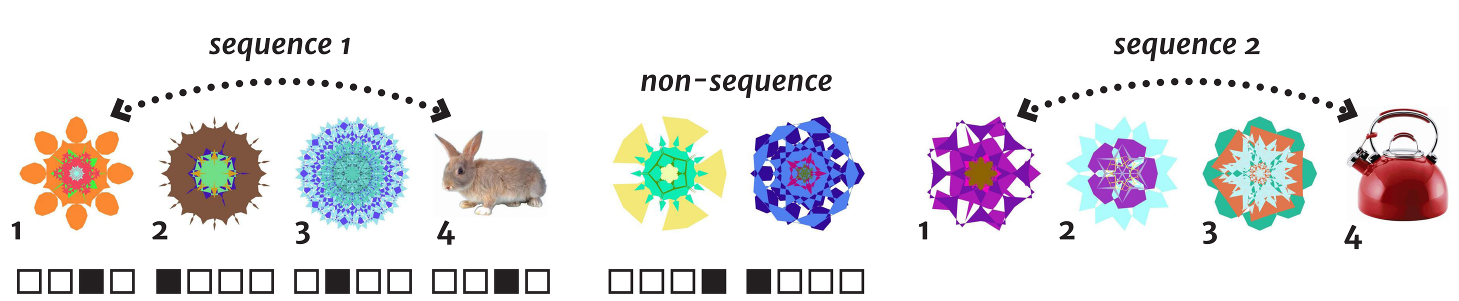
Stimulus set:

18 unique fractals per subject



- 3 human participants with at-home behavioral training every other day
- 24 functional MRI (fMRI) sessions / subject across 3 months
- fMRI scans: *stimulus localizers, sequence learning task, WM task, resting-state*

Sequence learning – serial reaction time task

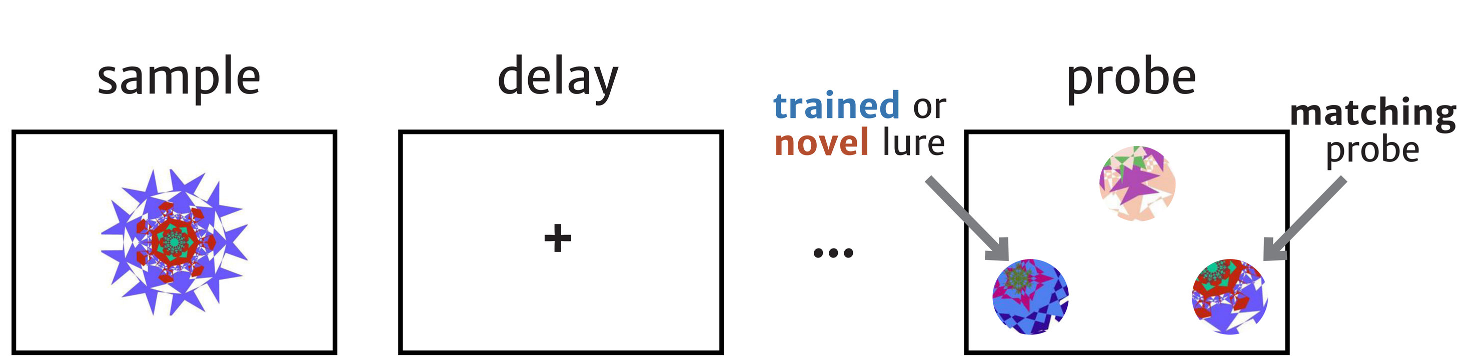


- sequences (4 total) occur with 0.75 probability
  - 12 sequence stimuli, 6 non-sequence stimuli per subject
- each stimulus associated with 1 correct response
- 1 unique stimulus presentation per block

fMRI session: 18 blocks (3 scanning runs)

