Enhanced Cortical Activity after n-back Working Memory Training: An Event-Related Potential Source Localization Study

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Background

Working memory (WM) is a core cognitive ability that involves the short-term maintenance and manipulation of information. We previously found that WM training resulted in enhancement of N2 and P3 event-related potential (ERP) component amplitude. Here, we seek to extend these findings by identifying the pattern of cortical activity that is associated with these training-related ERP effects. ERPs were obtained before and after cognitive training on a visual 3-back task. Study participants were randomly assigned to complete either an n-back WM training protocol, or a visual search training comparison protocol (20 sessions of training over four weeks for both groups). Cortical source activity for the pre/post 3-back task was estimated for the N2 and P3 components using the local autoregressive average (LAURA) method. Using this approach, we sought to identify the functionally associated networks of cortical activity that were associated with improved cognitive performance following n-back working memory training (see Study Aims for details)

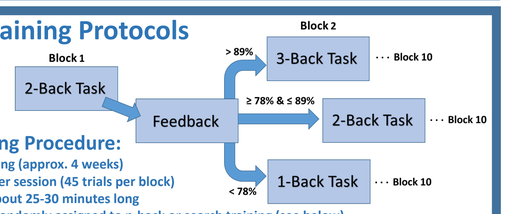
Study Aims

1. Identify cortical activity underlying the enhancement of N2 and P3 scalp amplitude after n-back working memory training → ERP source localization with LAURA method

2. Extract latent variables of training related cortical changes that represented functionally associated activity, i.e., network activity → Exploratory Factor Analysis

3. Determine if variables that represent training-related changes in cortical network activity are predictive of individual differences in improved cognitive performance following training (i.e., transfer effects) → Correlations

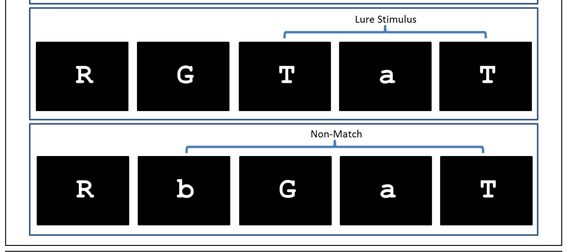
Cognitive Training Protocols



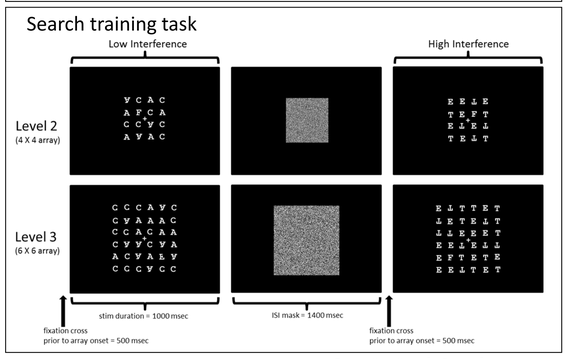
Adaptive Training Procedure:

- 20 sessions of training (approx. 4 weeks)
- 10 blocks of trials per session (45 trials per block)
- Each session was about 25-30 minutes long
- Study participants randomly assigned to n-back or search training (see below)

n-back training task (3-back level example)



Search training task



EEG/ERP Processing Pipeline

EEG Acquisition:
257-channel HydroCel Geodesic Sensor Net (Electrical Geodesics, Inc., Eugene OR); Impedances < 50 kΩ; Filtered during acquisition from 0.1-100 Hz, digitized at 250 Hz; Vertex (Cz) reference

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25 Hz low-pass filter

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Epoch window:
1,050 msec total, post-stimulus = 900 msec, baseline = -150 to 0 msec; Epochs for Match, Non-Match, and Lure trials

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Artifact Detection:
Reject data if: (1) amp > 100 μV, 40 msec moving average, (2) amp < 1.0 μV, window size = 200 msec, (3) amp > 200 μV; Eye blink artifact, amp > 100 μV, window size = 150 msec, 40 msec moving average, blink duration extended by 5 msec; Eye movement artifact, amp > 55 μV, 40 msec moving average, 200 msec window; Channel bad if 20% segments bad; Segment bad if ≥ 20 bad channels, eye blink, or eye movement. Epochs were also visually inspected after automated processing.

