Dynamic Configuration of the EEG Functional Network During Response Inhibition Differs Between ADHD Subtypes in a Non-clinical Population

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Introduction

• The DSM-V recognizes 3 subtypes of Attention-Deficit/ Hyperactivity Disorder (**ADHD**): (1) Inattentive; (2) Hyperactive-Impulsive; and (3) Combined. These traits exist on a continuum in the general population.

• **Response Inhibition** (ability to withhold prepotent motor responses) is a primary deficit in those with ADHD[1]. Each subtype shows distinct response inhibition deficits:
- **Inattentive**: variable & and delayed responses, reduced N2 ERP, increased oscillatory alpha power[2,3,4]
- **Hyperactive-Impulsive**: incorrect & early/anticipatory responses[2]
- **Combined:** increased beta power[4]

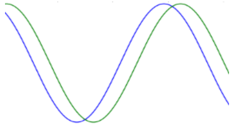
• Shift in our understanding of response inhibition neural correlates[5]:
- **Modular** perspective: right inferior frontal gyrus (rIFG) activity is crucial to inhibition; Vs.
- **Network** perspective: frontoparietal network dynamically shifts towards efficient configuration to promote response inhibition[5].

• Unknown whether specific deficits in this dynamic shifting of network configuration may be associated with each ADHD subtype.

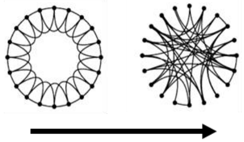
Present Study: We explore how ADHD traits relate to:

N2 ERP: Activation of specialized area in the frontoparietal network

Phase Synchronization:
Consistency of phase differences between two EEG signals. Thought to reflect the mechanism used by populations of neurons to communicate during cognition[6].



Global efficiency:
Reflects a shift towards functional integration. Global efficiency during processing is thought to promote a wide range of executive functions[7].



This research could:
(1) Elucidate various brain mechanisms used during response inhibition in people with different ADHD subtype traits;

(2) Inform our understanding of why response inhibition is challenging for people with ADHD and how targeted intervention may help.

Methods

Participants
• 62 university students aged 18 – 24, 28 females and 34 males.

Preprocessing and ERPs
• Continuous 128-channel EEG (500 Hz sampling rate); Referenced to average
• Filter: 40 Hz low-pass (ERPs), 100Hz low pass/60Hz notch (phase synchrony).
•Artifact removal: ICA for eye movements; threshold rejection set at +/- 100 mV
• ERPs: 200ms pre-stimulus baseline; cluster based permutation test (200-300ms)

Connectivity (Phase Synchronization)
• Single trial data z-scored; filtered into canonical frequency bands (delta 1-3Hz, theta 4-7Hz, alpha 8-12Hz, beta 13-25Hz, gamma 30-90Hz)
• Hilbert transform for phase estimates (±3 s from stimulus onset)
• **Phase Lag index (PLI):** consistency of phase differences between signals across trials while attenuating phase differences of 0, π, and 2π. This attenuation reduces the likeliness of measuring synchronization due to volume conduction[8].

Psychometric Tests
• Self-report measures of ADHD traits were collected with the Conner's Adult ADHD rating scale-long version and the DSM-IV ADHD rating scale.

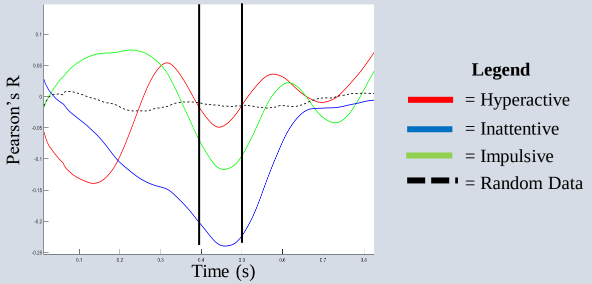
Network Analysis
• NoGo - Go PLI values = Undirected Weighted Network
Nodes = 128 electrodes
Edges = PLI values of top 20% strongest connections

