European Journal of Applied Physiology (2019) 119:1195–1201
https://doi.org/10.1007/s00421-019-04109-6

ORIGINAL ARTICLE

# Regional differences in facial skin blood flow responses to thermal stimulation

**Akane Miyaji[1,2] · Shohei Hayashi[3] · Naoyuki Hayashi[2,3]**

Received: 3 May 2018 / Accepted: 21 February 2019 / Published online: 28 February 2019


## Abstract

**Purpose** The facial skin blood flow (SkBF) shows regional differences in the responses to a given stimulation. The facial SkBFs, especially in the eyelid and nose exhibit unique response to physiological and psychological stimuli, but the mechanisms inducing those regional differences remain unclear. To investigate whether the regional differences in the local control of vasomotion in facial vessels correspond to the regional differences in facial SkBF response, we monitored the relative change of facial SkBF to regional thermal stimulation. We hypothesized that heat stimulation dilates the cutaneous vessels in the eyelid, while cold stimulation constricts those in the nose, which was based on previous findings

**Methods:** A thermal stimulator was used to apply temperature increase (from 20 to 40 °C at 2 °C/min) and decrease (from 40 to 20 °C at 2°C/min) in a randomized order to the right eyelid, nose, right cheek, and forehead of 14 healthy young males. The facial SkBF was measured for 10 s using laser-speckle flowgraphy when temperatures of 20 °C, 30 °C, and 40 °C had been applied for 30 s in both trials.

**Results** The SkBF in the eyelid did not change significantly during any thermal stimulation, and the nasal SkBF did not decrease significantly during cold stimulation. The SkBFs in the cheek and forehead increased significantly with the applied temperature.

**Conclusions** These findings indicate that a large regional variation exists in facial skin blood flow response to local heating or cooling and that the regional variation did not correspond to the unique SkBF responses in the previous studies.

**Keywords** Facial vascular response · Regional differences · Autonomic nerve activity · Thermal stimulation

## Abbreviations

| | |
|---|---|
| ANOVA | Analysis of variance |
| MAP | Mean arterial pressure |
| NO | Nitric oxide |
| SE | Standard error |
| SD | Standard deviation |
| SkBF | Skin blood flow |
| TD | Trial temperature-decrease trial |
| TI | Trial temperature-increase trial |

Communicated by Keith Phillip George.

✉ Naoyuki Hayashi
naohayashi@ila.titech.ac.jp

[1] Division of Medical Nutrition, Faculty of Healthcare, Tokyo Healthcare University, Setagaya, Tokyo 154-8568, Japan

[2] Institute for Liberal Arts, Tokyo Institute of Technology, Meguro, Tokyo 152-8852, Japan

[3] Graduate School of Decision Science and Technology, Tokyo Institute of Technology, Meguro, Tokyo 152-8852, Japan

## Introduction

The facial skin blood flow (SkBF) might show regional differences in the response to psychological stimuli. We previously reported changes in the facial SkBF induced by taste stimulation to the oral cavity (Kashima and Hayashi 2011; Kashima et al. 2014). Those studies found that a pleasant emotion associated with taste stimulation was related to an increase in the eyelid SkBF, while an unpleasant emotion was related to a decrease in the nasal SkBF. The other groups also reported that unpleasant emotion decreases the nasal skin temperature, probably due to vasoconstriction in the nasal arteriovenous anastomoses (Zenju et al. 2004; Nozawa and Tacano 2009). These findings suggest that pleasant and unpleasant emotions induce regional differences in the facial SkBF responses, which implies that it is possible to objectively estimate the emotional state by measuring the SkBF without requiring verbal communication.

The actual mechanisms underlying these reported regional differences in the facial SkBF responses are still

unclear. In particularly, no previous study has investigated the relationship between pleasant emotions and the SkBF response in the eyelid. We therefore investigated two possible mechanisms that could underlie regional differences in the responses of the facial SkBF.

One possible mechanism is autonomic control; sympathetic stimulation elicits vasoconstriction of cutaneous vessels, and parasympathetic stimulation elicits vasodilatation in the face. The regional differences in facial SkBF responses indicated above were observed as rapidly as within 3–5 s (Kashima and Hayashi 2011; Kashima et al. 2013). An autonomic control of vessels can induce within several seconds. From these, we assumed that the regional differences in facial SkBF responses are due to regional differences in degree of autonomic control of facial vessels.

