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Pain Classification using Evoked EEG Induced by Thermal Grill Illusion – Deep Neural Network Approach

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Abstract*—As the quantification of pain has emerged in biomedical engineering today, studies have been developing biomarkers associated with pain actively by measuring bio-signals such as electroencephalogram (EEG). Recently, some EEG studies of cold and hot pain have been reported. However, they used one type of stimulus condition for each trial and a relatively long stimulation time to collect EEG features. In this study, EEG signals during Cool (20 °C), Warm (40 °C), and Thermal Grill Illusion (TGI, 20-40 °C) stimuli were collected from 43 subjects, and were classified by a deep convolutional neural network referred to as EEGNet. Three binary classifications for the three conditions (TGI, Cool, Warm) were conducted for each subject individually. Classification accuracies for TGI-Cool, TGI-Warm, and Warm-Cool were 0.74$\pm$0.01, 0.71$\pm$0.01, and 0.74$\pm$0.01, respectively. For subjects who rated the TGI significantly hotter than the Warm stimulus, the classification accuracy for TGI-Cool (0.74 $\pm$ 0.01) was significantly higher than for TGI-Warm (0.71$\pm$0.01). In contrast, the classification accuracy for TGI-Cool (0.72$\pm$0.03) did not differ statistically from TGI-Warm (0.73 $\pm$ 0.01) in subjects without illusion. We found that the TGI and Cool stimuli were classified better than the TGI and Warm stimuli, implying that objective EEG features are consistent with subjective behavioral results. Further, we observed that most discriminative features between the TGI and the Cool or Warm conditions appeared in the parietal area for subjects who perceived the illusion. We postulate that the somato-sensory cortex may be activated when TGI is perceived to be hot pain.

I. INTRODUCTION

Quantitative measurement of pain levels is important, particularly for unconscious patients, people who suffer from a speech disorder, those who are too young to verbalize their pain, or the elderly, etc., to report their pain and receive proper aid. However, measuring and evaluating the intensity of pain with an objective standard with individuals' verbal or behavioral response is complicated because of subjectivity. More objective quantification of pain levels can be achieved by observing brain signals when a pain-evoking stimulus is given. An electroencephalogram (EEG), which is non-invasive and economical, and has a good temporal resolution, enables brain signals to be measured rapidly and efficiently [1].

In processing thermal stimuli, the anterior cingulate cortex (ACC), somato-sensory cortex, and prefrontal cortex have been reported to be regions responsible for pain recognition [2]. Some EEG studies have shown an increase in the gamma band (30-80 Hz) power and a decrease in the beta band (13-30 Hz) power as the pain level increases [3-4]. Nezam et al. reported an alpha band (9.8 Hz) power increase in the frontal region and a decrease in the parietal region in cold pain. Pain levels were classified using K-nearest neighbor (KNN) and support vector machine (SVM) after a decision tree was organized, and low/moderate pain versus high pain was classified with an accuracy of 0.68 and 0.70 by KNN (K=10) and SVM, respectively [5]. Tayeb et al. reported brain activity in the right parietal region under cold (16~24.99 °C) and hot (35~40 °C) stimuli, and the binary classification accuracy for the two stimuli was 0.85±0.03 using common spatial pattern (CSP) and linear discriminant analysis (LDA) [6]. Further, Vijayakumar et al. studied hot pain with a random forest model, and reported that EEG during pain cognition showed the greatest difference in gamma band power [3].

Previous studies have focused on non-pain and pain states with a stimulation time of over 30 s. In addition, the pain level was divided primarily into subjective responses during stimulation at one fixed temperature, or at a range of stimulus temperatures [3-6]. However, in the real world, pain is perceived quickly, and internal/external factors, such as indoor temperature, humidity, or the subject's mental state, may affect an individual's perception of pain [7]. Thus, quantitative measurement of thermal pain using EEG requires short time measurement or analysis, and many other factors that may affect perception should be considered to study and apply EEG in clinical fields.

