

Pain Modulation of the Prefrontal Cortex Following Diagnostic Nerve Blocks in Chronic Pain Patients: A Functional Near-Infrared Spectroscopy Study

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Background

Chronic pain affects millions, impairing daily functioning and often resisting conventional treatments.^{1,2} Current pain assessments rely on subjective reports, such as numeric pain rating scales, which lack objective biomarkers for pain perception and treatment response.³ While straightforward, these scales can vary widely between individuals and even within the same patient over time, influenced by emotions, context, and patient-provider interactions.⁴



- Recent fMRI studies have identified objective biomarkers for pain and analgesia, but its high cost and impracticality limit clinical translation.^{5,6} More accessible neuroimaging tools could improve pain assessment, enable earlier intervention, reduce chronic pain progression, and decrease reliance on opioids, leading to more effective and personalized pain management strategies.
- Functional Near-Infrared Spectroscopy (fNIRS) is a non-invasive neuroimaging tool that measures cortical hemodynamic changes, offering real-time insights into brain activity related to pain.⁷ While fNIRS has been well-documented for studying pain states and resting neural activity, its application in clinical pain settings remains largely unexplored.^{8,9}
- Diagnostic nerve blocks are widely used to identify pain sources and provide temporary relief, yet their cortical mechanisms remain poorly understood.¹⁰ Although clinically effective in reducing pain, how these procedures alter brain activity remains unclear.
- This study examines prefrontal cortical modulation in chronic pain patients undergoing diagnostic nerve blocks, exploring how these procedures influence brain activity to reinterpret and alleviate pain, and providing a potential objective neural marker of pain relief.

Methods

Study Inclusion Criteria:

- This IRB-approved study (Pennsylvania State University, STUDY00025253) recruited chronic pain patients scheduled for diagnostic nerve blocks at Penn State Health’s Pain Clinic.

Procedure for fNIRS Collection:

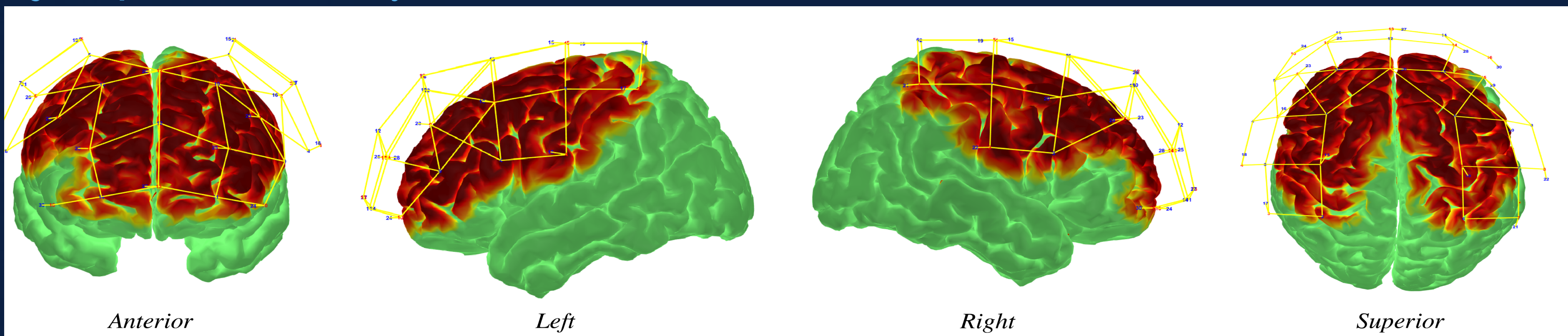
- Patients underwent two 10-minute resting-state fNIRS sessions (pre- and post-procedure), with signals collected using a NIRScout system (16 sources, 14 detectors, 2 short-distance channels) and NIRx 15.3 software.
- Pain scores were recorded pre- and post-procedure using a 0–10 numeric rating scale (NRS).
- Clinical data, including demographics, medications, and comorbidities, were extracted from medical records.
- Healthy controls (HCs) with no pain conditions, recent trauma, or hospitalizations provided baseline resting-state fNIRS data in a single 10-minute session. Resting-state functional connectivity (RSFC) was analyzed using the NIRS Brain AnalyzIR Toolbox in MATLAB R2022b, focusing on 15 prefrontal channels from the total 48.¹¹

Table 1: Study Inclusion

Patient	Age	Sex	Diagnostic Blocks	Pain Score (Pre/Post)	Δ HbO
1	62	Female	Bilateral genicular nerve branches Bilateral nerve to vastus medialis & intermedius	6 → 0	- 0.1067
2	68	Male	Right-sided C3-C5 medial branch blocks	8 → 3	- 0.0070
3	58	Female	Bilateral L3-L4 medial branch blocks Bilateral L5 dorsal ramus block	7 → 5	+ 0.0215
4	69	Female	Bilateral 3rd occipital nerve block	10 → 0	- 0.103
5	37	Female	Bilateral L3-L4 medial branch blocks Bilateral L5 dorsal ramus block	8 → 2	+ 0.2724