Another possible mechanism is regional differences in local control of vasomotion. The facial SkBF also shows regional differences to pressor responses elicited by the cold pressor test and hand grip exercise (Kashima et al. 2013). That study found that only the cutaneous vessels in the nose exhibited vasoconstriction against the pressor response induced by both stimuli, with no vasoconstriction in the cheek, eyelid, or forehead. From these observations, we assumed that the nasal skin vessels might readily constrict against any given stimuli, and that the eyelid skin vessels might readily dilate more than other regions in face.

The objective of the present study was to determine whether the regional differences in the degree of local control of vasodilatation/constriction in facial vessels to find possible factors explaining the regional differences in facial SkBF responses to a given stimulus. We observed facial SkBF responses to local thermal stimulation to achieve this objective. The local heating induces vasodilatation in forearm skin vessels, and local cooling induces vasoconstriction (Hodges et al. 2006; Yamazaki et al. 2006; Kellogg et al. 2009). Local thermal stimulation can be used to minimize changes in systemic and autonomic control of vasomotion (Minson et al. 2001). We simply hypothesized that the SkBF in eyelid dilated in response to local heating, while that in the nose constricted in response to local cooling, based on the regional differences in the responses of the facial SkBF to the taste stimulation found in the previous studies.

## Methods

### Subjects

Fourteen healthy males (age, 27 ± 10 years, mean ± SD; height, 173.1 ± 5.0 cm; body mass, 65.5 ± 5.9 kg) participated in this study. All of the subjects were free of any known autonomic dysfunction, cardiovascular diseases, atopic dermatitis, and metallic allergy, and were not taking any medications. The study was approved by the ethics committees of Tokyo Institute of Technology, Japan (Ethical approval number: 2,015,056). All of the protocols used conformed with the standards set by the Declaration of Helsinki. Each subject received verbal and written explanations of the objectives, measurement techniques, and risks and benefits associated with the study, and then provided written informed consent. Subjects were requested to abstain from strenuous exercise, alcohol ingestion, and excessive spice intake for at least 1 day, and from consuming caffeinated beverages and food for at least 2 h prior to the measurements.

### Experimental protocol

Before starting the measurements, each subject rested in a seated position for 20 min in an air-conditioned room maintained at 22 °C for temperature acclimation. Subjects wore long sleeve and long pants for their comfort. During the resting period, the probe of an autonomic sphygmomanometer was attached to the left middle finger (Finometer, Finapres Medical Systems, Amsterdam, The Netherlands), and this was subsequently used to continuously monitor the beat-by-beat arterial pressure throughout the experiment.

We conducted trials of temperature increase (from 20 to 40 °C; TI) and decrease (from 40 to 20 °C; TD) using a thermal stimulator controlled by a Peltier element (Intercross-210, Intercross, Tokyo, Japan). We conducted TI and TD trials to exclude possible effects of basal vasoconstriction/dilatation state before stimulation on the vessel responses to thermal stimulation. Supposing that low ambient temperature before stimulation had induced full vasoconstriction, thermal stimulation of cold temperature of 20 °C would not have masked vasoconstriction. Using temperature increasing and decreasing protocols as TI and TD could allow us to observe vasoconstriction/dilatation to thermal changes. The surface area of the stimulator was 10 mm × 10 mm, and this was held against the face by the subject's hand. In the TI and TD trials (Fig. 1), the stimulator caused the skin surface temperature to increase and decrease at a rate of 0.03 °C/s (i.e., 2 °C/min), respectively. The thermal stimuli were applied to four regions (i.e., right eyelid, nose, right cheek, and forehead) in a randomized order, with a washout period of longer than 10 min. The SkBF was recorded for 10 s without application of the thermal stimulator immediately after applying 30 s of thermal stimulation at 20 °C, 30 °C, and 40 °C in both trials. After each recording, the subjects placed the stimulator against the same area again with guidance from the investigator. Each TI or TD trial on the four facial regions was conducted within 2 h, and then another trial was performed with a washout period for at least 1 h. Each subject participated in eight trials, comprising combinations of TI and TD in four measurement regions.