at-home training: 26 blocks

Working memory task

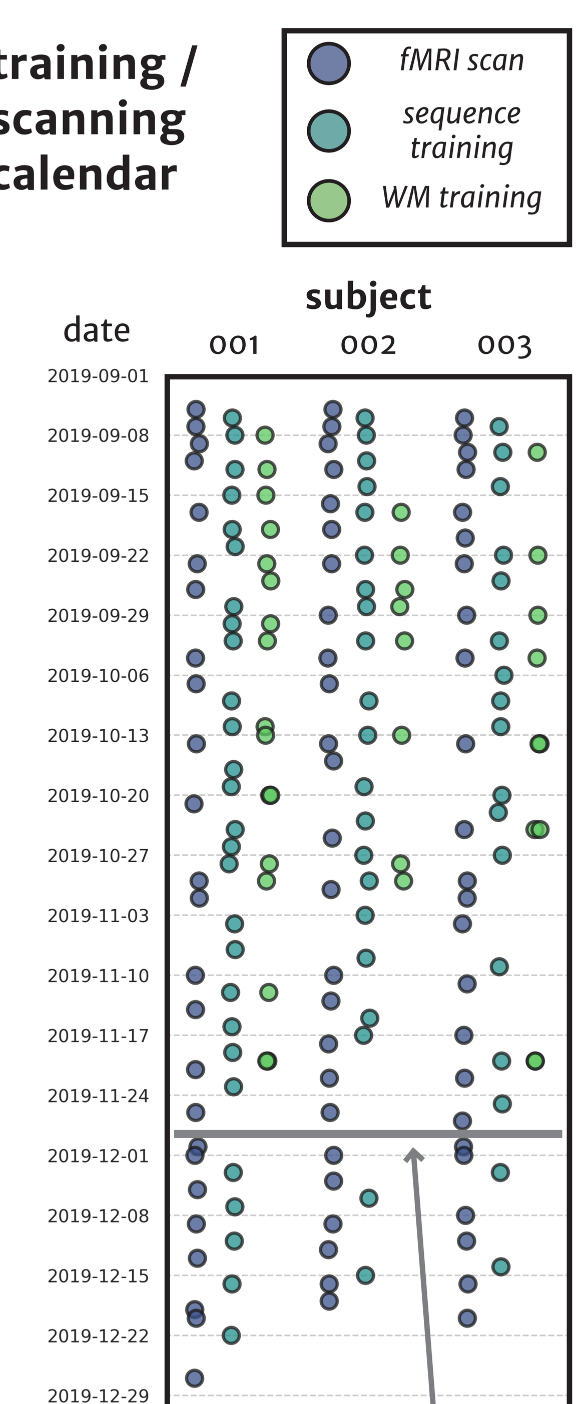


- 1 unique stimulus presentation per block

fMRI session: 24 trials * 4 blocks

at-home training: 24 trials * 2 blocks

training / scanning calendar



*new stimuli introduced, present data includes only first 17 sessions before new stimuli

