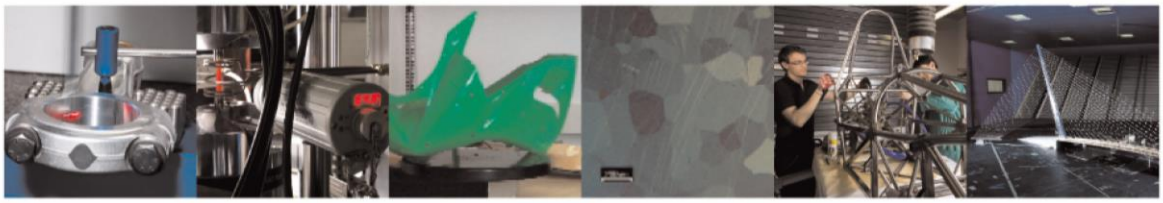

# Dynamic Quantification of Migrainous Thermal Facial Patterns - A Pilot Study

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This is a post-peer-review, pre-copyedit version of an article published in IEEE JOURNAL OF BIOMEDICAL AND HEALTH INFORMATICS. The final authenticated version is available online at: http://dx.doi.org/10.1109/JBHI.2018.2855670

# Dynamic Quantification of Migrainous Thermal Facial Patterns - A Pilot Study

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***Abstract*— This article documents thermophysiological patterns associated with migraine episodes, where the inner canthi and supraorbital temperatures drop significantly compared to normal conditions. These temperature drops are likely due to vasoconstriction of the ophthalmic arteries under the inner canthi and sympathetic activation of the eccrine glands in the supraorbital region, respectively. The thermal patterns were observed on eight migraine patients and meticulously quantified using advance computational methods, capable of delineating small anatomical structures in thermal imagery and tracking them automatically over time. These methods open the way for monitoring migraine episodes in non-clinical environments, where the patient maintains directional attention, such as his/her computer at home or at work. This development has the potential to significantly expand the operational envelope of migraine studies.**

***Index Terms*— migraine, headache, thermal imaging, face tracking, facial features, supraorbital, periorbital, maximum likelihood estimation**

## I. Introduction

The diagnosis of migraine headache is performed clinically and relies heavily on specific criteria outlined in the International Classification of Headache Disorders, 3rd Edition (ICHD-3) [1]. Screening tools, such as the ID Migraine™, facilitate diagnosis by improving migraine recognition [2]. Children's drawings have also proven to aid in the diagnosis of migraine in this population [3]. All currently available diagnostic methods, however, require effective communication between the examiner and patient, as an accurate migraine diagnosis is not based on pain presence alone, but also on the presence or absence of migraine-associated symptoms such as photo- and phono-phobia, nausea, or aura. Available scales relying on observation of pain behaviors can assist pain assessment in those with significant cognitive impairment and limited communication ability [4], but cannot assess migraine-associated symptomatology.

Significant advances have recently been made in understanding the pathophysiology of migraine headache, in part due to neuroimaging techniques using functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET) [5] [6]. These modalities allow observation of distinct cerebral regions (e.g., dorsal pons) and networks, as they become activated and involved during a migraine headache attack [7]. Migraine's mechanisms, however, remain incompletely understood [8]. Its episodic nature creates challenging logistic problems when attempting to study spontaneous headache events. A conclusion drawn from these studies that is of practical significance is that treating the patient with triptans early in the migraine attack (before the development of cutaneous allodynia), increases the likelihood of pain-freedom [9]. We are interested in developing a field (vs. a clinical) method for the quantitative study and possibly detection of migraines. We have focused on thermal imaging of the face, because the face is most often exposed in daily living conditions and thermal imaging is passive and hence safe for prolonged monitoring [10]. Our investigation aims to contribute towards three open problems in the study and treatment of migraines:

- Facilitate the investigation of the episodic nature of the condition. The thermal imaging sensor can be attached as a peripheral on a personal computer, enabling monitoring during work hours or at home. Such monitoring can cover a substantial portion of the day and thus, it would significantly increase the chances of capturing the development of migraine attacks. To make such monitoring feasible, however, the thermal imaging system should be capable of tracking facial features of interest in the presence of natural head motion.
- Localize with precision migrainous thermal patterns in facial areas of neurophysiological importance, aiding reproducibility and the understanding of underlying processes.
- Bridge the communication gap between the patient and

Initial submission. This work was supported in part by the National Science Foundation under Grant IIS-0414754.

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the clinician. Assuming that thermal facial patterns are found to be associated with migraines, the method can be especially useful as a diagnostic aid for patients with limited communication abilities.

Consequently, the central research question is how exactly migraine headache attacks affecting facial thermophysiological responses and what methods to use in order to capture such responses dynamically. To answer this question we conducted an observational study, with methods and results that are presented in the remainder of the paper.

This is not the first attempt to investigate the diagnostic potential of thermal imaging in migraine and other types of headaches. Considerable interest in migraine evaluation using thermography took place in the 1970s and 1980s hoping to better understand the disorder and use it as a diagnostic and therapeutic tool [11]. Some studies, however, failed to find specific thermographic patterns. Wood documented a pattern of cooling seen in one supraorbital region and periorbital areas in 63% of cluster headache patients, but this only rarely occurred in migraine [12]. Others subsequently reproduced very similar results [13].