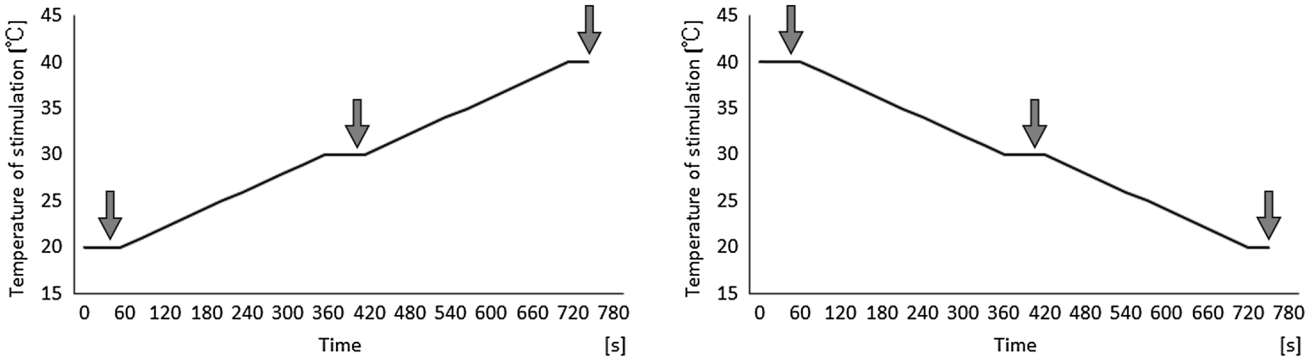



**Fig. 1** The experimental protocol. Left panel shows the temperature-increase trial, and the right panel shows the temperature-decrease trial. The thermal stimulator changed the temperature from 20 to 40 °C or from 40 to 20 °C at a rate of 0.03 °C/s (i.e., 2 °C/min). Arrows indicate periods when the skin blood flow was measured

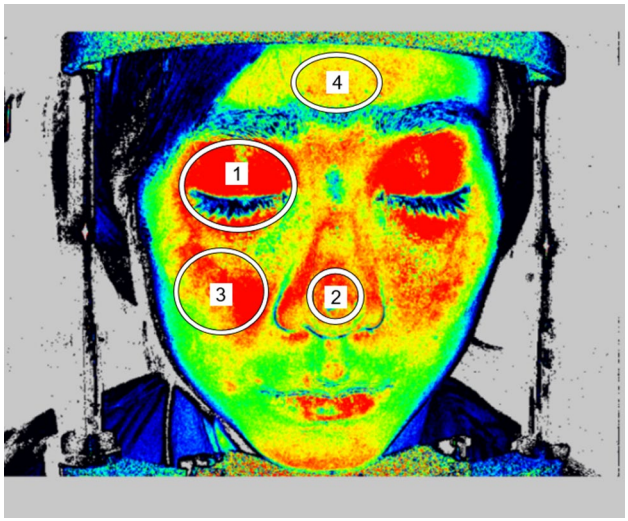



**Fig. 2** Laser-speckle flowgraphy image of the facial skin blood flow (not subject's face in the present study). White circles indicate the regions of interest: 1, right eyelid; 2, nose; 3, right cheek; and 4, forehead

## Measurements

The mean arterial pressure (MAP) was calculated from the beat-by-beat arterial pressure using analysis software (LabChart v5, ADInstruments, Sydney, Australia). The facial SkBF was measured using laser-speckle flowgraphy (LSFG-PI-E, SoftCare, Fukuoka, Japan) for 10 s before each trial as the baseline, and then at temperatures of 20 °C, 30 °C, and 40 °C. Subjects were instructed to keep their chin on a pedestal to stabilize their face, to keep their eyes closed, and to not move their facial muscles while the facial SkBF was being recorded. The focal length was set at 230 mm so that the SkBF could be measured over the entire face. SkBF data were obtained from the right eyelid, nose, right cheek, and forehead (Fig. 2).

## Data analysis

All statistical analyses were performed with the SPSS software (Statistics 21.0 for Windows, IBM, Tokyo, Japan). The data are expressed as mean ± SE values, and the cutoff for statistical significance was set at $P < 0.05$.