WM behavior improves for trained stumli

accuracy

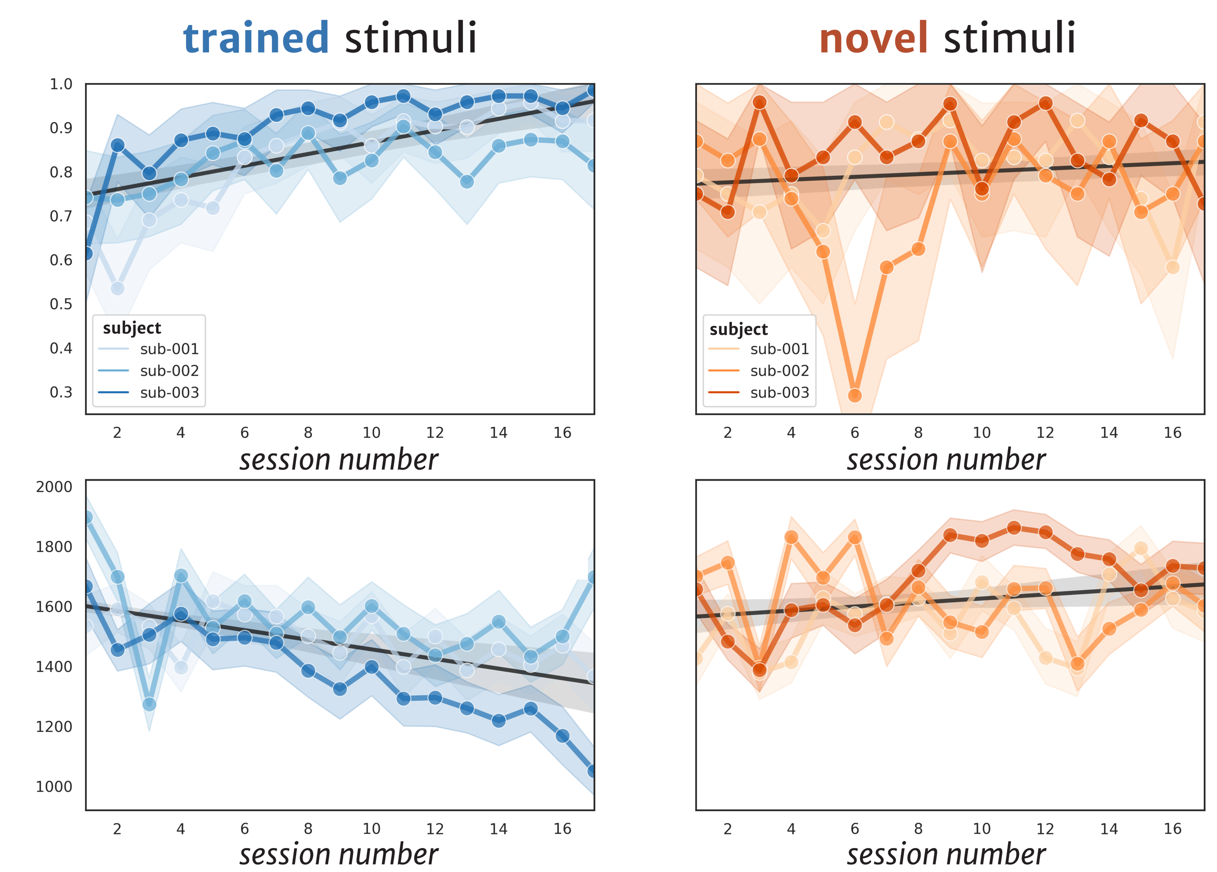
mixed linear model

session (1 -> 17)
x training (trained vs novel)
interaction:
β = 0.01, p = 0.006

response time (ms)

mixed linear model

session (1 -> 17)
x training (trained vs novel)
interaction:
β = −22.7, p < 0.001