Other investigators found evidence suggesting specific thermographic patterns could be seen during a migraine headache attack and normalize interictally. Such findings, however, were not uniform. Drummond reported a higher average orbital temperature of 35.6 °C during a migraine headache and 35.4 °C when headache free [14]. Higher temperatures during migraine headache vs. the asymptomatic period when using the angular orbit and supraorbital arterial reference points have also been documented [15].

In contradistinction to these results, multiple other studies suggested facial cooling during migraine might be a more specific pattern seen during acute migraine. Lance reported forehead cooling in 8 of 12 subjects during spontaneous hemicranial migraine headache ipsilateral to the pain, the temperature progressively dropped as pain intensified [16]. Similarly, a cold patch in the external carotid territory ipsilateral to the prevailing side of pain was seen in 13 out of 17 subjects with migraine with and without aura in Dalla Volta's study. The cold patch disappeared or attenuated in parallel with clinical improvement following treatment [17]. Subsequently, the same group replicated and extended the prior findings now with a larger sample of 246 migraine patients. Of these, 206 exhibited the typical cold patch in the forehead. Among the 136 patients who experienced complete or substantial relief from headache the cold patch disappeared or markedly improved in 85% of the cases. The authors suggested thermography could be useful to monitor the clinical course of the disease and could represent a useful criterion for the decision of discontinuing preventive therapy [18].

A key difference between our study and prior efforts is in the technical methods. We use semi-automated computational methods that operate on dynamic (video) and not static imagery, affording continuous measurement on anatomical markers despite small head motions. In the present study, applying these methods to data collected via a high definition thermal imaging sensor, clarified the underlying physiological mechanisms in the periorbital and supraorbital regions, during and after a migraine attack. Importantly, our methods can potentially be used in free-living scenarios featuring directional attention, such as computer work at the office - a development that could significantly expand the operational envelope of migraine studies.

## II. Methods

### A. Approvals

Approvals were obtained from the Institutional Review Boards of Mayo Clinic and University of Houston. Each subject underwent an informed consent process and provided written informed consent prior to participation.

### B. Subject Inclusion and Exclusion Criteria

We searched for patients seen for migraine in the Department of Neurology at Mayo Clinic, Rochester MN. Using medical record retrieval, we identified 1576 subjects. Of these, we identified 70 as having episodic migraine on no preventive medication and living in the vicinity of Mayo Clinic to facilitate the study. We sent a letter to them inviting them to participate and of the 70 patients, 31 responded with interest. We interviewed all 31 subjects to confirm the diagnosis and review inclusion and exclusion criteria. Of the 31 candidates, we excluded 13 because they had other coexistent headache disorders, did not have episodic migraine, were overusing acute treatments, or were using migraine preventives.

### C. Collection of Subject Data

We instructed all 18 subjects who were included in the study to come to the laboratory for thermal video recording at the beginning of a migraine headache. We also instructed them to not treat the headache before the recording. In such visits, an examiner from our clinic determined if the subject had indeed an episode of migraine headache with or without aura according to the International Classification of Headache Disorders, 3rd Edition (ICHD-3) [1]. Then, the study coordinator recorded a thermal video of the subject's face for 5 min ('Migraine' session). At that time, the subject was free to treat her headache and leave the lab. We asked the subject to return when her symptoms had stopped and the headache was gone. In this second visit, the study coordinator recorded again a thermal video of the subject's face for 5 min ('Baseline session). We obtained from all subjects their age, sex, and medication history.

### D. Imaging Parameters

We used a mid-wave infrared camera (FLIR SC 4000 FLIR Systems, Boston, MA, USA) for thermal video recording. The camera featured an InSb focal plane array of $320 \times 256$ pixels and thermal sensitivity of 0.025 °C; the recording speed was set at 54 fps. We focused on the supraorbital and periorbital areas two facial regions of neurophysiological importance, for which other researchers reported migrainous thermal patterns, but in a rather qualitative, non-algorithmic manner (e.g., 'cold patch in [17] [18]). From each thermal video we extracted the following thermophysiological responses:

1) Supraorbital thermal signal $\mathbf{S}$
2) Periorbital thermal signal $\mathbf{P}$

Each signal point represented the mean temperature in °C in the respective area of the face at a particular time.

As the signals $\mathbf{S}$ and $\mathbf{P}$ were extracted from imaging measurements with no restrictions imposed on the subjects, other than sitting on a chair, we needed methods for virtual probing and tethering. These are the computational equivalents for the actual probe and its attachment paraphernalia in traditional clinical measurements (e.g., thermistor). In medical imaging terminology virtual tethering is called tissue tracking, while virtual probing is called tissue segmentation. Tracking and segmentation are important to the envisioned practical application of this methodology, as subjects who work in front of personal computers frequently exhibit small motion and have differing facial characteristics.