This study observed and analyzed 7 s (relatively short compared to 30 s) of EEG signals during Thermal Grill Illusion (TGI). TGI is an illusionary stimulus that is perceived to be very hot when a Warm stimulus (40 °C) and a Cool stimulus (20 °C) are applied simultaneously on one's hand [8]. While existing studies of EEG evoked by thermal stimuli have focused on measuring brain signals of one type of stimulus at a time, this study measured EEG with illusionary conditions that two simultaneous stimuli induced. Further, a deep learning method was introduced to perform binary classification for each of the three dyadic (TGI-Cool, TGI-Warm, and Warm-Cool) from the EEG data induced by TGI, Cool, and Warm stimuli.

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II. METHODS

A. Experimental Procedure

Fourty-three healthy subjects (24.77±1.33 yrs. mean±SEM. 29 male) participated in this study. Before the experiment began, the subjects tested thermal stimuli. They filled out a questionnaire that asked about their current states, experiences of sensory abnormality, and symptoms of depression through Patient Health Questionnaire-9, described in [9]. We enrolled subjects who reported tolerating the thermal stimuli and performed the entire tasks. The Gwangju Institute of Science and Technology (GIST) Institutional Review Board approved this experiment (20220628-HR-67-03-02), and all subjects signed informed consent.

The thermal stimulation task paradigm was implemented using a Matlab-based Psychophysics toolbox. The thermal stimulus was delivered by a lab-made thermal grill, which consists of a Peltier element and adjusts the temperature ±3 °C/s at the maximum in the range of 10 °C to 50 °C using custom-built Matlab scripts [10-11]. During the experiment, subjects were instructed to place their left hand on the thermal grill for thermal stimulation. Before the first block of the task, 80 s of EEG were collected during the resting state while a subject had their hand on the 32 °C grill. For each block, nine different stimuli were applied in a random order: TGI (20-40 °C, 23-37 °C, and 26-34 °C), Cool (20 °C, 23 °C, and 26 °C), and Warm (34 °C, 37 °C, and 40 °C), as shown in Fig. 1. A thermal stimulus was given for 20 s during each trial. Subjects evaluated the stimulus's intensity on an 11-point Likert scale (0: very cold, 5: no stimulation, 10: very hot) after the first 10 s. The next stimulus was given after 15 s without a stimulus (32 °C). The subjects performed ten blocks of this thermal stimulation task.

B. EEG Acquisition and Preprocessing

During each task, including the resting state, 32-channel EEG was collected with a 1,024 Hz sampling rate according to the international extended 10-20 system (ActiveTwo, BioSemi Inc. Netherland), by OpenViBE software [12].

EEGLAB and FieldTrip are used primarily to preprocess the EEG data [13-14]. After the EEG data were down-sampled to 512 Hz and re-referenced to both mastoids, they were band-pass filtered with 0.5-55 Hz and band-stop filtered with 58-62 Hz with the fourth-order Butterworth filter to avoid line noise. During thermal stimulation, 7 s of data before screen changes were used for classification. For deep learning analysis, this study used three stimuli (TGI: 20-40 °C, Cool: 20 °C, and Warm: 40 °C) cases.

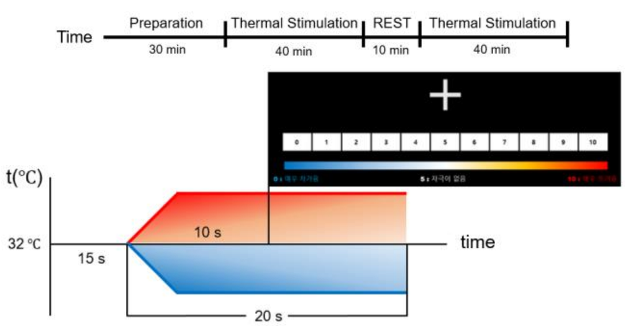

Figure 1. Thermal stimulation task paradigm.

C. Thermal Stimuli Classification and Statistics

Three stimuli (TGI and two single-type thermal stimuli, Warm and Cool) were compared using pairwise binary classifications (TGI-Cool, TGI-Warm, and Warm-Cool). To evaluate performance, we conducted 5-fold cross-validation and the mean classification accuracy was used to measure performance. All of the classification accuracies given in this paper represent the mean ± SEM. The performances were compared across thermal stimuli using a paired Student's *t*-test.

