

# Multimodal Neuroimaging (fMRI and fNIRS) at WPI

# **PracticePoint**

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Data Processing in Functional Near-Infrared Spectroscopy (fNIRS) Steady State Research for

Future Collation with fMRI Data.

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#### Abstract

Chronic pain presents a complex challenge in medical science that affects a substantial portion of the population. The most common technique to analyze how chronic pain manifests in the brain is by the way of functional magnetic resonance imaging (fMRI). While this method provides reliable, insightful data, it has large downsides. In recent studies, however, there has been promising data that suggest that fNIRS may offer a unique opportunity to investigate the neural foundations of pain perception in real-time. This study focuses on analyzing cortical neural hemodynamics during resting-state using fNIRS for future collation with fMRI data and applications in chronic pain identification and research. To analyze this, a sample set of 7 participating healthy individuals over the age of 18, underwent multimodal neuroimaging utilizing both fMRI and fNIRS imaging techniques simultaneously. This data was processed in nirsLAB software using GLM analysis to derive what areas of the cortex experienced significant increases in hemoglobin. The results of this study did find spontaneous increases in hemoglobin in the 4 valid samples analyzed as would be expected with resting-state data. However, the overall consensus was that overall, the sample set was not ideal due to the substantial loss of data integrity across the 20 channels observed for each subject.

### 1. Background/Introduction

What is chronic pain? Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."<sup>1</sup> Chronic pain is classified as "pain that persists past normal healing time and hence lacks the acute warning function of physiological nociception." Physiological nociception is when pain detects some level of damage. Pain is considered chronic when it lasts for 3 to 6 months.<sup>2</sup>

A review of several studies achieved an estimate that 15% of adults suffer from chronic pain while one of the studies estimated that 40% of adults suffer from chronic pain.<sup>3</sup> The CDC estimates that 20.9% of adults in the United States suffer from chronic pain.<sup>4</sup> Neuroimaging is believed to be able to detect pain. Despite this most studies agree that neuroimaging should not be used to replace patient reports on pain, as a distinction between perceived pain and imageable pain could lead to poor treatment. Still, neuroimaging is useful for detecting chronic pain.<sup>5, 6</sup>

The areas of the brain most implicated in pain perception include the frontal and parietal lobes, particularly the prefrontal cortex and the primary somatosensory cortex [xx]. Notably, the prefrontal and limbic regions play a crucial role in regulating emotional and motivational responses to pain stimuli, thereby influencing the subjective experience of pain. Numerous

<sup>&</sup>lt;sup>1</sup>Merskey, H. A. F. D. (1979). Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. Pain, 6, 249-252.

<sup>&</sup>lt;sup>2</sup>Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., ... & Wang, S. J. (2015). A classification of chronic pain for ICD-11. Pain, 156(6), 1003-1007.

<sup>&</sup>lt;sup>3</sup>Verhaak, P. F., Kerssens, J. J., Dekker, J., Sorbi, M. J., & Bensing, J. M. (1998). Prevalence of chronic benign pain disorder among adults: a review of the literature. Pain, 77(3), 231-239.

<sup>&</sup>lt;sup>4</sup>Rikard, S. M., Strahan, A. E., Schmit, K. M., & Guy Jr, G. P. (2023). Chronic pain among adults—United States, 2019–2021. Morbidity and Mortality Weekly Report, 72(15), 379.

<sup>&</sup>lt;sup>5</sup>Robinson, M. E., Staud, R., & Price, D. D. (2013). Pain measurement and brain activity: will neuroimages replace pain ratings?. The Journal of Pain, 14(4), 323-327.

<sup>&</sup>lt;sup>6</sup>Davis, K. D., Flor, H., Greely, H. T., Iannetti, G. D., Mackey, S., Ploner, M., ... & Wager, T. D. (2017). Brain imaging tests for chronic pain: medical, legal and ethical issues and recommendations. Nature Reviews Neurology, 13(10), 624-638.

neuroimaging studies have demonstrated morphological changes in these regions among individuals with chronic pain, highlighting the interplay between pain processing and emotional regulation [2012 study].



Figure x: Illustrates how the cortex of the brain is sanctioned into lobes. The frontal, parietal occipital and temporal lobe make up the entirety of the cerebral cortex.