### E. Thermal Imaging - Tissue Tracking

The virtual tissue tracker encompassed and tracked of the segmented region of interest, despite small motions of the subject's face (Fig. 1). This ensured that the thermophysiological signal extractors operated on consistent and valid sets of data over the data collection timeline. We used the tissue tracking algorithm we reported in [19]. It is capable of handling various head poses, partial occlusions, and thermal variations. On the initial frame, the operator initiated two trackers by selecting via mouse the subject's supraorbital and orbital regions as follows:

**Localization of Supraorbital Tracker.** The supraorbital tracker was a rectangle with a base that bridged the inner ends of the subject's eyebrows and extended halfway up the height of the forehead (Fig. 1).

**Localization of Periorbital Tracker.** The periorbital tracker was a rectangle that included the two orbits height-wise, but left out their outer halves width-wise (Fig. 1).

After tracker selection in the initial frame of the thermal clip, the rest of the computational process was automated. Each tracker estimated the best matching block for the next frame of the thermal clip based on particle filtering driven by spatiotemporal smoothing. Particle filtering can handle nonlinear motion, which head motion mostly is, while spatiotemporal smoothing does away with the unrealistic assumptions of pixel and frame independence, thus, increasing accuracy and reducing tracking oscillation.

### F. Thermal Imaging - Segmentation & Signal Extraction

The supraorbital and periorbital signals were extracted by computing the mean temperature of the corresponding anatomical landmarks in each time step. These anatomical landmarks were segmented within the supraorbital and periorbital trackers, respectively.

**Segmentation of Supraorbital Landmark.** For the supraorbital region the signal was extracted by computing in each time step the mean temperature in the entire tracking area; therefore, segmentation of the supraorbital landmark was trivial (Fig. 1). This landmark was chosen because it includes the supraorbital arteries and a preponderance of eccrine glands both of neurophysiological importance.

**Segmentation of Periorbital Landmark.** For the periorbital region the signal was extracted by computing in each time step the mean temperature in the thermal footprints of the left and right ophthalmic arteries - a small portion of the overall tracking area located in the inner canthi. A segmentation algorithm, operating within the periorbital tracker, was delineating the arteries' apparent footprints in each incoming frame (Fig. 1). We reported the details of this algorithm and its operational characteristics in [20]. In every frame the algorithm delineated the region of interest in each orbit by starting from the local maximum (seed) and expanding according to a probabilistic cost function. This cost function factored in geometry, temperature homogeneity, and temperature gradient space adjacency. The local maximum corresponded to the hottest local pixel, which based on heat transfer laws was bound to be in the center of arterial blood flow. This landmark was chosen because the ophthalmic arteries anchor neurophysiological responses in the orbital area, as they supply with blood the ocular muscles.

### G. Statistical Analysis

We sought to find if there were significant differences in the thermophysiological responses between the baseline and the migraine sessions. Because we used two tests (supraorbital temperature comparison and periorbital temperature comparison) we applied Bonferroni correction for the level of significance ($\alpha = 0.05/2 = 0.025$).

We adopted a two-stage analysis. In the first stage we examined what happened in each subject. In the second stage we tested if any significant trends observed in individuals held for the entire group of subjects. Table I lists all the experimental variables used in the analysis. Please note that we treated the pain as a binary entity present in the migraine session and absent in the baseline session).

The mean supraorbital and periorbital temperatures for the migraine and baseline sessions ( $\overline{\mathbf{S}}_m, \overline{\mathbf{S}}_b, \overline{\mathbf{P}}_m, \overline{\mathbf{P}}_b$, respectively) were computed by averaging over $16,200$ measurements ($54$ fps $\times$ $60$ s $\times$ $5$ min per session) a highly dense temporal support of non-trivial duration.

## III. Results

### A. Subject Characteristics

At the time the study ended, eight subjects completed the study and were recorded while 10 did not have a migraine attack to study. None of the completers had prior or active autonomic disorders. All completers ($n = 8$) were female; seven had episodic migraine without aura and one episodic migraine with aura per ICHD-3. Age range was 21-57 years old, mean 37, median 37.

