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# Monitoring Blood Oxygenation Changes due to Acute Pain Stimuli using functional Near-Infrared Spectroscopy (fNIRS)

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*Abstract*—**We've used Near-Infrared Spectroscopy (fNIRS) as a noninvasive tool to monitor blood oxygenation due to the acute pain stimuli. The aim of the study was to find a relationship between the signals recorded by activation of the anterior cingulated cortex (ACC) in healthy subjects, who experience pain via stimulation, and the subject reported pain. These findings will shed light on pain related cognitive studies. Based on our findings, we believe that the fNIRS can be used as a tool for monitoring pain in the brain as well as an effective tool for monitoring the objective efficiency of the pain treatments. Results have shown a correlation between the fNIRS signal and patients' subjective pain level (mild, moderate and severe) which is evidence that the fNIRS is a useful tool for monitoring objective pain response.**

## I. Introduction

Functional Near-Infrared Spectroscopy (fNIRS) which uses near infrared light, in the range of 700-900 nm, to estimate levels of oxygenated hemoglobin and deoxygenated hemoglobin changes during brain activities. This light can pass through skin, bone and other tissue easily and thus can be used to study the absorption and scattering properties of living tissues by measuring the quantitative spectroscopic concentration of oxygenated and deoxygenated hemoglobin at different wavelengths.

Pain is a major cause of suffering in individuals at different levels. Most often, there is not adequate understanding of the pain which makes it hard to treat it. The failure rate of the current treatments is a good witness for the clinical needs toward deeper studies of the pain processing system which will help both in prevention and treatment of pathological pain. At basic levels, pain is often a symptom of injury, but when persists past normal healing, it becomes a pathological disorder. Past researches revealed a close connection between the ongoing cortical neuronal activity of the brain and its underlying hemodynamics (i.e., the need for oxygenated blood) [1], [2]. This concept has become the basis for several brain study techniques such as functional Magnetic Resonance Imaging (fMRI). These studies are based on the premise that "the magnetic signal characteristics of hemoglobin is blood oxygenation level dependent (BOLD)" [3]. There had been several fMRI studies and cortex analysis which demonstrated pain-related modulation of cortical activity in sensory, affective, and cognitive processing regions in accordance with the noxious stimulus [3], [4]. However, the many limitations of fMRI technique, such as cost, size, lack of portability, emphasize the importance of other alternative approaches, such as fNIRS, which provides a portable, cost-effective and accessible tool for clinical settings and daily patient care. fNIRS provides a continuous and accurate spatial monitoring of the cortex, much like fMRI, but with a low cost.

Recently, there have been several published studies, using fMRI and PET technologies, which aimed to identify the areas of the brain that are activated when a person experiences acute and chronic pain. Both technologies are based on measuring regional cerebral blood flow (CBF), and the brain regions which have been described as increasing their activity in response to painful stimuli are well identified. During low intensity pain in the right hand, the left side of the brain activates initially, and then it spreads bilaterally with more intense pain. This is associated with activation in the inferior parietal cortex, which has dense interconnections with the prefrontal cortex [5].

In this paper, we describe the changes of cortical cerebral blood oxygenation during precisely controlled painful stimuli in control healthy subjects. Our ultimate goal is to develop a brain monitoring system that can objectively quantify the level of pain in pain patients by monitoring cortical responses to the chronic pain, using a portable fNIR sensor. Such an objective quantification of pain can contribute significantly to the use of drug therapy for pain disorders.

## II. FNIR TECHNOLOGY

Near infrared spectroscopy (NIRS) is an emerging technology that uses near infrared (NIR) light to probe through the intact scalp for monitoring the state of the cortical tissue of brain during neural activity. The technology is based on monitoring and quantifying the changes in oxygenated hemoglobin (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) concentrations, which are the primary light absorbing components of the blood flowing in the brain and have different optical properties [6-10].

Typically, a functional near-infrared (fNIR) sensor is

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comprised of a light source that is coupled to the participant's head via light-emitting diodes (LEDs) and with a light detector that receives the light after it has interacted with the tissue.

While pain is experienced and processed in the brain, like any other cognitive task, the active areas of the brain start consuming more oxygen than before. In response to this consumption, the blood flow to those active areas increase to support the brain functions [6-9]. This relation between the neural activity and hemodynamics of the brain is known as neurovascular coupling (NVC) and forms the basis of most imaging modalities.

## III. MEASUREMENT SYSTEM

We did our measurements using the fNIR system in Drexel University (see Fig. 1) which is a flexible panel (5cm x 10cm) and consists of an array of light emitting diodes and detectors (16 Voxels). This system has been extensively tested and used in a variety of studies. It was designed by scientists at the University of Pennsylvania and by biomedical and electrical engineers from the Optical Brain Imaging Group of the Drexel University School of Biomedical Engineering, Science and Health Systems. The system has been presented in more details in [11]-[13].