Functional Near-Infrared Spectroscopy (fNIRS) scans use an optode configuration to measure oxygenated and deoxygenated blood. There are eight sources and eight detectors, otherwise known as leads. The sources are LEDs pressed at various points along a person's scalp. A red light that is almost the wavelength of infrared comes from the source and is then reflected back by blood. Detectors then measure the reflected light, determining at what points in the brain there is blood activation. There are 20 channels in which this is measured. These scans are blood oxygenation level dependent (BOLD). This makes fNIRS an optimal proxy for fMRI since fMRI is also BOLD.

Recent advancements in neuroimaging techniques, such as fNIRS, offer a unique opportunity to investigate the neural foundations of pain perception in real-time. For instance, a study utilizing fNIRS revealed elevated concentrations of oxygenated hemoglobin (HbO) in the

prefrontal cortex of patients with cervical shoulder syndrome (CSS) experiencing painful stimuli [2023 study]. This heightened HbO concentration was accompanied by increased neural activity in regions associated with cognitive and emotional pain processing, shedding light on the complex interplay between physiological and psychological factors in chronic pain conditions.

Additionally, neuroimaging studies have identified structural alterations in brain regions involved in emotional and cognitive processing among individuals with chronic pain. Reduced gray matter volume in the hippocampus and amygdala, as observed in patients with chronic pain, suggests a strong correlation between pain perception and emotional-cognitive changes in the brain [xx]. These findings emphasize the multifaceted nature of chronic pain and the importance of integrating neuroimaging techniques like fNIRS to explain its underlying mechanisms.

fNIRS offers a more compelling alternative to MRI, which provides data to researchers and clinicians as a tool for studying brain activity with advantages that include portability, patient comfort, cost-effectiveness, and improvement in computer interface technology.

MRI is oxygen-dependent, while fNIRS can separately measure oxygenated, deoxygenated, and total hemoglobin. This can be advantageous in measuring brain activity and hemodynamics as clinicians better understand the involvement of neural activity and mapping brain activity in clinical settings [xx].

MRI requires a person to sit still for up to 60 minutes in order to be completed successfully, which can be difficult for patients to go through especially those that are younger or have chronic pain. The concept of being contained in a small space, having to stay still with noise/exposure to radio frequency pulses in the background, and possibly needing to insert a needle for intravenous contrast administration can increase anxiety levels that sometimes lead to the patient going under anesthesia. Sedating patients has its own risks when a patient is over-sedated including respiratory depression, which can lead to airway obstruction and a decrease in function in protective reflexes. The sedation process can add extra time to the scanner and cost hospital billing due to the use of additional staff, hospital equipment, and drug administration. A big issue for children getting MRIs is that they aren't usually well educated in how the machine works and this feeling of uncertainty is what leads to high levels of anxiety and can lead to anxiety-related psychological disorders like claustrophobia that can develop into adulthood. Studies suggest children experience similar levels of anxiety as adults [xxx].

fNIRS is a noninvasive process that doesn't expose patients to strong magnetic fields or any loud noises that remove the fear factor, especially those patients that have a chronic illness, which requires the use of magnetic devices like a pacemaker. As opposed to MRI, fNIRS is less sensitive and can tolerate motion artifacts, which is important for patients who have a hard time staying still. People with movement disorders would benefit from this greatly as this larger threshold for assessment along with the faster testing rate allows patients to be more comfortable with the procedure. fNIRS, like fMRI, observes changes in oxygen concentrations in the brain tissue, but instead of relying on the paramagnetic properties of hemoglobin, it utilizes the different absorption properties of biological chromoph<sup>7</sup>ores and detects these light changes from anywhere between 700 and 900 nm. Some of the more notable biological chromophores detected in the brain include hemoglobin, myoglobin, and cytochrome oxidase. fNIRS is portable, which is one of the most important characteristics of the system. They are smaller, less expensive, and more portable than MRI systems. This feature of the machine makes it very viable in clinical<sup>8</sup> settings that allow for greater accessibility to brain imaging [xx].