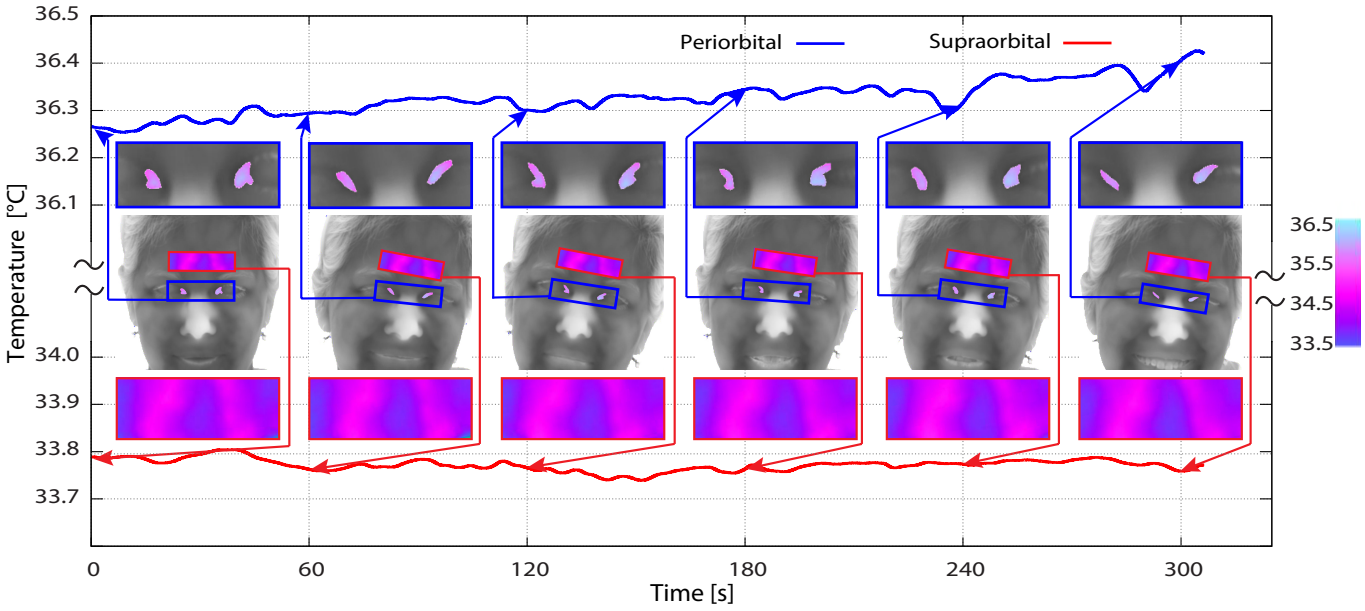


Fig. 1. **Middle Row:** Supraorbital and periorbital tissue trackers at work as subject D006 exhibits small head motion during the baseline session. **Top Row:** Motion-corrected periorbital snapshots with the segmented thermal footprints of the ophthalmic arteries - the corresponding signal points are indexed above. **Bottom Row:** Motion-corrected supraorbital snapshots with the corresponding signal points indexed below.

TABLE I
EXPERIMENTAL VARIABLES.

| VARIABLE | DESCRIPTION |
|---|---|
| SUB | Subject ID |
| SESS | Session indicator: b=Baseline, m=Migraine |
| $\mathbf{S}_b$ | Supraorbital thermal signal during baseline |
| $\mathbf{P}_b$ | Periorbital thermal signal during baseline |
| $\mathbf{S}_m$ | Supraorbital thermal signal during migraine |
| $\mathbf{P}_m$ | Periorbital thermal signal during migraine |
| $\overline{\mathbf{S}}_b$ | Mean Supraorbital temperature during baseline |
| $\overline{\mathbf{P}}_b$ | Mean Periorbital temperature during baseline |
| $\overline{\mathbf{S}}_m$ | Mean Supraorbital temperature during migraine |
| $\overline{\mathbf{P}}_m$ | Mean Periorbital temperature during migraine |

### B. Supraorbital Temperatures in Baseline vs. Migraine - Subject Level

Every subject had significantly lower mean supraorbital temperature $\overline{\mathbf{S}}_m$ in the migraine session with respect to the mean supraorbital temperature $\overline{\mathbf{S}}_b$ in the baseline session ($p < 0.0001$, two-sample t-test for all). Figure 2 shows detailed results for a representative case (Subject D003), while Figure 3 shows the supraorbital temperature distributions for the entire subject set.

### C. Periorbital Temperatures in Baseline versus Migraine - Subject Level

In 7 out of the 8 subjects the migraine session had significantly lower mean periorbital temperature $\overline{\mathbf{P}}_m$ with respect to the periorbital temperature $\overline{\mathbf{P}}_b$ in the baseline session ($p < 0.0001$, two-sample t-test); for one subject (D009) there was no significant difference ($p = 0.0458$, two-sample t-test). Figure 2 shows detailed results for a representative case (Subject D003), while Figure 4 shows the periorbital temperature distributions for the entire subject set.

### D. Hypothesis Validity across Subjects

From the analysis thus far we have formed the hypothesis that during migraine sessions the subjects have lower supraorbital and periorbital temperatures with respect to their baseline sessions. This is true for all eight subjects regarding the supraorbital response and for seven out of the eight subjects regarding the periorbital response.

Next, we test whether this finding is a significant (at $\alpha = 0.025$) result or not at the group level. For each subject $i = 1, 2, ..., 8$ we define the random variables $X_i$ and $Y_i$ as:

$$X_i = \begin{cases} 0, & \text{if } \overline{\mathbf{S}}_b \leq \overline{\mathbf{S}}_m \\ 1, & \text{if } \overline{\mathbf{S}}_b > \overline{\mathbf{S}}_m \end{cases} \quad \text{and } Y_i = \begin{cases} 0, \text{if } \overline{\mathbf{P}}_b \leq \overline{\mathbf{P}}_m \\ 1, & \text{if } \overline{\mathbf{P}}_b > \overline{\mathbf{P}}_m \end{cases} \tag{1}$$

The random variable $X_i$ ($Y_i$) is 1 if the research hypothesis is true for the supraorbital (periorbital) temperatures and 0 otherwise. Each of the $X_i$ and $Y_i$ forms a Bernoulli random variable with probabilities of success (assumed constant across subjects):

$$\theta = \Pr(\overline{\mathbf{S}}_b > \overline{\mathbf{S}}_m) \text{ and } \phi = \Pr(\overline{\mathbf{P}}_b > \overline{\mathbf{P}}_m) \tag{2}$$