The sensor is attached comfortably to the forehead of the subject using a medically graded tape as well as a Velcro strap. Outputs of the amplifiers are fed into a medical data acquisition device with a sampling rate of 1.9 Hz, which is controlled by a laptop PC. The recorded data is stored in the laptop. The signals from these voxels are amplified and converted to a voltage signal. Our system uses three different wavelengths: 705 nm, 730 nm and 850 nm. In our experiments, after initial investigations to find the most suitable wavelength, we focused on the data gathered in 850nm wavelength since it is more specific to oxy-Hb content.

## IV. PATIENT RECORDINGS

We obtained IRB approval for patient recordings and enrolled six healthy, free of any medication and neurological/psychiatric disorder history, volunteers (ages 18-65). Subjects were trained with the recording protocol. Each subject completed a set of three tests per day. We tried to provide a comfortable and relaxing environment for the participants and asked them to focus on the experiment as much as possible and avoid any kind of mind distraction. For creating pain in these healthy subjects, we used cold water as the stimuli source. All recordings were monitored by a neurologist to ensure that there would be no problems for the participants during and after the stimuli.

## V. MEASUREMENT PROTOCOL

For stimulation, we used hand immersion (left hand) in cold water (~ -0.8°C). Each subject was asked to take part in three tests, each test with different duration of stimuli (4 sec, 8 sec and 12 sec) to create different levels of pain: mild, moderate and severe. The timing of the tests were investigated on the basis of the traditional 0-10 scale for subjective pain assessment, where zero represents no pain and 10 represents the maximum pain that the subject can bear. After each test we also asked the subjects to rate the level of their perceived pain on the traditional 0-10 scale. This was both to ensure that the subject will not suffer any severe pain, and for later use in the statistical analysis to investigate the accuracy of our system.

We also recorded the subjects' data for 30 seconds before hand immersion, which is considered as the pre-stimulus state of the subject. In each test, after the defined stimulus time, the subject moves his hand out of the water. During this time which is known as "recovery time" the pain from the stimuli decreases till there is no pain sensed in subject's hand. This is the "no pain" status which is reported by the subject and its time is saved as the no pain time indicator. Then, we recorded subject's data for 3 minutes, which were considered as the recovery time. After each test, we let the subject to rest for 5 minutes as the gap between the

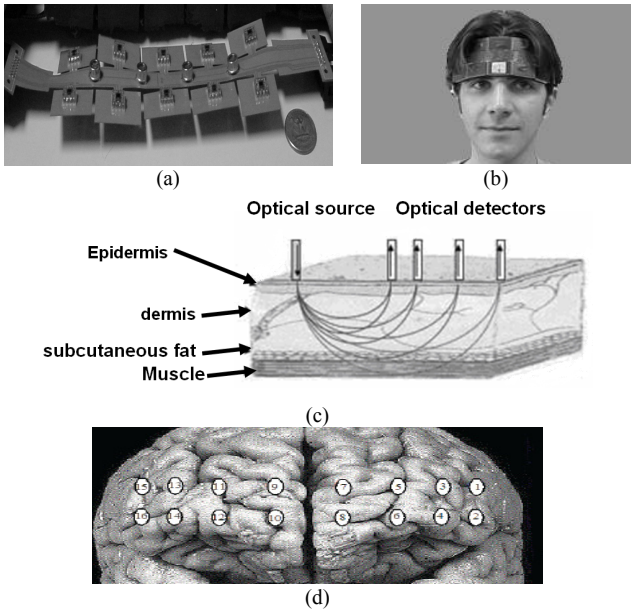


Figure 1. The fNIR system used in Drexel University: a) Optical sender/receivers located in a headband; b) Fixed headband on subject's head; c) Demonstrates route between optical sender and receivers; d) position and indexes of Voxels V1 to V16.

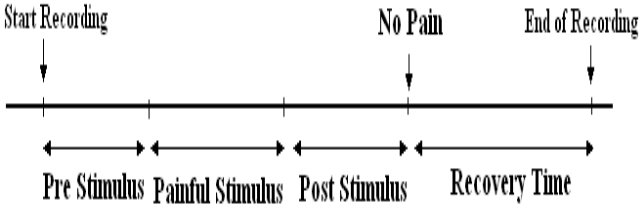


Figure 2.The fNIR system data acquisition protocol on healthy control subjects.

recordings (Figure 2).

We tried to minimize noise sources during the experiments by reducing unnecessary subject movements, talking, etc., as much as possible through both subject training and protocol design, while maintaining an environment similar to a normal clinic. The total time commitment for each subject was approximately 30 minutes per session

## VI. METHODOLOGY

As stated, our goal was finding a relationship between subjective perceived pain and cortical blood flow, while trying to correlate these signals with their evoked cortical activity detected by our system. The raw intensity measurements at wavelength 850nm are first gathered to form data arrays v1 to v16 which have a direct relation with oxy-Hb (Figure. 1 (d)).