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Interpolation for bad channel replacement

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Averaging

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Re-reverence to averaged reference

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Baseline correction (-150 to 0 msec as baseline)

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Source Localization:
Minimum Norm Least Squares (MNLS) for estimating dipole sources; Local Autoregressive Average (LAURA) method for constraining source solution; Finite Difference Model (FDM) for head model, using the MNI average (305 subjects), with 2,447 dipoles; regularization = 10^{-3};

Statistical Analyses

1. ERP Source Analyses: Source analyses were completed for the visual letter 3-back task, which was completed before and after the cognitive training procedure. The root-mean-squared was calculated for each dipole set (within a voxel), and data were then averaged for each gyrus (66 gyri in total). Source data were then averaged across two distinct time windows for the N2 (200-300 msec) and the P3 (350-550 msec). Pre-training activity was subtracted from post-training activity to obtain a change score that represented increase/decrease in activity after training. This served as the initial dependent measure. The n-back and search training groups were compared on this dependent measure with paired samples t-tests. No comparisons survived FDR correction (Benejamini-Hochberg) – an uncorrected alpha level of $p < .05$ is reported. This exploratory analysis identified the cortical regions that were most strongly associated with n-back training specifically, in comparison to another training protocol (search training).

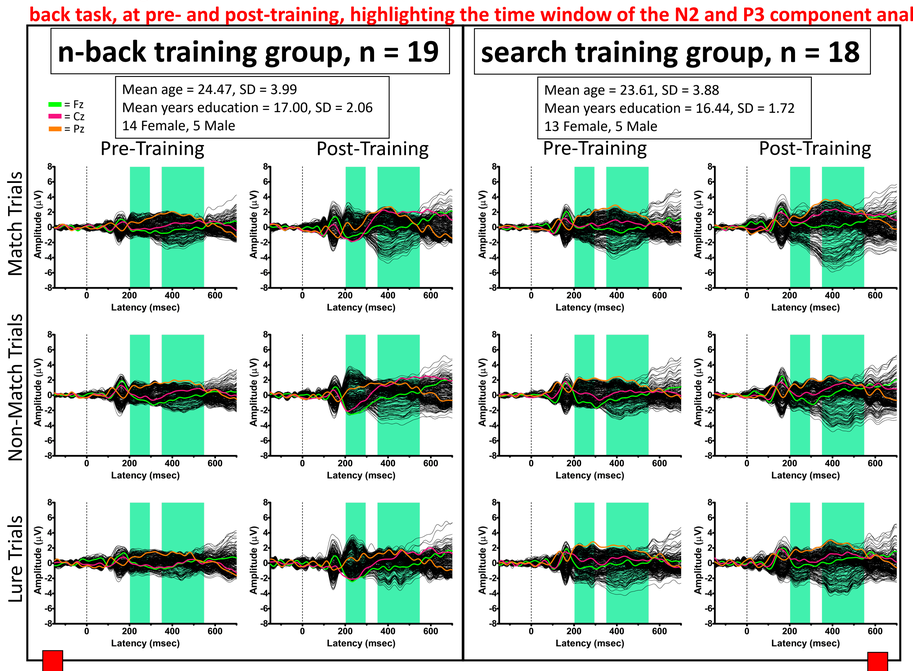
2. Factor Analysis with Cortical Source Data: An exploratory factor analysis was conducted using the regions that were identified at each time window in the initial analysis. Principal component analysis was used, with varimax rotation, and subsequent plots (see upper far right) present coefficient weights that were greater than .40.

3. Correlation Analysis: Pearson correlations were conducted for latent variables derived from the factor analysis vs. behavioral performance variables. Change scores (post-training minus pre-training) were derived for the following behavioral measures: n-back training task measures (gains in first training session, best training session); Letter 3-back (pre, post outcome measure, separately for Match, Non-Match, Lure trials); Spatial 3-back (Match, Non-Match, Lure trials); Paced Auditory Serial Addition Test (PASAT) performance; Working memory composite performance (composite of accuracy from letter 3-back, spatial 3-back, and PASAT); Fluid reasoning composite measure (composite performance from Raven's Advanced Progressive Matrices, Analysis-Synthesis test, Concept Formation test, and Letter Series test).

This work was supported by a Mark Diamond Research Fund Grant and a National Multiple Sclerosis Society Pilot Grant

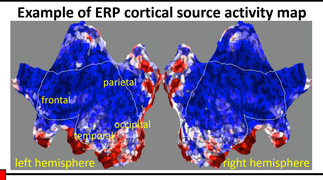
1. Cortical source activity associated with n-back training

Grand Averaged Event-Related Potentials (butterfly plots for 257 channels) obtained for the letter 3-back task, at pre- and post-training, highlighting the time window of the N2 and P3 component analysis



Source Localization (LAURA method) of N2 and P3

Example of ERP cortical source activity map



Cortical source activity was estimated for the N2 (200-300 msec) and P3 (350-550 msec) time windows. This was done using the LAURA method (MNLS, FDM). Activity was averaged across voxels within 66 pre-defined gyri (MNI). The pre-to-post-training change in activity was then calculated for each gyrus, and pairwise contrasts between the n-back and search training groups were then carried out for each gyrus.