Thermal stimuli were classified in this study using the EEGNet model, one of the best deep convolutional neural network models used widely for brain-computer interface (BCI) [15]. The hyperparameters tuned for this study are as follows:

Kernel length: 32; number of temporal filters: 8; number of spatial filters: 2; number of pointwise filters: 16; regularization dropout rate: 0.5; batch size: 32; epochs: 300; loss function: binary cross-entropy; Adam optimizer, activation function: sigmoid.

In addition to classification accuracy, we compared self-evaluation scores, which denote the subject's response to the thermal stimuli, across the three stimuli using a Paired Student's *t*-test. All self-evaluation scores given in this paper represent the mean±SEM.

Class weights that contributed to training were extracted using the DeepLIFT method [16]. After the binary classification, each class's training attribution weights were normalized in the range from -1 to 1, averaged within each class, and analyzed using the Wilcoxon signed-rank test over the entire head to determine where the difference between two stimuli appeared most frequently. The statistical test decisions (logical value, 1; $p<0.05$) were summed for all subjects and plotted as a brain scalp map.

III. RESULTS AND DISCUSSION

A. Classification Accuracy

The data of just 41 subjects (24.09±1.12 yrs. 28 male) were analyzed, as 2 subjects stopped the task in the middle of the experiment because of personal issues. The classification accuracy for TGI-Cool, TGI-Warm, and Warm-Cool conditions are shown in Fig. 2. The subjects' mean total accuracy was 0.74±0.01, 0.71±0.01, and 0.74±0.01 for TGI-Cool, TGI-Warm, and Warm-Cool respectively. Subjects were divided into two subgroups depending upon their response to TGI stimulation assessed by self-evaluation scores. On average, the subjects rated the Warm stimulus within the range of 7.3 to 9.7. Based upon this result, we assigned subjects to the TGI group for those who rated TGI stimulus higher than 7.3 (33 subjects, 24.03±1.30 yrs.) and the no-TGI group for those who rated TGI stimulation lower than 7.3 (8 subjects, 24.36±2.20 yrs.).

In the TGI group, the classification accuracy of the TGI-Cool (0.74±0.01) was significantly higher than that of the TGI-Warm (0.71±0.01) condition ($p < 0.05$) as shown in Fig. 3. On the other hand, neither the accuracies of the TGI-Cool (0.72±0.03) nor Warm-Cool conditions (0.73±0.01) differed statistically significantly. Nezam et al. reported that the binary classification accuracies of 'Low & Moderated Versus High &