<sup>&</sup>lt;sup>7</sup>Scarapicchia, V., Brown, C., Mayo, C., & Gawryluk, J. R. (2017). Functional Magnetic Resonance Imaging and Functional Near-Infrared Spectroscopy: Insights from Combined Recording Studies. *Frontiers in human neuroscience*, *11*, 419. <u>https://doi.org/10.3389/fnhum.2017.00419</u>

<sup>&</sup>lt;sup>8</sup>Hallowell, L. M., Stewart, S. E., de Amorim e Silva, C. T., & amp; Ditchfield, M. R. (2007). Reviewing the process of preparing children for MRI. Pediatric Radiology, 38(3), 271–279. <u>https://doi.org/10.1007/s00247-007-0704-x</u>

fNIRS measures brain activity by detecting changes in blood oxygenation and flow that occur in response to neural activity. When a brain area is more active, it consumes more oxygen, and to meet this increased demand, blood flow to the active region increases. The device uses near-infrared light (wavelengths between 650 and 900 nanometers) because it can penetrate the skull and is absorbed differently by oxygenated and deoxygenated blood. Light sources, usually LEDs or laser diodes, emit near-infrared light. This light is then directed into the scalp and skull. As the light travels through the brain tissue, it is absorbed and scattered by different components within the tissue. Oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) absorb light differently, affecting the light's intensity and wavelength. Optical sensors placed on the scalp detect the light that has traveled through the brain tissue and bounced back. These sensors measure the amount and properties of the light that returns. By analyzing these light signals, the fNIRS machine can determine the relative concentrations of oxygenated and deoxygenated blood in the brain. This information is used to infer brain activity in the regions where the light was emitted and detected. Through complex algorithms, the data obtained from these measurements is then used to map out which areas of the brain are more active (indicated by higher levels of oxygenated blood) during specific tasks or stimuli.

One of the biggest strengths of fNIRS machines is its ability to integrate with other neurocognitive devices like electroencephalography (EEG). The purpose of this pairing is to improve the brain-computer interface technologies including the spatial resolution from fNIRS and temporal resolution of EEG. This would help in mapping areas of the brain activity, which can have potential in treating psychological disorders like anxiety [xx].

Functional Magnetic Resonance Imaging (fMRI) has several important advantages for studying the brain. It's safe because it doesn't require surgery or anything invasive. It's really

good at showing where brain activity happens, so researchers can figure out which parts of the brain are involved in different tasks or problems. People use it for all sorts of studies about how our minds work. And it can be combined with other brain imaging methods to give us even more information. In hospitals, doctors use it to find problems in the brain and plan treatments. It's also used to study things like memory, learning, and how our brains change over time. So, fMRI is a powerful tool for understanding the brain and helping people with brain-related issues (Toronov, 2001).

Previous studies utilizing fNIRS have provided valuable insights into the hemodynamic changes associated with specific cognitive tasks and brain dysfunction. For instance, a study demonstrated a significant increase in HbO levels in the lateral superior frontal and left parietal cortices, along with a substantial decrease in HbR levels in the right parietal cortex during certain cognitive tasks [xx]. These findings were corroborated by our own data, which revealed a pronounced concentration of HbO in the right frontal lobe, consistent with the observed pattern in the external study.

Similarly, another investigation employed fNIRS to compare hemoglobin levels between patients with prefrontal cortex dysfunction and healthy controls following cognitive tasks such as verbal fluency and visual spatial working memory tests [xx]. The results indicated significantly higher concentrations of both HbO and HbR in the prefrontal cortex of healthy individuals compared to those with dysfunction, suggesting a link between altered brain function and conditions affecting this brain region, such as traumatic brain injury (TBI).

fMRI offers a range of compelling advantages in the field of neuroscience and medical research. One key benefit is its non-invasiveness, as fMRI does not require any surgical procedures or physical intrusion into the body (Logothetis, 2008). This makes it an ethical and

safe method for investigating brain function. Researchers can observe brain activity without the need for risky procedures, making it more comfortable for study participants and suitable for a wide range of populations, including clinical patients.

Moreover, fMRI excels in providing high spatial resolution, allowing researchers to precisely pinpoint brain activity within specific regions (Bandettini et al., 1992). This advantage is critical for mapping the functional organization of the brain and identifying brain regions associated with particular cognitive functions or disorders. The detailed spatial information enables researchers to create precise brain activity maps, enhancing our understanding of the brain's functional architecture. In combination with its non-invasiveness, high spatial resolution makes fMRI a valuable tool for both basic neuroscience research and clinical applications.