Analysis design for n-back vs. search training group contrasts

n-back training group	search training group
post-training source activity – pre-training source activity	post-training source activity – pre-training source activity
Cortical Activity Δ	Cortical Activity Δ

→ Pairwise t-tests comparing magnitude of activity change for each gyrus

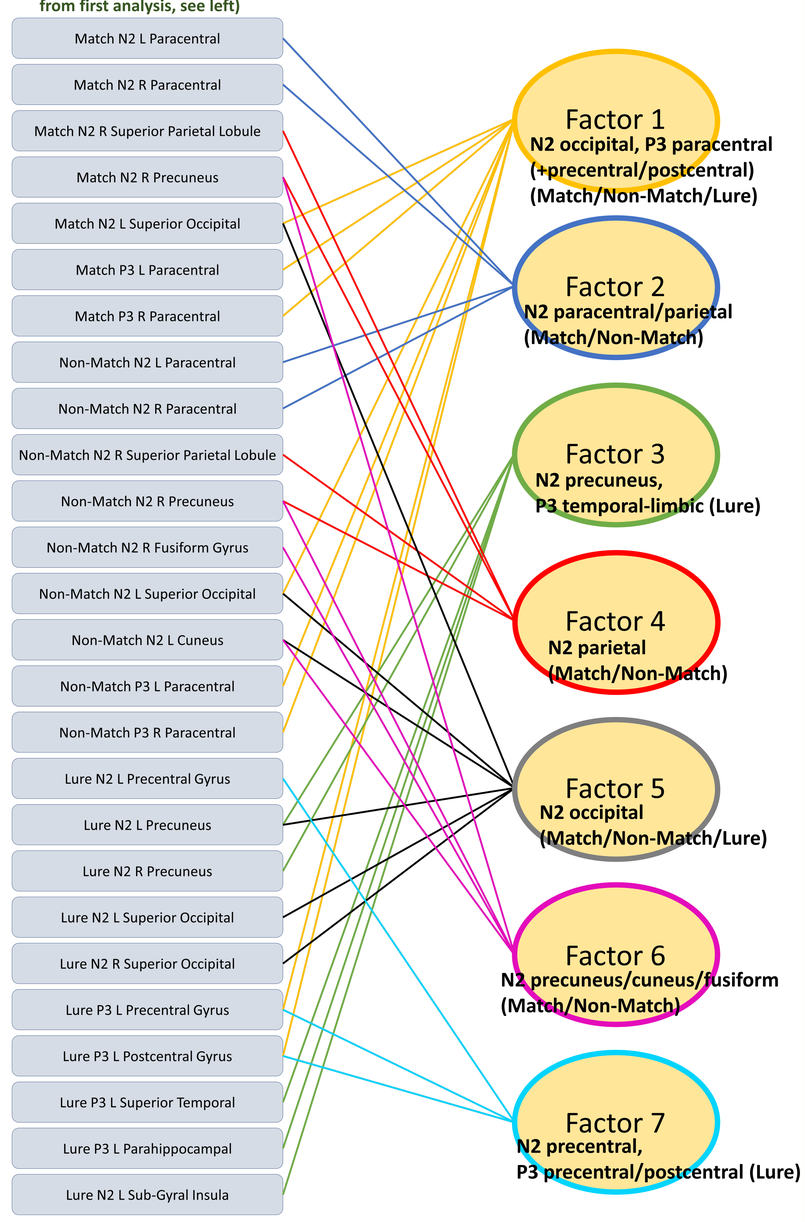
Regions in which n-back > search contrast for pre-to-post-training cortical enhancement was statistically significant

Region	Gyrus	Match N2	Match P3	Non-Match N2	Non-Match P3	Lure N2	Lure P3
L Frontal	L precentral gyrus					●	●
L Frontal-Parietal	L paracentral lobule	●	●	●	●		
R Frontal-Parietal	R paracentral lobule	●	●	●	●		
L Parietal	L postcentral gyrus						●
	L precuneus					●	
R Parietal	R superior parietal lobule	●		●			
	R precuneus	●		●		●	
L Temporal	L superior temporal gyrus						●
R Occipital-Temporal	R fusiform gyrus			●			
L Occipital	L superior occipital gyrus	●		●		●	
	L cuneus			●			
R Occipital	R superior occipital gyrus					●	
L Limbic	L parahippocampal gyrus						●
L Insula	L sub-gyral						●

● = $p < .05$ $d = 0$ — $d = 0.8$

CONCLUSIONS: Similar training related changes in cortical activity were observed for Match and Non-Match trials in the N2 window; and Match/Non-Match trials in the P3 window. Changes in cortical activity underlying N2/P3 for Lure trials were observed in a different set of gyri, in comparison to Match/Non-Match trials.