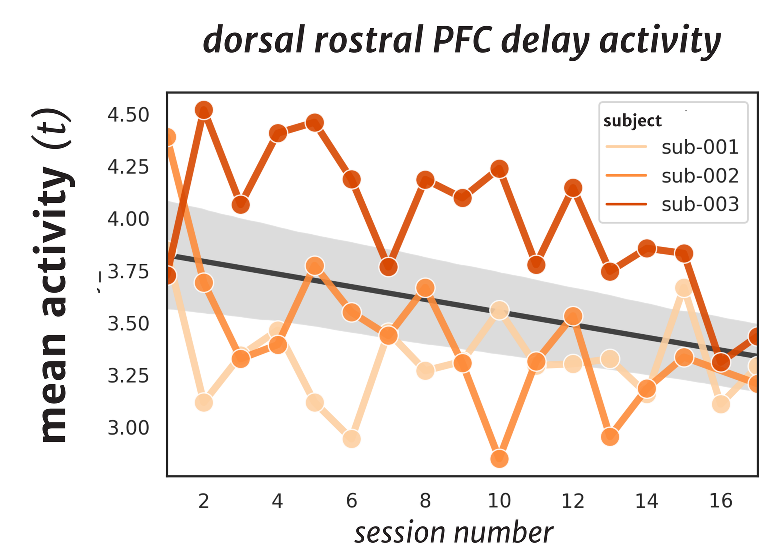


Cortical activity patterns change across training

WM delay activity decreases overall, but spreads across PFC

high delay activity voxels

voxels within *dorsal rostral PFC* **decrease** activity with training



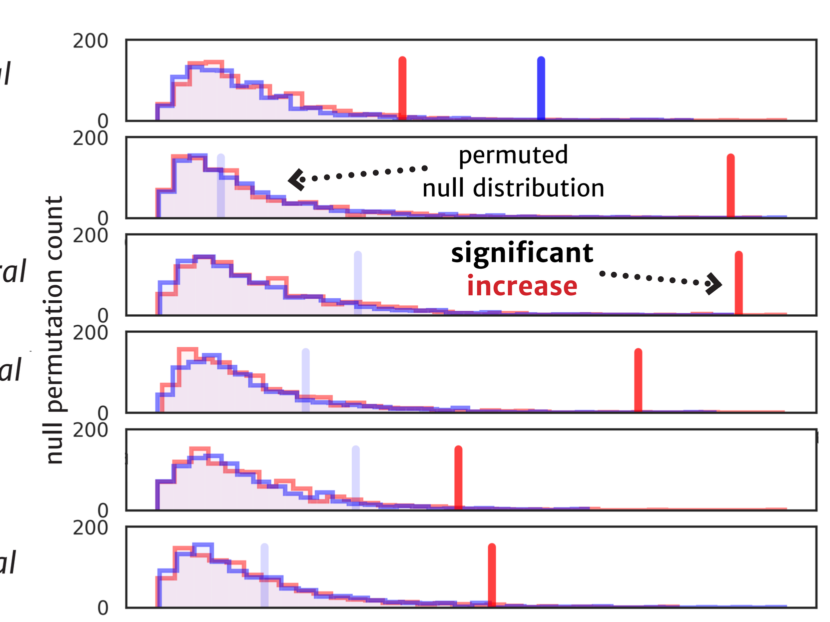
mixed linear model

session (1 -> 17) main effect:
β = −0.03, p = < 0.001

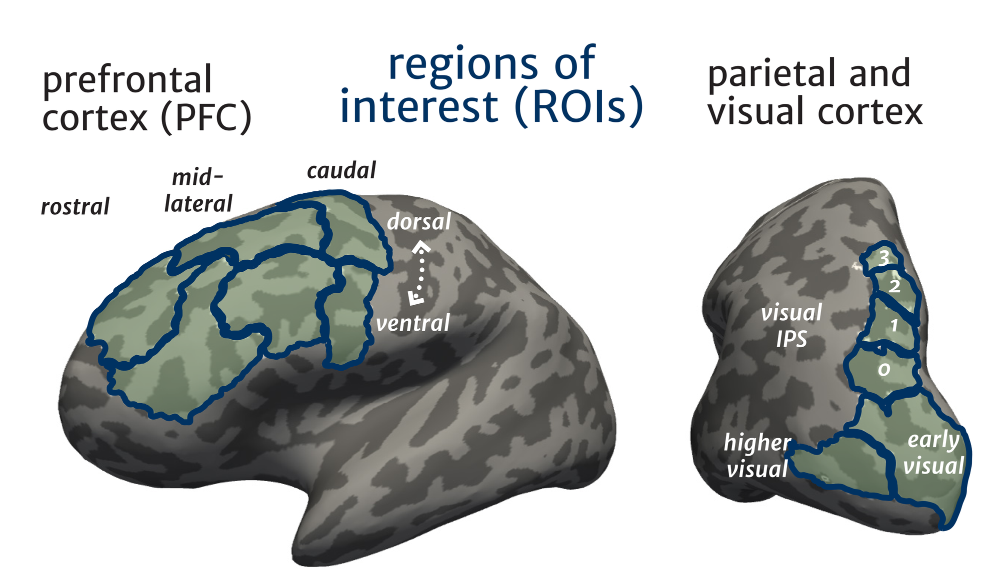
all voxels

high proportions of **all** voxels in PFC **increase** activity with training

what % of voxels in each ROI show an increase or decrease in activity across sessions?