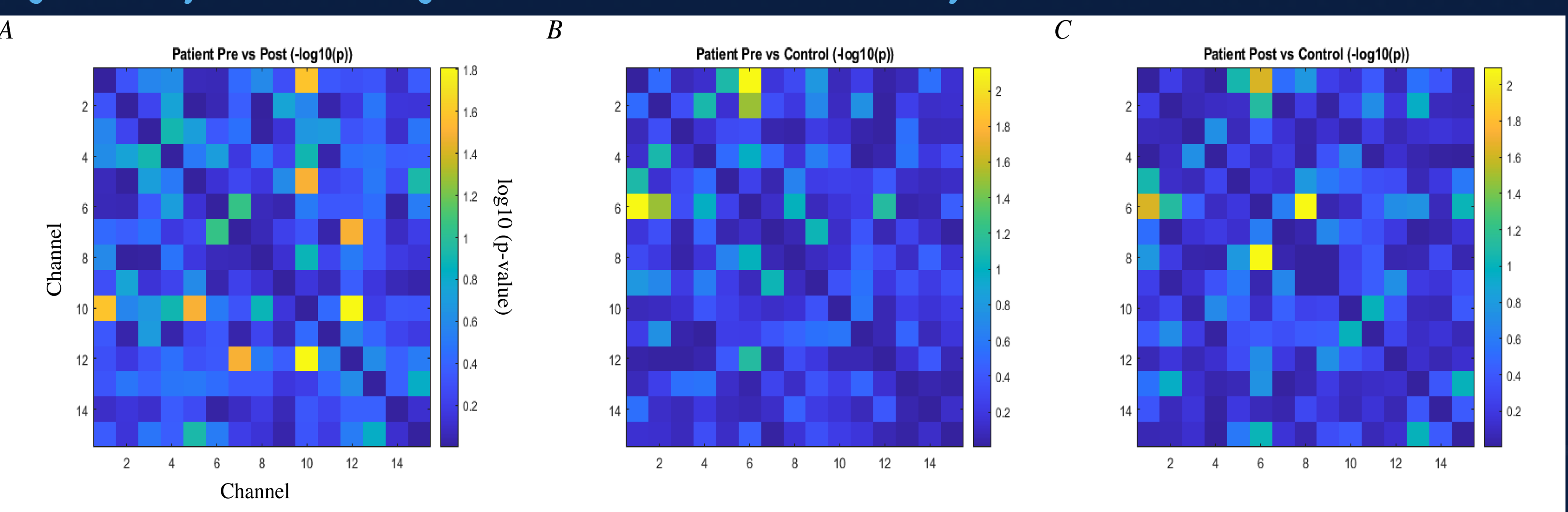
- Five patients (one male, four females) and four HCs were included. The median age of patients was 62 years (IQR: 58–68).
- The average NRS pain score significantly decreased from 7.8 (SD = 1.5) to 2.0 (SD = 2.1) post-procedure (t = 4.53; p = 0.011).
- The difference mean oxygenated hemoglobin concentrations [HbO] across 15x15 channels Z-values reflected as Δ HbO.

Fig 1: Spatial Sensitivity of fNIRS Measurements



- Monte Carlo simulations using the Homer3 AtlasViewer toolbox to simulate and visualize the efficacy of the optical sensors.

Fig 2: Analysis of Resting-State Functional Connectivity Across fNIRS Prefrontal Channels



- Preliminary cortical activity data, illustrating trends in resting-state functional connectivity (RSFC) differences between pre- and post-block conditions. Brighter spots indicating measurable modulation of prefrontal cortical connectivity following the diagnostic nerve block.

Discussion

Key Findings

- ✔ Patient self-reported pain scores significantly decreased post-block (mean Δ pain: -5.8, t = 4.53; p = 0.011), supporting the efficacy of diagnostic nerve blocks.
- ✔ Although no statistical differences were found in Δ HbO, descriptive trends suggest variability in prefrontal cortical modulation among patients following diagnostic nerve blocks. 3 out of 5 patients exhibited a decrease in HbO, while 2 patients showed an increase, suggesting individual differences in cortical pain processing [Table 1].
- ✔ Figure 2A highlights RSFC differences between pre- and post-block conditions, showing scattered significant differences (bright spots), indicating that the diagnostic block produces measurable prefrontal modulation.
- ✔ Figure 2B shows altered prefrontal connectivity in patients before the block compared to HCs, likely reflecting heightened pain perception and processing associated with chronic pain.
- ✔ Figure 2C suggests partial normalization of prefrontal activity post-block, with post-block recordings becoming more comparable to those of HCs. However, residual differences remain, suggesting incomplete modulation or persistent pain-related neural adaptations.

Points for Interpretation

- 💡 Variability in HbO responses suggests that individual differences may influence how the prefrontal cortex processes pain relief.
- 💡 Residual differences in certain cortical regions post-block suggest that modulation may be incomplete or that patients may have lasting neural adaptations from chronic pain exposure.
 - While nerve blocks provided meaningful pain relief, chronic pain may involve persistent cortical alterations that extend beyond immediate treatment effects.
 - These procedures were diagnostic in nature, the true pain generator may not have been fully targeted, which may result in incomplete treatment.
 - In clinical pain management, it’s common for multiple sources to contribute to pain, and treating only one of these may lead to partial cortical changes that don’t fully reflect pain resolution.

Future Directions

- 🔮 Expand sample size to improve statistical power ➔ A larger cohort will help detect subtle cortical modulation effects and clarify whether individual differences in prefrontal responses correlate with pain relief.
- 🔮 Longitudinal studies to assess sustained neural adaptations ➔ Future work should track fNIRS activity over multiple time points post-block to determine whether cortical modulation evolves over time or if residual neural adaptations persist despite pain relief.

Contact + References:



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