• Global efficiency measured for each participant at each time point
Global efficiency = local efficiency (∈) averaged across every pair of nodes (i and j) in the network,
Local efficiency = inverse of the distance between node pairs
Distance = minimum number of connections to travel between nodes[9]:

$$E_{glob} = \frac{1}{n(n-1)} \sum_{i \neq j} \in (v_i, v_j)$$

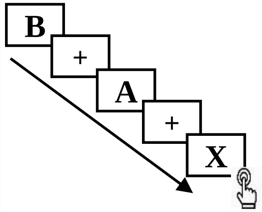
• Pearson correlations between global efficiency at each time point and Conner's Adult ADHD Rating Scale (CAARS)

Global Efficiency and ADHD



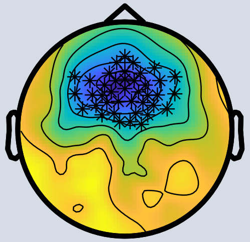
Correlations between ADHD subtype traits & global efficiency of **alpha (8-12 Hz)** functional network over time. **Shift towards less efficient network configuration in those with Inattentive traits** (400-500ms; $r = -.27$, $p = .03$).

Stimuli

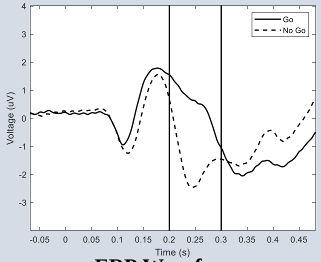


1270 Letters were presented quasi-randomly. Participants were told to respond quickly and accurately to the letter **X**, but only when it was preceded by the letter **A.**
50% of letters following **X** were **A.**
Go = Trials requiring a response, 50 total
NoGo = Trials NOT requiring a response, 50 total

N2 ERP



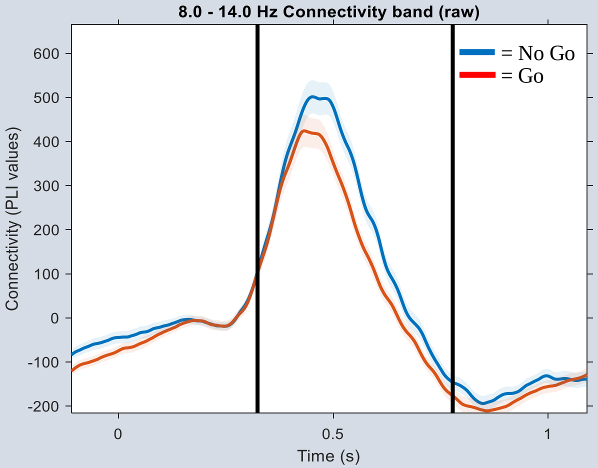
Topographical Distribution



ERP Waveforms

Mean N2 amplitude (200-300 ms) greater (more negative) for NoGo vs. Go trials ($p < .001$). **This effect was smallest in those with higher trait measures of hyperactivity:** CAARS Hyperactivity/Restlessness: $r = -.307$ ($p = .015$), DSM-IV Hyperactive/Impulsive: $r = -.279$ ($p = .028$)

Phase Synchronization Over Time



Alpha-band (8-13Hz) functional network communication between frontal N2 electrodes and the global brain network over time.
→ More communication from N2 areas for NoGo vs. Go trials

(492 – 728 ms; *pcorr* < .05; electrodes selected from ERP results)
No other frequency bands showed significant condition differences.

Conclusion

• People with **hyperactive** traits showed smaller N2 effect
→ Reduced specialization of local areas within frontal-parietal network during response inhibition

• People with **inattentive** traits showed a **less globally efficient** alpha network configuration when inhibiting motor responses
→ More functionally segregated frontal-parietal network
→ Reduced ability to dynamically shift towards an efficient configuration during response inhibition

Clinical Implications for ADHD diagnosis & intervention:
Differentiating subtype-specific deficits with neurophysiological measures of inhibition could allow clinicians to tailor remediation efforts early in diagnosis.

Future Research Directions:

How do networks modulate over the course of processing?
We could use dynamic networks (rather than the static networks constructed at each time point here) to better capture the degree to which networks configure themselves in response to task demands[3], a defining characteristic of executive functions.

Which network characteristics best predict ADHD subtype?
We could use machine learning methods to understand which network features (of the many measures of integration, segregation, and information transfer, for each frequency band, at both local/global level) are best able to predict the severity of ADHD subtype.

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