functional MRI (fMRI) analyses and methods



univariate activity

- session-level general-linear model (GLMs)
- time-series convolved with canonical HRF
- separate regressors for trained vs novel stimuli
- mean activity from each ROI and contrast extracted from each session at t > 2.5

representational similarity (RSA)

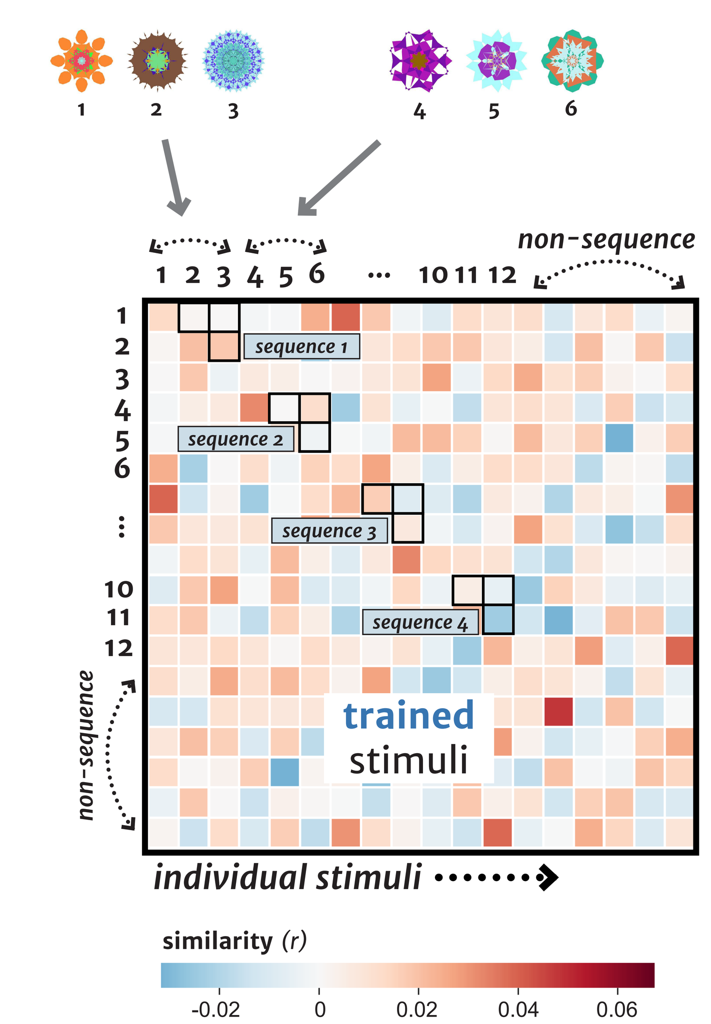
- single-trial activity from least-squares-all (LSA) GLMs for each separate run
- between-run correlations calculated for each individual stimulis within each session
- data cleaned with multivariate noise decomposition (Walther et al., *Neuroimage*, 2016)

Summary

- Frequent WM training increases accuracy and decreases response times for trained stimuli across learning
- While delay activity decreases with training in dorsal rostral PFC regions that were highly active early on, ***more*** voxels are recruited and increase their activity with training across all of PFC
- Different PFC ROIs develop item-level selectivity (similar activity patterns for item sequences) versus task-level selectivity (all trained WM stimuli)