### 2. Methodology

### 2.1 Participants

This prospective multimodal study was conducted in collaboration with UMass Medical to investigate the steady-state neural activity of healthy individuals and compare their data with patients experiencing chronic pain. The overall study involved 7 participating healthy individuals over the age of 18, who underwent the multimodal neuroimaging utilizing both fMRI and fNIRS imaging techniques. This report focuses on the fNIRS data analysis of the participants to better understand the cortical hemodynamics of the brain and the resulting data's prospective role and application in the complementary analysis of fMRI data.

The set up of a fNIRS machine involves several steps to ensure accurate and effective brain activity measurement. The following sections 2.2 - 2.5 delineates a comprehensive overview of the experiment's setup and procedure.

#### 2.2 Sensor and Optode Placement:

The scan involves using a cap, which comes in two different sizes including 42-48 cm for children over the age of 2 years old and 50-60 cm for adults. Optodes are the light-emitting and light-detecting components. Optodes are typically arranged in a cap that is worn on the head. The optodes are placed on the scalp according to a predefined sequence that targets specific areas of the brain. The placement is often guided by a standard brain atlas or based on the specific requirements of the study. It's important to ensure the cap or band is snug but comfortable, to maintain optimal sensor contact with the scalp without causing discomfort to the participant.



Figure (x): Illustrates the optode placement map used in this study, which serves as a foundational component for the subsequent neural connectivity mapping.

After samples are recorded, inferences can be made upon what regions of the brain were active, depending on the corresponding optode and area of the head for which that optode was placed. This study only utilizes 20 channels, therefore, only a select region of the cortex was analyzed. The below Figure shows the location key of the optodes utilized in this study.

Channel # (Left Hemisphere)	Channel # (Right Hemisphere)	Location	Location	Function
Ch 1	Ch 12	Precentral gyrus	lateral frontal lobe	voluntary motor movement
Ch 2	Ch 11	Postcentral gyrus	Lateral Parietal lobe	involuntary motor movement
				processing of language (triangular - semantic
Ch 3	Ch 13	Inferior frontal gyrus (Triangular)	frontal lobe (Broca's area)	processing of language)
Ch 4	Ch 15	Precentral gyrus	lateral frontal lobe	voluntary motor movement
Ch 5	Ch 14	Postcentral gyrus	Lateral Parietal lobe	involuntary motor movement
			(central fissure) divides pre-& postcentral	
Ch 6	Ch 16	Central sulcus (Postcentral & Precentral gyri)	gyri along dorsal-ventral plane	motor and sensory function
Ch 7	Ch 17	Middle frontal gyrus	middle prefrontal cortex	Left (development of literacy), right (numeracy)
Ch 8	Ch 18	Middle frontal gyrus	middle prefrontal cortex	Left (development of literacy), right (numeracy)
Ch 9	Ch 19	Middle frontal gyrus	middle prefrontal cortex	Left (development of literacy), right (numeracy)
Ch 10	Ch 20	Superior frontal gyrus (Dorsolateral)	prefrontal cortex	higher cognitive functions/working memory

Figure(x):

### 2.3 Calibration and Baseline Measurement:

Before starting the measurement, the system is calibrated to ensure the accuracy of light detection and signal processing. A baseline measurement is often taken with the participant at rest or in a neutral state, to serve as a reference for detecting changes in brain activity.

2.4 Connecting to Data Acquisition System:

Optodes are connected to the data acquisition system, which records the light signals. Before starting the experiment, it's crucial to check the quality of the signals to ensure that the optodes are functioning properly and are receiving clear signals.

#### 2.5 Task Administration:

Depending on the study design, participants may be asked to perform specific tasks or be exposed to certain stimuli while neural activity is being recorded. Because this study focuses on methods of collation with fMRI data, the recorded neural activity was sampled during resting-state. Resting-state fNIRS (also known as steady-state) measures the spontaneous hemodynamic fluctuations in the four lobes of the cerebral cortex of the brain (frontal, temporal, parietal and occipital lobes) while there are no explicit tasks or stimuli performed [9].

#### 2.6 fNIRS Software - NirsLab:

After the experiment, the collected data is analyzed using specialized software. This analysis includes filtering, signal correction, and statistical testing to interpret the brain activity patterns.

NIRS signals detect changes in the attenuation of light in several brain regions including somatosensory and motor regions in order to measure the concentration changes in HBO and Hbr in brain tissue. This data uses a series of time-dependent signals measured between each light source and the detector positions of the probes [xx]. The software used to record the data was done using NirsLab. This imaging system is intended for NIRS of blood perfusion movement in the brain region.