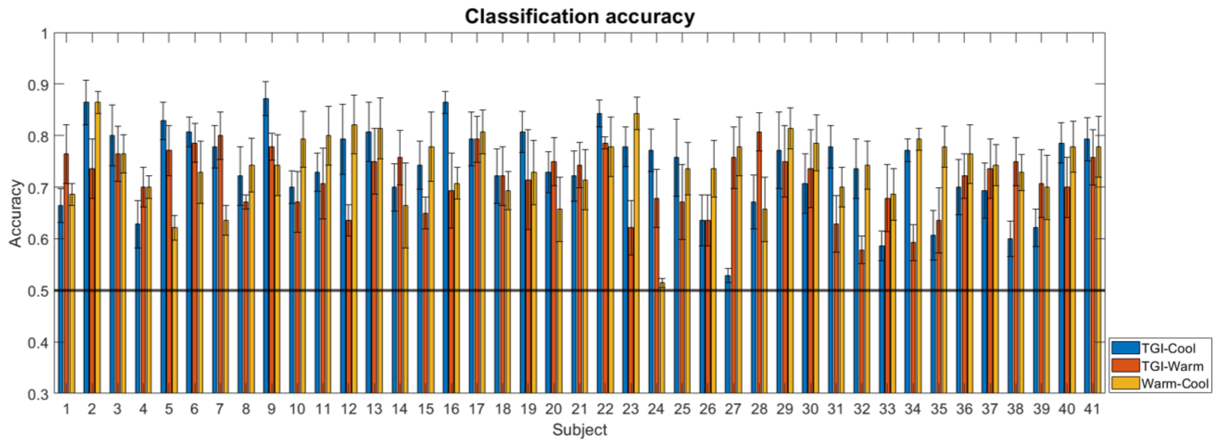

Figure 2. Classification accuracy for individual subjects. Total accuracy is 0.74±0.01, 0.71±0.01, and 0.74±0.01 for TGI-Cool, TGI-Warm, and Warm-Cool respectively, and the black line stands for the random probability (0.5).

Intolerable' were '0.681 and 0.696 using KNN (K=10) and SVM,' respectively [5]. The tuned EEGNet in this study classified TGI versus Cool and TGI versus Warm well with relatively short time data.

The subjects in the TGI group rated TGI (9.17 ± 0.12) significantly hotter than the Warm stimulus (8.54 ± 0.12), which implies that TGI was perceived as hot rather than cold or cool, although both the Cool and Warm conditions were given equally (left of Fig. 3). The TGI-Cool classification accuracy was higher than that of the TGI-Warm. This is congruent with the result that the subjects' cold-hot rating response characteristics to TGI stimuli are closer to Warm than Cool stimuli.

On the other hand, in the no-TGI group, TGI-Cool classification accuracy did not differ significantly from the TGI-Warm condition. Subjects in the no-TGI group rated TGI 4.54±0.71, where 5 is the no-stimulation state. The TGI-Cool and TGI-Warm conditions were classified with an accuracy of 0.72±0.03 and 0.73±0.01, respectively (right of Fig. 3). This suggests that the TGI stimulus could also be perceived as a different stimulus from the Cool or Warm stimuli, although the TGI stimulus consisted of both Cool and Warm conditions, and the illusion did not occur, which resulted in a high standard error of the mean scores.

B. Feature Analysis

Scalp topography, in which the weights of trained features differed significantly between the two conditions ($p < 0.05$) is shown in Fig. 4. For both the TGI and no-TGI groups, Warm and Cool conditions were classified most in the right centro-parietal and central regions (Fig. 4). Tayeb et al. and Nezam et al. addressed the brain activity in those areas during both cool and warm conditions; however, similar regions were also responsible for the classifying Warm-Cool conditions [5-6].

Within the TGI group (Fig. 4a), we observed that the feature weights that classified the TGI and Cool conditions significantly were positioned in the left temporal, parietal, and right frontal regions. Further, the right parietal region contributed to classifying the TGI and Warm stimuli. Given that the somato-sensory cortex is one of the regions responsible for the pain cognition process, the difference in the parietal area between the TGI and Cool conditions might be interpreted as activity in the somato-sensory cortex during subjects feeling TGI as hot pain [2].

However, the common regions that classified two stimulus conditions significantly were the left temporal region for the