If we assume that the subjects are independent of each other, then the sum of the random variables $X_i$ over the eight subjects forms a binomial distribution and so does the sum of the random variables $Y_i$:

$$X = \sum_{i=1}^{8} X_i \sim \text{Bin}(8, \theta) \text{ and } Y = \sum_{i=1}^{8} Y_i \sim \text{Bin}(8, \phi) \tag{3}$$

In our data set we get $X = 8$ and $Y = 7$. Our interest lies in the probabilities of success $\theta$ and $\phi$. Specically, we are interested to determine if these probabilities are significantly higher than 0.5, which represents random guess. We have a relatively small number of subjects in the study ($n = 8$) and the point estimates in both experiments are near or at the edge of the parameter space [0,1] (the Maximum Likelihood Estimates of $\theta$, $\phi$ are $\widehat{\theta} = 8/8 = 1$ and $\widehat{\phi} = 7/8 = 0.875$). Hence the standard frequentists methods relying on the asymptotic performance are questionable; thus, we opted for a Bayesian analysis.

We have two Binomial experiments with likelihoods:

$$X|\theta \sim \text{ Bin}(8, \theta) \text{ and } Y|\phi \sim \text{ Bin}(8, \phi), \tag{4}$$

and we are interested in drawing an inference about the success probabilities $\theta$ and $\phi$. Initially we need to provide prior distributions for $\theta$ and $\phi$. Since no prior knowledge is available to us, we adopt the Uniform distribution in the range $[0, 1]$ for both parameters:

$$\pi(\theta) \sim U[0, 1] \text{ and } \pi(\phi) \sim U[0, 1] \tag{5}$$

Bayes theorem provides the posterior distribution for each parameter given the observed data. Specically, it is easy to show that:

$$\theta|X = 8 \sim \text{Beta}(9, 1) \text{ and } \phi|Y = 7 \sim \text{Beta}(8, 2). \tag{6}$$

The distribution plots in Figure 5 show that the posterior probability mass of the parameters $\theta$ and $\phi$ lies to the far right and away from 0.5. This can be quantified by computing the Highest Posterior Density (HPD) interval for each parameter when the confidence level is at 0.025, to match the Bonferroni corrected value in the earlier tests:

97.5% HPD interval for $\theta$ is $[0.664, 1.000]$
97.5% HPD interval for $\phi$ is $[0.515, 0.995]$.

In neither case the value of 0.5 is included, which means that the random guess scenario is excluded and our hypothesis is accepted.

## IV. Discussion

There are significant temperature decreases in the supraorbital and periorbital areas during a migraine attack - a pattern that our analysis shows is likely to be widespread. The mechanism and rationale for this reduction are not completely understood. But in the case of the supraorbital region the temperature reduction appears to be partly due to the onset of perspiration, as evidenced by the blobby thermal pattern. And in the case of the periorbital region the reduction appears to be due to vasoconstriction of the ophthalmic arteries, the thermal footprints of which are centered next to the lacrimal ducts. Should this etiology of the temperature reduction be correct, then both responses are likely to be of sympathetic origin. This fresh insight is afforded in part by the new generation high definition thermal imaging sensors and in part by the computational methods we used.

Irrespective of the phenomenon's origin, migraines appear to be associated with a characteristic facial thermal pattern, which can be detected based on simple t-tests between the evolving mean temperature distributions in the supraorbital and periorbital areas and their baseline values. Real-time measurements and comparisons can be performed via a thermal imaging system mounted atop a personal computer. Importantly, the tissue areas where these measurements are performed are defined and tracked algorithmically, facilitating reproducibility and quantification.

A legitimate question is if this thermophysiological pattern on the face characterizes other activities in which subjects engage when they are in front of a computer. In a series of past studies we documented characteristic facial thermophysiological patterns associated with common desktop activities - none appears to be in conflict with the observed migraine pattern. Specifically, we documented that cognitive loading is associated with gradual warming of the supraorbital area [21], startle is associated with instantaneous warming of the periorbital area [22], and chewing is associated with gradual warming of the mandible area [23]. One unsettled issue is if headaches other than migraines produce the same facial themophysiological signature - something that calls for further research.

There are some practical limitations regarding the application of the method. The periorbital area is not accessible in subjects who wear glasses. There is, however, redundancy in the methodology and in this case monitoring could be based on the supraorbital signal only. The supraorbital area itself may be inaccessible in subjects with hair banks, but this problem can easily be solved with bobby pins.