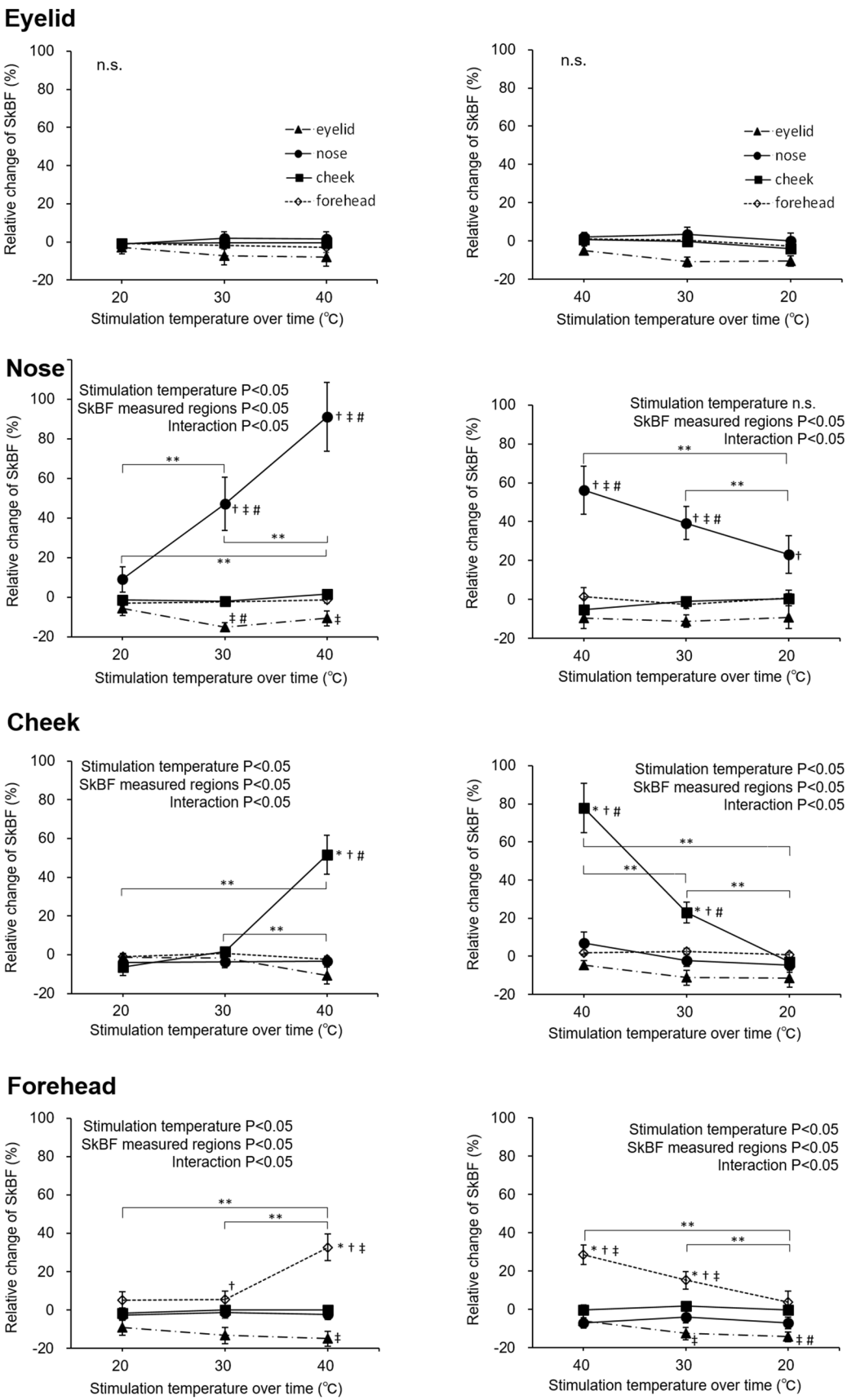
Facial SkBF data were used in the analysis only when artifact-free laser-speckle imaging data were obtained. The regions of interest were the same in each subject. The SkBF was expressed as the change relative to baseline since the laser-speckle technique does not provide absolute values.

The effects of stimulation temperature (20 °C, 30 °C, and 40 °C) and SkBF measurement region (eyelid, nose, cheek, and forehead) on the changes in SkBF were tested by two-way repeated ANOVA. This analysis was conducted in eight trials: two temperature conditions × four measurement regions. When a significant $F$ value was detected, this was further examined using Bonferroni's post-hoc test to assess for the main effect of temperatures and SkBF measurement regions, respectively. The effects of stimulation temperature (20 °C, 30 °C, and 40 °C) and measurement region on the changes in SkBF in the different measurement regions were tested by two-way repeated ANOVA. This analysis was conducted separately in TI and TD trials. When a significant F value was detected, Bonferroni's post-hoc test was conducted.

## Results

Thermal stimulation in both the TI and TD trials resulted in mean change in the MAP in the various regions of less than 2 mmHg from baseline, and these changes were not statistically significant.

The SkBFs in the cheek and forehead increased significantly from the baseline in both the TI and TD trials when these regions were heated to 40 °C (52 ± 10% for the cheek


Eyelid
n.s.
eyelid
nose
cheek
forehead
Relative change of SkBF (%)
Stimulation temperature over time (℃)
Nose
Stimulation temperature P<0.05
SkBF measured regions P<0.05
Interaction P<0.05
Stimulation temperature n.s.
SkBF measured regions P<0.05
Interaction P<0.05
Cheek
Forehead