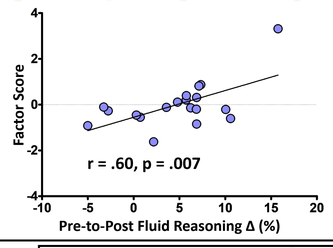
2. Functionally associated network activity: Latent variables derived from factor analysis



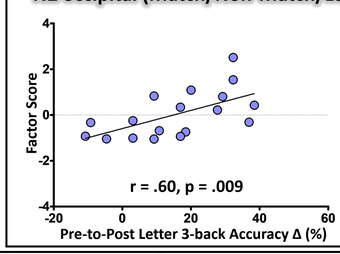
CONCLUSIONS: The factor analysis produced seven latent variables that may underlie the structure of network activity associated with changes in cortical activity following n-back training.

3. n-back training induced network activity vs Δ in cognitive performance: Correlations

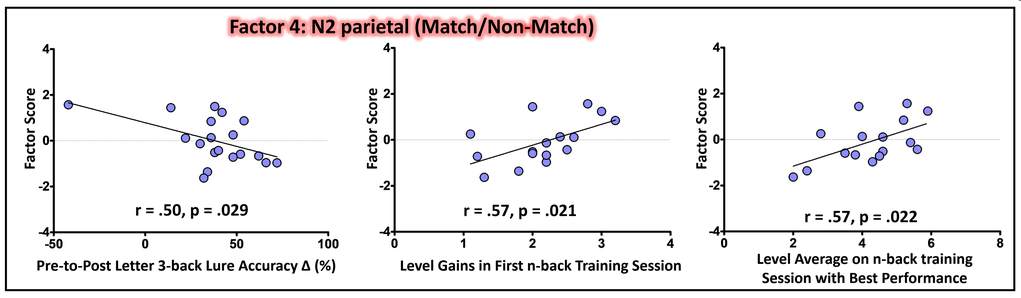
Factor 3: N2 precuneus, P3 temporal-limbic (Lure)



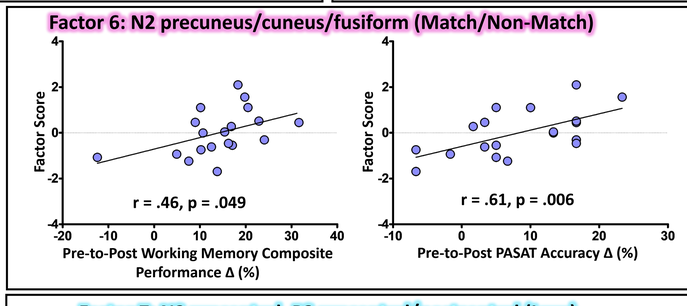
Factor 5: N2 occipital (Match/Non-Match/Lure)



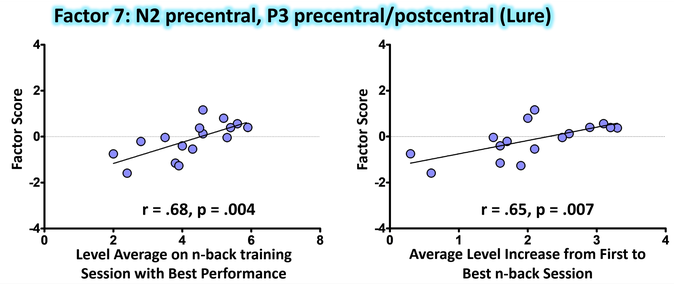
Factor 4: N2 parietal (Match/Non-Match)



Factor 6: N2 precuneus/cuneus/fusiform (Match/Non-Match)



Factor 7: N2 precentral, P3 precentral/postcentral (Lure)



CONCLUSIONS: Network activity in the N2 time window (parietal, occipital, temporal involvement) was associated with gains on the training task and untrained working memory tasks. Network activity spanning the N2 and P3 time windows (frontal, parietal, temporal, limbic involvement) was associated with gains on the training task and untrained fluid reasoning tasks (cautious interpretation, note outliers)