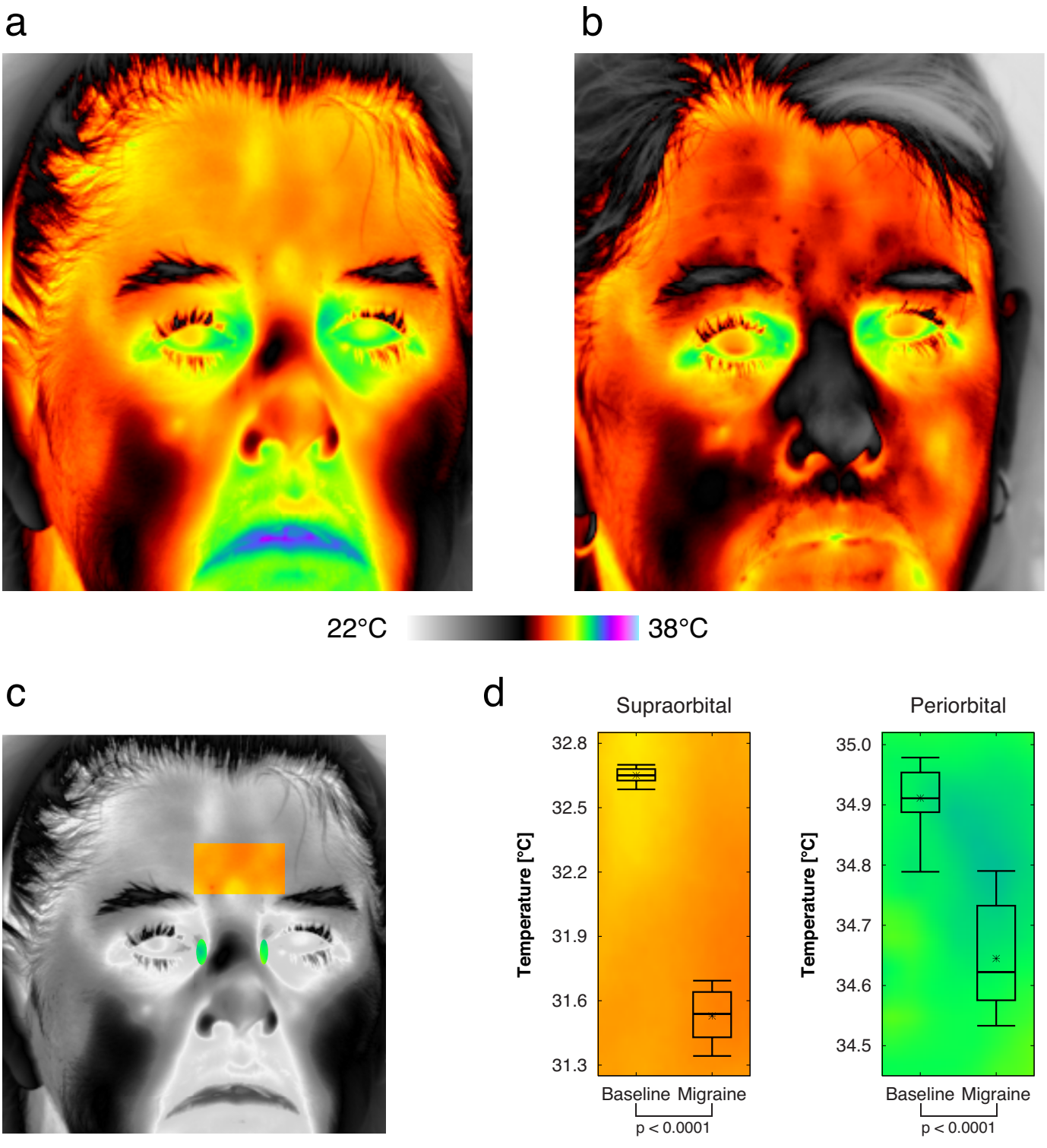


Fig. 2. **a.** Facial thermal image of subject D003 representative of her baseline condition and **b.** of her migraine condition. **c.** Measurement areas. **d.** Comparative boxplots. Each box plot contains the thermal signal values in the specic area (supraorbital or periorbital) and for the specic condition (baseline or migraine). The mean values are indicated by the '*' symbol.