#### 2.7 Data Pre-Processing

Channel signal visualization was completed in MatLab using the files derived from the raw fNIRS data. The unfiltered signal data was plotted using a tiled chart layout in order to compare the signal quality across the individual channels. The Total Hb, Oxygenated Hb and Deoxygenated Hb were plotted for each data sample to evaluate the amount of good channels established for each sample. A threshold number of channels was determined based upon the prevalence of good channels across all the given data samples. By establishing a threshold, certain data samples that don't meet the required amount of functioning channels can be eliminated from consideration in the later data analysis. This prevents the data from being skewed by outlier variables in signal quality.



Figure (x): Illustrates a MATLAB figure of the data recorded for each of the 20 channels for sample 2023-06-21-002. Notably, this specific sample demonstrated complete data integrity across all of the 20 channels.

Analysis of the visualized channel data across all 7 subjects revealed that none of the observed channels had clean signals across the entirety of the 7 samples taken. Moreover, an assessment of channel quality across all subjects showed that a substantial 46.4% of channels across all

subjects were bad (meaning no signal was recorded by the channel). The coefficient of variation (CV) for the instances of bad channels across all subjects, as visualized in graph [x], was adopted as the criterion to discern between channels exhibiting acceptable vs subpar signal quality. This metric is automatically calculated by the nirsLAB software and was computed at 15%. Specifically, within this dataset, there were 5 channels identified that had over 4 instances of missing data/bad signal quality across the samples. Furthermore, a subset of 12 channels (1, 3, 5, 6, 7, 9, 10, 11, 12, 13, 14 and 18) displayed a recurring pattern of having 3 instances of compromised or absent data.



Chart [x] : The left chart displays the bar graph of Instances of Bad Channels Across All Subjects where the CV was quantified at 34.4%. The right image shows an example of the resulting hemoglobin map with missing and/or bad channels.

A total of 7 samples collected for analytical purposes. To mitigate data dimensionality, and ensure the integrity of subsequent/future analysis, subjects characterized by less than 50% of channels displaying good signal quality were discarded from the examined dataset. Here, Subjects 2023-06-21-001, 2023-07-07-002 and 2023-07-07-003 had 9, 7 and 2 good channels

respectively, which was sufficient for these samples to be removed. By eliminating these instances, the remaining dataset, composed of 4 subject samples, demonstrated a collective reduction in total bad channel quality to 27.5%.

After establishing what samples would be considered in the final analysis, the raw data files were pre processed and analyzed using nirsLAB. Data preprocessing was completed with SPM Level 1 using a generalized linear model (GLM) based analysis on each subject, which has been shown in past literature to be better representative of fNIRS data. GLM is a statistical linear model utilized to show data by modeling it as a linear combination of an explanatory variable plus an error term. In this context, GLM is employed to specifically measure the temporal variational pattern within the signals.



Figure (x): Illustrates the baseline HRF curve that is used to model the expected pattern of changes in hemoglobin concentration over time in response to a task or stimuli.

In nirsLAB, the data was truncated and checked for quality, but no filter was applied. The hemodynamic states parameters were from a Gratzer filter. The data was pre-whitened with AR(n) (NIRx's autoregression formula that is specifically suited towards fNIRS data) and a hemodynamic response function (HRF) was used as a basis function. There was no temporal filtering applied. The GLM coefficients were then estimated to create the SPM contrast data, and a series of p and t values were saved thereafter as Matlab files, and visually as hemodynamic maps for both the beta images and the residual mean square images (as shown below in Figure x). The resulting SPM analysis .mat files were additionally evaluated in Matlab in order to obtain the calculated statistics (parameter tables as well as the estimated beta values) for each of the respective data samples analyses. These values will be considered in the later data analysis to evaluate and compare fNIRS data against the general linear model (GLM) to make inferences about brain activity characteristics.



Figure x : Illustrates an example beta image hemodynamic map of the brain for sample 2023-06-21-002. The colors denote the magnitude of total hemoglobin measured during steady-state.

## 3. Results

Sample 2023-06-21-002



Figure x: MATLAB figure shows the raw data of sample 2023-06-21-002 for the total hemoglobin measured in each channel. Notably, there are many channels that document a sudden drop in HbR. These drops are centralized around the front parietal lobe.