To cancel out most part of the motion artifacts in our fNIR signal which change the signal shape, we eliminated signal segments corresponding to hand-in and hand-out movements (2 seconds in total). In order to detect motion artifacts, for the other parts of the signals, we differentiated voxel signals in our pain level estimation algorithm. This will reject most part of motion artifact distributed in all voxels as common signals and increase the common mode rejection ratio (CMRR). This will not significantly cancel pain-related signals as they have different intensities according to our investigations but motion artifacts create common signals in neighbor voxels. We also used an amplitude/threshold separation method and cut-off any sharp intensities higher than normal.

To obtain a quantity measure of fNIR data, we used a statistical feature called 'Root Mean Square (RMS)' which is in fact a statistical measure of the magnitude of a varying quantity.

The pain signal recorded from the frontal cortex, is a non direct response from a part which is located deep inside the brain. To estimate pain level, we used fNIR data at wavelength of 850nm, which is more specific to oxy-Hb content. For each voxel, we removed the DC level by subtracting time average of each voxel from itself [vi=vi-mean(vi), i=i1:i2]; where vi is the signal from voxel number i. As we used stimulation of right hand we just need to consider the right side of the brain. So i1=9 and i2=16 in our case.

Another step is baseline removal. There are several ways to remove baseline activities. One is estimation of baseline wave form, using signal processing methods. But for simplicity, our aim was just to remove the hardware drift that was affecting our signals and changing intensity randomly. In order to remove very slow but high amplitude drifts, we applied linear estimation of baseline. We considered this baseline as a slope between the first point and the last point of each segment, and subtracted that from each segment.

Next step included noise cancellation of the data. Thus, we found the differences between the following voxels: [d1=v11-v12, d2=v13-v14, d3=v15-v16]. This is based on the fact that almost the common noise and motion artifacts exist in upper and lower voxel data. This subtractions doesn't have a significant effect on pain response. This can be proved as following. If we suppose that the pain response is F, then the upper signal (s1), collected from an upper voxel is a1F1 plus the system noise, n. Then, the lower signal, collected from a lower voxel (s2), is a2F2 plus the noise n. Eventually F1 and F2 reflect different responses. However, if we suppose that the F1 and F2 signals are similar, considering the fact that the distance between voxels are small, according to spatial distance between upper and lower voxels, a1 and a2 can't be the same. So, in the worst scenario, this differentiation will just attenuate pain response which can be amplified again. Thus the subtraction will cancel out major common mode signals and reduces the amount of noise.

In the next step, we search for the strongest signal among d1, d2 and d3, which has the highest intensity among three, and call it the 'signal of intrest' (S). The criterion to find S was to compute RMS values of the stimulus-no-pain segments of the signals d1, d2 and d3. In fact, the signal with the highest RMS within this segment was chosen as the strongest signal S. Searching for the strongest signal is necessary because there are different factors that make it possible for a person to have a "stronger" signal at a different location than others, such as the shape and size of the forehead, etc. Also, fMRI studies indicate that the side voxels, reflects stronger pain response compared to others, as the effect of pain, but there is no strong evidence to show that a special voxel usually reflects the highest response to pain. Thus in the area which lights up most, we should search for the strongest signal.

After choosing the strongest signal (S), next step is its segmentation. To do that, we defined the stimulus duration LL as the time difference between the starting and the ending point of pain stimulus. In this experiment there are three values for LL: 4, 8 and 12 seconds. In this step we segmented the signal S to pre-stimulus [S(L1:L2), where L2 is the starting point of the pain stimulus (time segment) and L1 is L2-30s], stimulus-no pain [S(L2:L3), where L3 is the point where the subject reported no-pain, plus M*Delta] and post-stimulus-recovery [S(L3:L4), where L4 is the end point of recording]. Delta is defined as the as the time difference between the starting point of pain stimulus and the point where the subject reported no-pain. We defined a scaling factor M for each test, in a way that we should have enough samples for RMS calculation. This means that M for mild pain test should be bigger than M for moderate pain test and M for severe pain test should be bigger than for moderate pain test. This definition can result a range of values for M. But this range should not be big to change signal to noise ratio of the segment. We recommend to just include few samples as adding more samples could affect signal to noise

ratio and performance of the algorithms. Initial values for M are discussed in the results section.