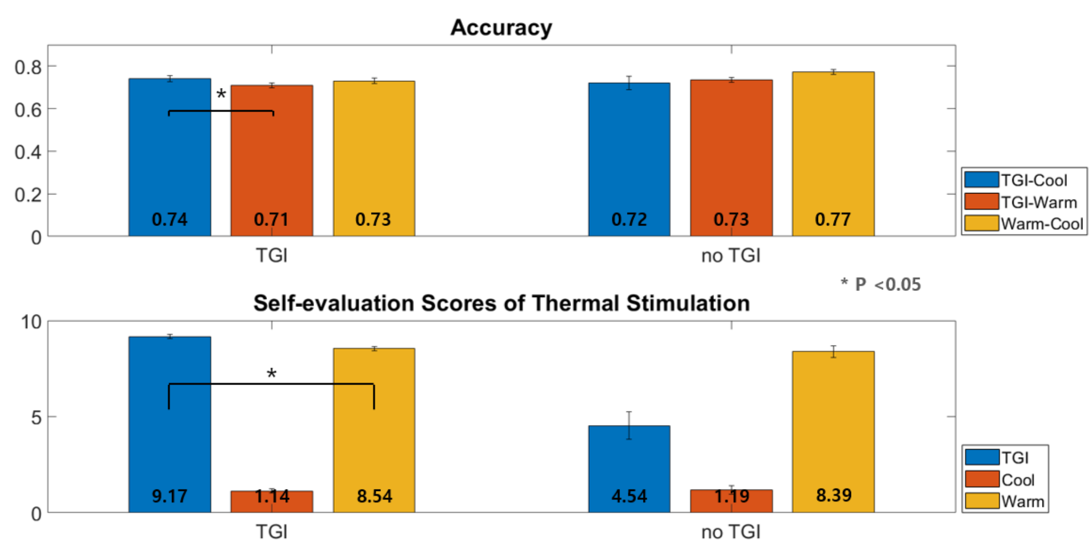

Figure 3. Classification accuracy and self-evaluation scores of thermal stimuli for TGI (left) and no-TGI (right) groups.

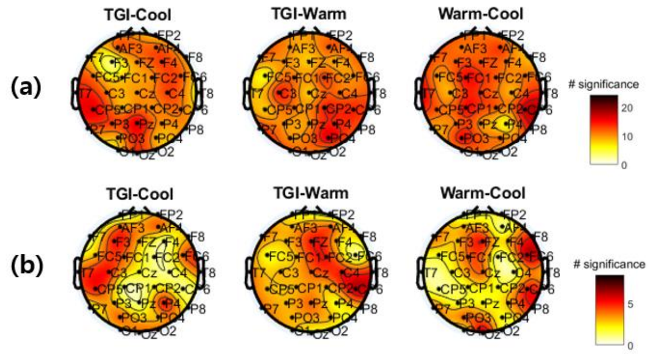

Figure 4. Scalp topography representing significantly different regions between two class weights for binary classification of (a) TGI group and (b) no-TGI group. # significance represents the number of subjects who showed a significant difference at each electrode.

TGI/Cool conditions and the frontal region for the TGI/Warm conditions (Fig. 4(b)). Interestingly, the left temporal region for the TGI-Cool stimuli and the right frontal region for the TGI-Warm stimuli classification dominated, while those two areas were responsible for classifying the TGI-Cool stimuli in the TGI group (Fig. 4(a)). The self-evaluation score for the TGI was 4.54 ± 0.71 and varied highly. We note that a score of 5 is no stimulation, i.e., TGI was considered two countervailing stimuli in the no-TGI group.

IV. Conclusion

We observed and analyzed 7 s of EEG signals during Thermal Grill Illusion (TGI; 20-40 ℃), Cool (20 ℃), and Warm (40 ℃) conditions for the 41 subjects. We tuned the parameters of the EEGNET for the short stimulation time data. We achieved a classification accuracy of the TGI-Cool condition (0.74 ± 0.01) that was significantly higher than the TGI-Warm condition (0.71 ± 0.01). In contrast, the accuracy was similar to the Warm-Cool condition (0.73 ± 0.01), for subjects who rated TGI significantly hotter than the Warm stimulus. We found that the signal in the parietal region, where activity at the somato-sensory cortex can be observed, is responsible for classifying the TGI and Cool or Warm conditions when subjects perceived that TGI was hot pain. The TGI stimulus was considered as two countervailing stimuli for subjects who rarely felt the illusion. However, the TGI condition was also classified from Cool or Warm stimuli.

In this study, the accuracy of three binary classifications demonstrated that the subjects' cold-hot rating test results are repeated in EEG. Several features of the TGI, Cool, and Warm conditions were investigated according to the self-evaluation scores for the TGI stimulus. Our results suggest that an EEG analysis using a deep neural network has the potential to measure and classify thermal stimuli accurately and band features could be extracted without verbal or behavioral expressions, even if a stimulus is illusionary. We will continue the studies on extracting EEG features for the remained six conditions, such as TGI (23-37 ℃ and 26-34 ℃), Cool (23 ℃ and 26 ℃), and Warm (34 ℃ and 37 ℃) from the EEG data already obtained, and classifying them using proper deep learning techniques.

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