Figure x: MATLAB figure shows the raw data of sample 2023-06-21-002 for the oxygenated hemoglobin measured in each channel.



Figure x: MATLAB figure shows the raw data of sample 2023-06-21-002 for the deoxygenated hemoglobin measured in each channel.



#### SPM Hemodynamic Maps

Fig (x): The left diagram illustrates the beta image hemodynamic map of the brain for sample 2023-06-21-002. The colors denote the magnitude of total hemoglobin measured during steady-state. As expected, the distribution of responses is random, as there was no coordinated

task or stimuli to activate a specific brain region. The diagram on the right shows the residual mean square ('ResMS') image which demonstrated the spatial distribution of values in the E (residual term) matrix.



Fig (x): Shows the connectivity matrix created for sample 2023-06-21-002.

### 4. Discussion

Looking at past literature, steady-state cortical neural hemodynamics are defined by spontaneous (non-task/stimulus induced) increases/decreases in hemoglobin. In the context of this study, which utilized GLM analysis to derive a mathematical model of the data in comparison to the expected baseline HRF curve as pictured in Figure (x), it was expected that there would be a lot of potential outliers in the data. The HRF curve assumes that an event, documented at a known time, has caused an increase in hemoglobin levels. In steady state neural analysis, increases in hemoglobin would occur sporadically, which would likely conflict with the event-based analysis method. While this isn't ideal for the given neural state being studied, it would provide valuable knowledge regarding if the sample data aligns with the aforementioned behaviors expected. Following data preprocessing, the finalized set of 4 samples that were analyzed included 2023-07-07-001, 2023-06-29-002, 2023-06-29-001, and 2023-06-21-002. After analyzing the data derived from the GLM analysis, a similar pattern of hemodynamics was found across the 4 valid samples as visualized in the beta images. For example in sample Figure(x), the red regions of the hemodynamic map of total Hb demonstrate large increases in total channels hemoglobin. These regions correlate to channels 5 and 12 which represent the postcentral gyrus and precentral gyrus, respectively. Notably, the functions of these areas of the brain correlates to both voluntary and nonvoluntary motor movement. This could signify that there was some degree of physical movement while this sample was being recorded.

This study does not provide sufficient data to determine the changes in connectivity between brains experiencing chronic pain from a control group of brains not experiencing chronic pain. This study does, however, contain information that could be used to compare with a control group to determine differences.

The average channel failure rate was 46.4%. The test administrator has noted that hair plays a role in the failure rate of channels. Hair may prevent a near-infrared emitter or a sensor channel from making appropriate contact with the scalp. Either case would cause affected sensor channels to have a reading of little to no magnitude. These are then detected as bad channels.

#### **Neural Activity Regions**

Assessing resting state functional connectivity across brain regions in fNIRS can be a useful tool in differential diagnoses for patients that have chronic pain, as it can be very practically applicable when it becomes translated in the medical setting.

A previous study done showed significant increase in HbO from baseline in the lateral superior frontal and left parietal cortices and HbR showed a massive decrease from baseline in right parietal cortex (p < 0.05). In the same study, the channels showed a significant decrease in HbO in the frontal lobe for performing active recall in the various sections of the frontal lobe [xx]. Our data is consistent with this outside study since we have a high concentration of HbO in the right side of the frontal lobe indicated by the blue color.

Another study was done using fNIRS to compare the HbO and HbR levels for patients with prefrontal cortex dysfunction and those of healthy patients after they have done a few tasks including verbal fluency test (VFT) and visual spatial working memory task (VSWMT). The results showed that for both tests, the control group exhibited higher oxyhemoglobin (p = 0.002 and p = 0.001 for right and left side respectively) and deoxyhemoglobin (p = 0.022 and p = 0.003 for right and left side respectively) concentrations in the prefrontal cortex than the patient group

for the VFT [xx]. There would also be a subsequent higher neural activity in the prefrontal cortex for the healthy group, which means the patient group would be linked to patterns of altered brain function that leads to conditions affecting the prefrontal cortex like TBI. In our study, we observed how fNIRS detects changes in HbO and HbR for healthy people and people with chronic pain, which can lead to changes in brain function including areas in the prefrontal cortex leading to cognitive impairments related to dysfunction. Our results show...(need channels mapped to each brain region)

The areas of the brain that perceive pain the most include the frontal and parietal lobes most notably the prefrontal cortex and the primary somatosensory cortex [xx]. The prefrontal and limbic regions are in charge of regulating emotional and motivational responses when dealing with pain processing. The degree of pain experience is affected by the changes of these responses. Many neuroimaging studies show that morphological changes in the limbic and emotional systems are linked to chronic pain [2012 study]. According to a neuroimaging study, patients with chronic pain are shown to have reduced gray matter in the hippocampus and amygdala region, which would show a strong correlation between chronic pain and emotional and cognitive changes in the brain [xx].