The reason for the need for a scaling factor is that the sampling rate for our recording is too low (2Hz) and therefore we need to have enough samples for each trial, so we take some samples from proceeding recorded samples. For instance for mild pain, we will have very few samples for the stimulus-no pain segment, therefore we need to take some additional samples from proceeding samples. Thus the samples we need for mild pain is more than the samples we need for moderate pain and the samples we need for moderate pain is more than the samples we need for severe pain. The above mentioned values are investigated during the experiments; however slight changes of the values shouldn't change the results.

Referring to our investigation, taking samples from proceeding recorded samples doesn't affect on the results as the hemodynamic response is very slow and neighbor samples are not very different than samples in the stimulus segment. That's why we attempted to use similar samples from neighbor with similar characteristics.

In the final step, we find the root mean square (RMS) value of each segment (y1, y2 and y3) and plot RMS values in a BAR format.

## VII. RESULTS

To run above mentioned pain-level estimation algorithm, we first need to initialize its parameters. First we needs to initialize scaling factor M. We have a flexibility in choosing value for M, but M should not be very big to change signal to noise ratio of the segment and performance of the algorithms. Our suggestion to choose M is as following but it can be chosen in other ways than our suggestion and should not affect result significantly: If stimulus duration (LL) <5 seconds, choose M=1.5; If 5 seconds <LL<10 seconds, M=0.8; If LL>10 seconds, M=0.2; These values are investigated during the experiment, however slight changes of the values shouldn't change the results.

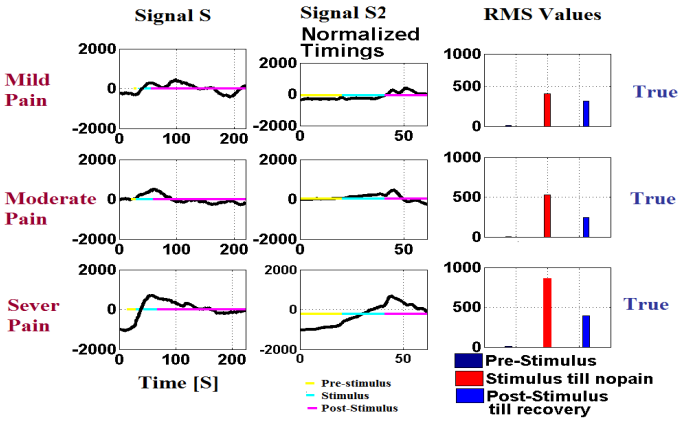


Figure 3. Pain level estimation results for a typical subject. Levels are mild, moderate and severe. S is the strongest signal calculated using an approach explained in the method part. For visualization purposes, signal S2 is the same signal as S with time normalization for pre-stimulus, stimulus-nopain and post-stimulus segments. RMS features were calculated for mild, moderate and severe segments of S

TABLE I
PAIN-LEVEL ESTIMATION RESULTS FOR 54 ICE-TEST TRIALS; LEVELS ARE MILD, MODERATE AND SEVERE

| Classifier | Number of Trials | Correct Estimation | Incorrect Estimation |
|---|---|---|---|
| Mild pain | 18 | 15 | 3 |
| Moderate pain | 18 | 18 | 0 |
| Severe pain | 18 | 17 | 1 |
| Overall | 54 | 50 (%92.5) | 4(%7.5) |

To evaluate the performance of our algorithm, we applied the pain-assessment algorithm with the above mentioned initializations for the mid, moderate and severe pain trials from six healthy subjects (6 participants: each participated in 9 tests in 3 different days; total: 54 ICE-test trials). Table 1 shows result of pain-level estimation based on RMS values for these 48 ICE-test trials. In this analysis, we compared each recording day with itself for pain assessment, since we have different conditions for different recording days. Figure 3 shows pain level estimation results for a typical subject. S is the strongest signal calculated using an approach explained in the method part. For visualization purposes, we normalized timings (time zooming) which created another signal called S2. This time normalization is just for visualization purpose and we didn't use in data analysis. We resample [shrink or expand] above-mentioned segments to obtain segments with the same duration (NT1=NT2=NT3=20 seconds; equivalent to 40 samples).

It can be seen from the results, presented in Table. 1, that the performance of our pain-level estimation algorithm is high with low estimation error. This shows that pain level has a direct correlation with intensity of RMS during stimulus.

## VIII. CONCLUSION AND DISCUSSION

Results showed that there is a clear correlation between the fNIR recorded brain signal and patients' subjective pain rating, which proves that the fNIRS is a useful test for objective quantification of the pain response. Using this modality, we also could estimate the level of the perceived pain in the subjects. This means that the fNIR sensor has the potential to be used as a noninvasive tool for monitoring pain in human brain as well as measuring the objective efficiency of the treatment along with or as a substitute for the commonly used subjective measurement methods.

However, this study needs more investigation for bigger population of both healthy and unhealthy subjects (including patients with chronic pain). We also aim to apply more advanced signal processing methods to improve pain stimulus level using fNIR data.

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