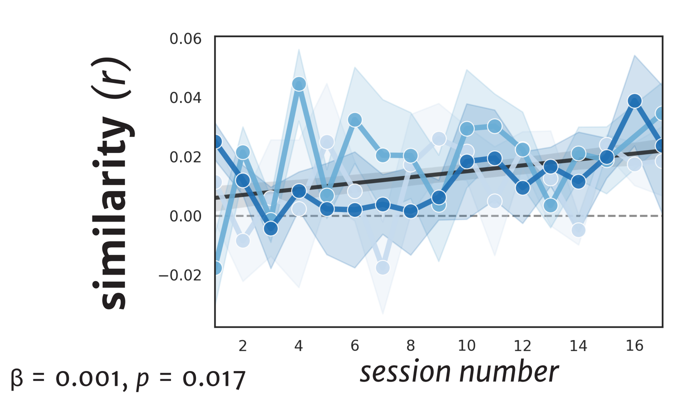
Selectivty of PFC delay activity changes across training

example RSA matrix



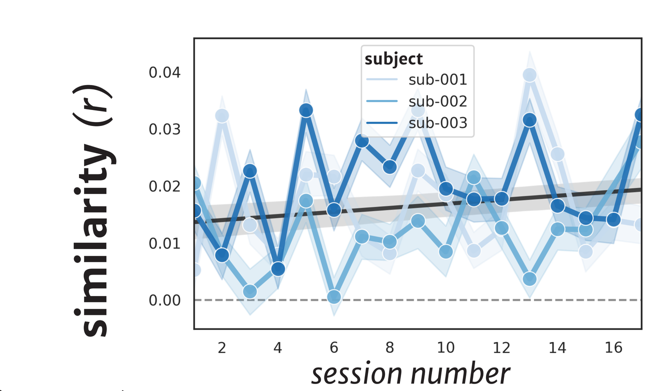
pattern similarity emerges between stimuli within trained sequences and across all **trained** stimuli

ventral mid-lateral PFC
(similarity to stimuli in ***same sequence***)



β = 0.001, p = 0.017

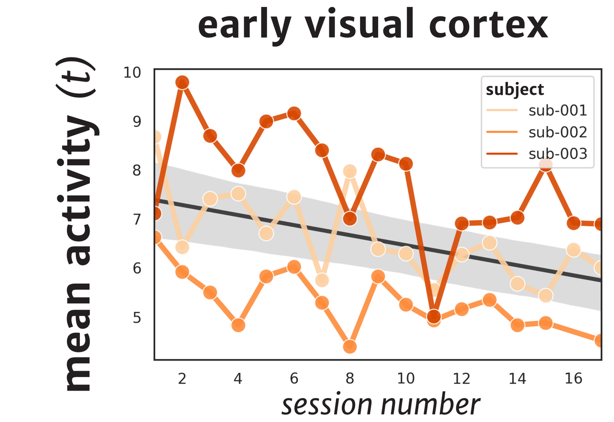
dorsal caudal PFC
(similarity to ***different*** trained stimuli)



β = 9 x 10^{-4}, p = 0.003

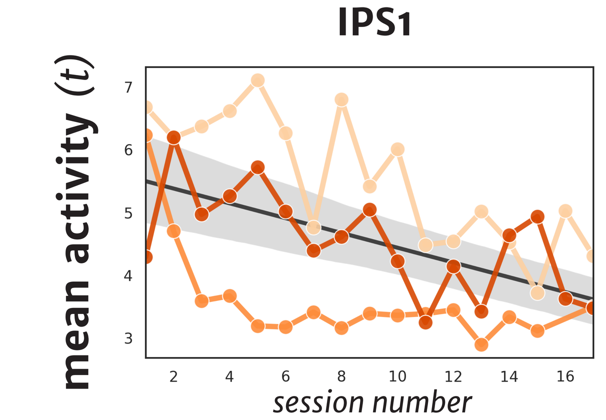
WM encoding activity decreases across cortex with training

early visual cortex



mixed linear model
session (1 -> 17) main effect:
β = −0.11, p = < 0.001

IPS1



mixed linear model
session (1 -> 17) main effect:
β = −0.12, p = < 0.001

* all ROIs decrease encoding activity across training

(all p < 0.05, FDR correciton)

Data, acknowledgements, funding

- complete dataset to be made openly available upon publication
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