A recent study was done using fNIRS showing high HbO concentrations in prefrontal cortex for patients with cervical shoulder syndrome (CSS) that experienced painful stimuli at the cerebral cortex, where they also had heightened neural activity reflective of the high cognitive and emotional pain processing [2023 study]. In our study...

### 5. Conclusion

#### Ethics:

It is important that we do not make the case that pain is only real if measured. This could lead to poor treatment for those for whom pain shows up differently and for those who perceive that they are in pain.

Future Work/Limitations: fNIRS holds significant promise within the neuroimaging realm as a valuable tool for measuring brain activity. Our hypothesis centers on fNIRS's potential to diagnose chronic pain by leveraging BOLD signals at the steady-state level. However, enhancing the technique's design remains a critical focus area. This includes refining spatial resolution through advanced signal processing algorithms, integrating multimodal approaches, enabling real-time data analysis during neurocognitive training, and standardizing processes to ensure reproducibility across studies. These advancements are essential for elevating fNIRS into a more viable neuroimaging modality with practical applications in clinical settings.

Both fMRI and fNIRS are ways to track blood changes in the brain. fNIRS is a more accessible option to both individual and research endeavors due to its lower cost, shorter acquisition duration, and portability. Its benefits make it particularly advantageous for those constrained by limited resources and/or time. This makes fNIRS a promising technological advancement for a wide span of research disciplines, especially chronic pain studies.

\*\*Add section about how laser is what is used to be fMRI safe so it's not as good as LED\*\*

#### **Future Direction:**

Although both fMRI and fNIRS are ways to track hemodynamic changes in the brain, fMRI requires a heavy, expensive magnet while fNIRS requires a wearable, more affordable cap. The wider use of fNIRS would bring the ability to track hemodynamic neuroimaging to situations where an MRI is not practical or available. fNIRS is more accessible to subjects and clinicians with less time and money available and can greatly benefit studies involving more mobile tasks.

However, for fNIRS to allow future studies and clinicians to track hemodynamic changes, it must become more reliable. 46.4% of the channels used in this study were unusable. Less than half the channels were usable in three out of seven of the subjects. The causes of these unusable channels are not unique to this study. When the scalp fails to make sufficient contact with a near infrared emitter or sensor channel, channels may become bad. The issue is compounded by the reality that this loss of data disproportionately affects subjects with hair; the thicker the hair, the more the data collected on the subject is likely to be affected. This may make subjects less likely to be included in a viable set of data. Therefore bad channels caused by hair may not only make initial data collection harder, but it may also affect the ability to use data from specific demographics. There are ethical concerns with excluding data from specific demographics from research, so it is vital that future development addresses this issue through designs or procedures.

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# Appendix

## Sample 2023-07-07-003









Sample 2023-07-07-002







Fig x:

Sample 2023-07-07-001



2023-07-07-001 Deoxygenated Hb							
	Channel 1	Channel 2	Channel 3	Channel 4	Channel 5		
0.5				0.5	0.5		
-0.5			****	-0.5	-0.5		
0	500 1000 1500 2000	0 500 1000 1500 2000	0 500 1000 1500 2000	0 500 1000 1500 2000	0 500 1000 1500 2000		
ī.	Channel 6	Channel 7	Channel 8	Channel 9	Channel 10		
0.5		0.5	and head the state of the shellow	0.5	0.5		
0		0	and a second	0	0		
-0.5		-0.5	which have been been been been been been been be	-0.5	-0.5		
			and the second second second				
-1 -1 -0	500 1000 1500 2000	0 500 1000 1500 2000	0 500 1000 1500 2000	0 500 1000 1500 2000	-1 0 500 1000 1500 2000		
152	10 <sup>-0</sup> Channel 11	Channel 12	A ×10 <sup>-3</sup> Channel 13	2 ×10 <sup>-3</sup> Channel 14	e ×10 <sup>-3</sup> Channel 15		
1.5 1 0.5	10 <sup>-3</sup> Channel 11	Channel 12	4 ×10 <sup>-3</sup> Channel 13	2 - 10 <sup>-3</sup> Channel 14	6 ×10 <sup>-3</sup> Channel 15		
1.5 1 0.5 -0.5	10 <sup>3</sup> Channel 11	Channel 12	4 10 <sup>-3</sup> Channel 13	2 = 10 <sup>-2</sup> Channel 14	6 -10 <sup>-3</sup> Channel 15 4 2 0 2 1 4		
1.5 1 0 -0.5 -1 0	10 <sup>-3</sup> Channel 11 <b>Channel 11</b> <b>Channel 11</b> <b>Channel 11</b> <b>Channel 11</b> <b>Channel 11</b> <b>Channel 11</b>	0.04 0.02 0.04 0.02 0.04 0.05	4 - 10 <sup>-3</sup> Channel 13 2	2 = 117 <sup>2</sup> Channel 14 2 = 0 4 = 0 3 = 0 5 = 500 1000 1500 2000	Channel 15		
1.5 1 0.5 -0.5 -1 0 1	10 <sup>-3</sup> Channel 11 000 1000 1500 2000 Channel 16	Channel 12 0.02 0.02 0.02 0.02 0.02 0.03 0.05 0.00	2 10 <sup>-3</sup> Channel 13 2 0 2 0 0 00 100 1500 200 2 2 <sup>-10<sup>-3</sup></sup> Channel 18	2 + 10-3 Channel 14 0	Channel 15		
1.5 1 0 -0.5 -1 0	10 <sup>-3</sup> Channel 11 00 100 1500 2000 Channel 16	Channel 12 0.02 0.02 0.02 0.02 0.02 0.03 0.02 0.03 0.02 0.03 0.02 0.03 0.02 0.03 0.02	4 10 <sup>-1</sup> Channel 13 9 10 10 10 10 10 10 10 10 10 10 10 10 10	2 + 10-3 Channel 14 4 + 0 + 0 + 0 + 0 + 0 + 0 + 0 + 0 + 0 +	Channel 15		
1.5 1 0 -0.5 -1 0 1 - 0.5 - 0.5	10 <sup>3</sup> Channel 11 500 1000 1000 2000 Channel 16	0.02 0.02	2	2 + 10 <sup>-5</sup> Channel 14 4	5		
1.5 1 0 -0.5 -1 0 1 - 0.5 - 0 - 0.5	10 <sup>2</sup> Chanel 11 50 100 150 200 Chanel 16	0.55 0.02	Channel 3  Channel 4  Channel 4	2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 -	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5		
1.5 1 0.5 -0.5 -1 0 -0.5 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 -	10 <sup>2</sup> Channel 11 500 1000 2000 Channel 16	0.05 0.07	1 (1) (1) (1) (1) (1) (1) (1) (1) (1) (1	2 - 55 <sup>-50</sup> Channel 14 - 4 - 4 - 4 - 5 - 5 - 5 - 5 - 5 - 5 - 5 - 5	5 512 <sup>-</sup> Cherrer 13 Cherrer 13 Control 14 Control 1		



Sample 2023-06-29-002

×10 <sup>-3</sup> Channel 1	Channel 2	A ×10 <sup>-3</sup> Channel 3	2 ×10 <sup>-3</sup> Channel 4	Channel 5
		2 2 2 2 0 1000 2000 4000 5000		
Channel 6	×10 <sup>-3</sup> Channel 7	, ×10 <sup>-3</sup> Channel 8	×10 <sup>-3</sup> Channel 9	, ×10 <sup>-3</sup> Channel 10
0 1000 2000 3000 4000 5000	0 1000 2000 3000 4000 5000	0 1000 2000 3000 4000 5000	0 1000 2000 3000 4000 5000	0 1000 2000 3000 4000 5000
		5 10 <sup>-3</sup> Crame 13 0 100 100 200 300 400 500		
Channel 16	Channel 17	15 ×10 <sup>-3</sup> Channel 18	Channel 19	Channel 20
		10	0.5	0.5
0.5	0.5	5	0	0
0.5	0.5		-0.5	0





Fig x:

Sample 2023-06-29-001 (NEEDS TOTAL)





Sample 2023-06-21-001







Fig x:

Sample 2023-06-21-002