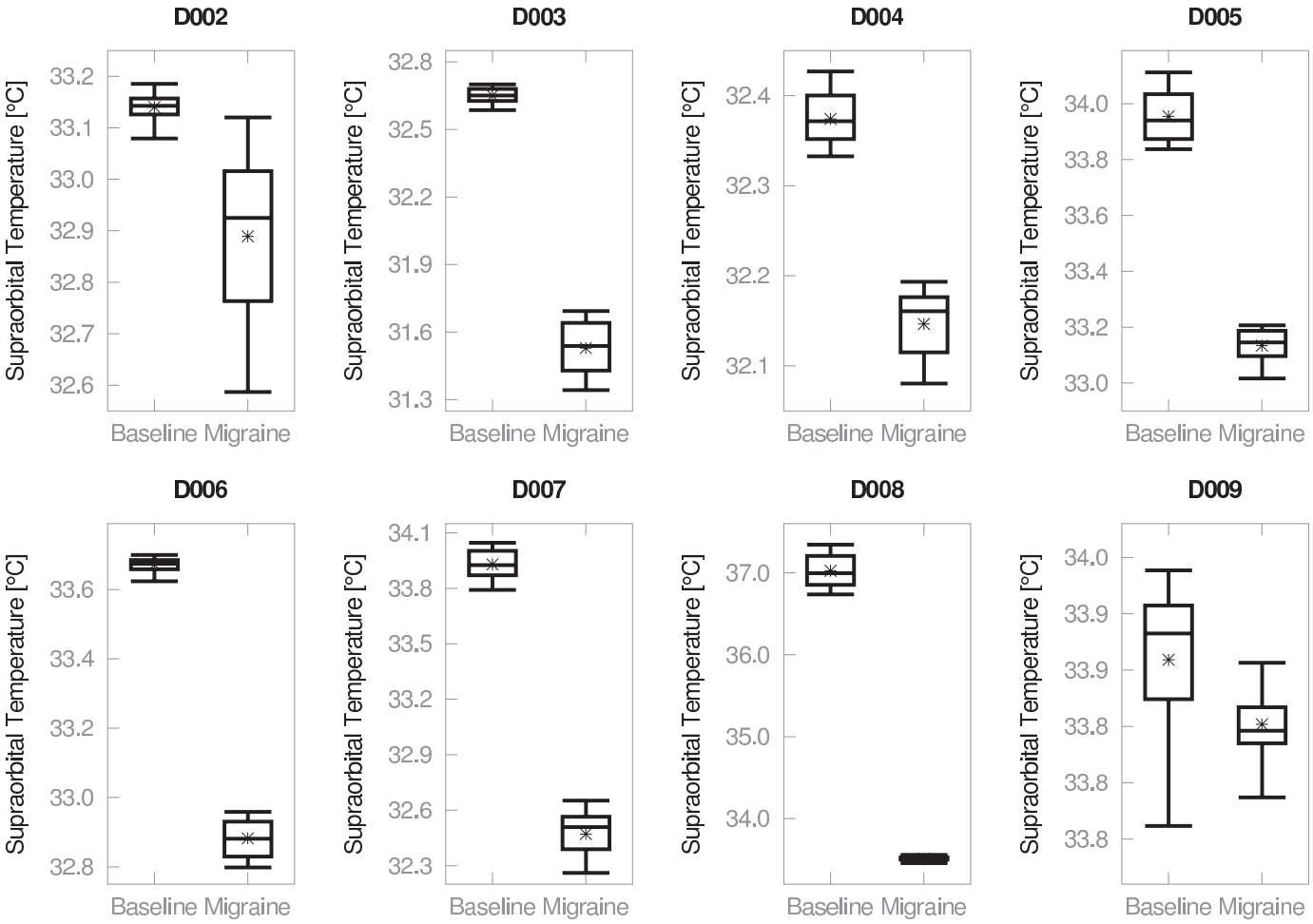


Fig. 3. Boxplots of the supraorbital thermal signals in the baseline and migraine sessions for each subject. We performed a two-sample t-test for each subject, to decide if the mean supraorbital response variable has significant differences between the baseline and migraine sessions. All the p-values are far less than $\alpha = 0.025$ ($p < 0.0001$). The mean values are indicated by the '*' symbol.

We note that all the subjects were female. This was not a deliberate study choice but reflects the fact that migraines are more prevalent in females than in the male population. It is likely that male migraine sufferers manifest the same thermophysiological pattern on the face. However, because there were no male subjects in our experimental set, this remains a question for a future study.

A method such as the one described in this study, could provide observational access in migraine studies outside the clinical setting and facilitate gaining a better understanding of the episodic nature of the ailment. Migraines are not fully understood, partly because it has been difficult to study them during daily living activities. The problems associated with studying migraines are exacerbated when patients have communication difficulties. The methodology described in this paper may provide a useful means of conducting field studies of migraine patients and better understanding the etiology of the attacks.

## Acknowledgment

This material is based upon work supported by the National Science Foundation award IIS-0414754 entitled 'Interacting with Human Physiology'. It was also supported in part by grants from the Texas Medical Center, the Methodist Hospital, and the Mayo Clinic Foundation for Research. Any opinions, findings, and conclusions or recommendations expressed in this paper are those of the authors and do not necessarily reflect the views of the funding agency.

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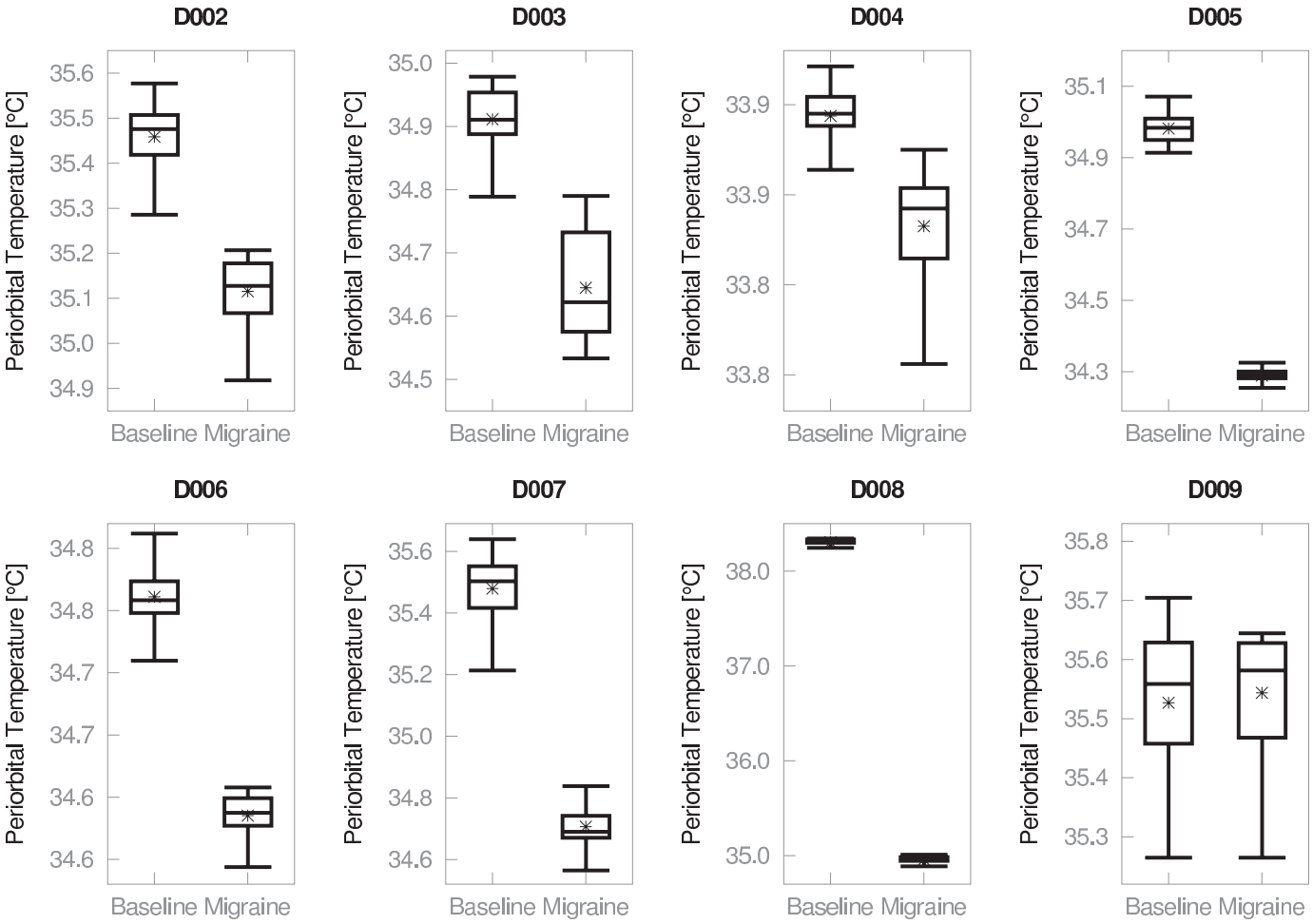


Fig. 4. Boxplots of the periorbital thermal signals in the baseline and migraine sessions for each subject. We performed a two-sample t-test for each subject, to decide if the mean periorbital response variable has significant differences between the baseline and migraine sessions. All the p-values but one are far less than $\boldsymbol{\alpha = 0.025}$ ($\boldsymbol{p < 0.0001}$ for all but subject D009, for which $\boldsymbol{p = 0.0458}$). The mean values are indicated by the '*' symbol.

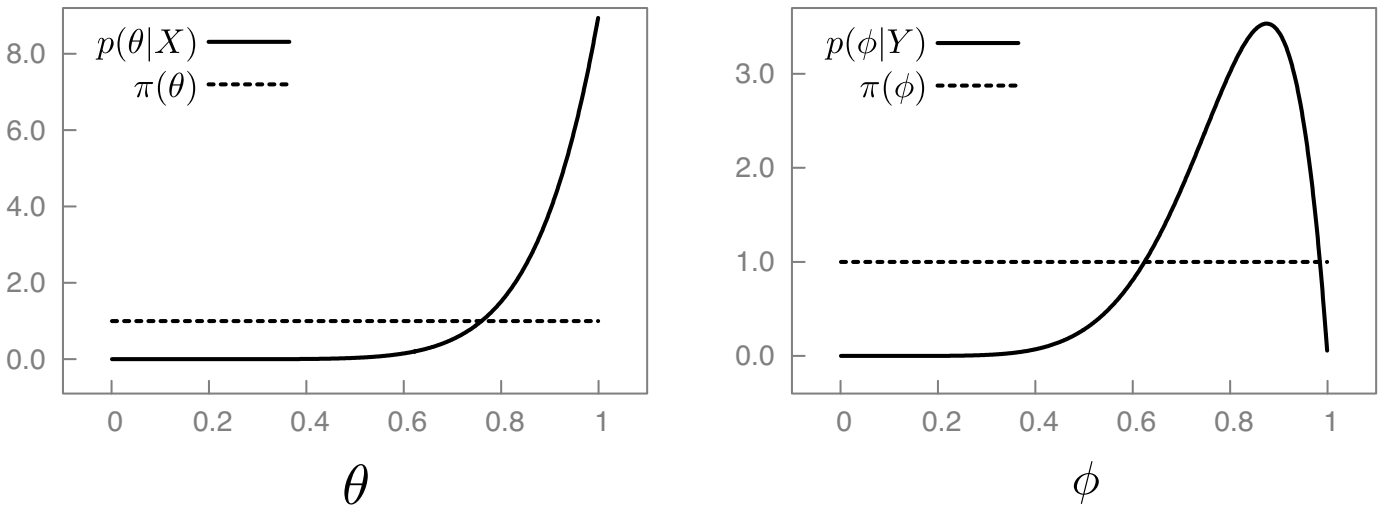


Fig. 5. Plots of the prior and posterior distributions for the supraorbital and periorbital random experiments.

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