◂**Fig. 3** Relative changes in skin blood flow associated with changes in the stimulation temperature. Left panels show the temperature-increase trial and right panels show the temperature-decrease trial for the eyelid, nose, cheek, and forehead. Filled squares, triangles, and circles and the open diamond denote the skin blood flows in the eyelid, nose, cheek, and forehead, respectively. $^{*}P<0.05$ vs. nose, $^{\dagger}P<0.05$ vs. eyelid, $^{\ddagger}P<0.05$ vs. cheek, $^{\#}P<0.05$ vs. forehead, $^{**}P<0.05$ between each stimulation temperature

and 33 ± 7% for the forehead in the TI trial, and 78 ± 13% and 29 ± 5%, respectively, in the TD trial) (Fig. 3). However, there were no significant changes in SkBF relative to baseline in any regions for stimulation at 20 °C or 30 °C. The nasal SkBF increased significantly at 40 °C only in the TI trial (91 ± 18% from baseline), with no significant change at 20 °C in either trials. The SkBF in the eyelid did not change significantly in any trial at any temperature.

There were significant interactions of stimulation temperature and measurement regions in eight conditions, i.e., TI and TD multiplied by four regions, whereas no significant effects were shown in TI and TD for the eyelid (Fig. 3). Multiple comparisons among these trials performed at 40 °C revealed that the relative change in the SkBF in the region that was stimulated showed significantly greater than the changes in other measurement regions that were not stimulated.

There were significant interactions of stimulation temperature and stimulated regions in both the TI and TD trials (Fig. 4). Main effects of stimulation temperature and stimulated regions were detected in both trials. Multiple comparisons of both trial types showed that the relative changes in the SkBFs in the nose, cheek, and forehead for stimulation at 40 °C were significantly greater than that in the eyelid. There were no significant differences in the relative changes at 20 °C and 30 °C among all regions, with the exception that the relative change in nasal SkBF at 30 °C in the TI trial was significantly greater than the changes in other regions.

## Discussion

This study aimed to determine whether the regional differences in the degree of local control of vasomotion in facial vessels explain the regional differences in facial SkBF responses to physiological and psychological stimulations; relatively large blood flow changes in eyelid and nose (Kashima and Hayashi 2011; Kashima et al. 2013, 2014). This was achieved by observing the facial SkBF responses elicited by local thermal stimulation. The SkBF in the eyelid was not changed significantly by any thermal stimulation, and cold stimulation did not significantly decrease the nasal SkBF. The SkBF in the cheek, forehead, and nose increased significantly in response to local heating, with this increase observed only within the heated region itself. These findings indicate that a large regional variation exists in facial skin blood flow response to local heating or cooling, and do not support our hypothesis, which had been based on previous reports, and they provide clues to the underlying mechanisms of those regional differences in facial SkBF response.

We assumed that there are two possible mechanisms that could underlay regional differences in facial SkBF, i.e., the autonomic control, and local control of vasomotion in facial skin vessels. The present result suggests that the regional differences in the degree of local control of vasomotion could cause regional differences in facial SkBF, since the forehead and cheek readily responded to any thermal stimulation whereas the nose and eyelid did not. This can not, however, explain the previous observations of vasodilatation in the eyelid and vasoconstriction in the nose (Kashima and Hayashi 2011, 2013; Kashima et al. 2014).

We used local thermal stimuli to examine the role of local control of vasomotion in regional differences in facial SkBF responses. Cutaneous vessels exhibit vasodilatation during local heating and vasoconstriction during local cooling (Johnson et al. 2014). Local heating enhances the production of NO by endothelial cells (Kellogg et al. 2009), and NO induces the relaxation or vasodilatation of smooth muscle. This mechanism was responsible for the vasodilatation in the forehead, cheek, and nose seen in the present study. Local cooling inhibits NO synthase and enhances the Rho kinase that induces vasoconstriction (Hodges et al. 2006; Yamazaki et al. 2006), this mechanism also contributed to vasoconstriction in the forehead and cheek in the TD trial.

Any thermal stimulation did not significantly change the eyelid SkBF, and cold stimulation at 20 °C did not significantly decrease the nasal SkBF. These findings indicate that the local control of vasomotion can not fully explain the vasomotion observed in the face. The facial cutaneous vessels are richly innervated by both sympathetic and parasympathetic nerves (Kuchiiwa et al. 1992; Drummond 1994). Facial sympathetic nerves evoke vasoconstriction while parasympathetic nerves evoke vasodilatation (Drummond and Lance 1987; Kuchiiwa et al. 1992; Izumi and Karita 1993; Drummond 1994, 1995). The present results suggest that the SkBFs in the face—and especially those in the nose and eyelid—are affected by autonomic control of vasomotion (Kashima and Hayashi 2011, 2013; Kashima et al. 2013, 2014).

Cold stimulation in the TD trail tended to increase the nasal SkBF than the baseline value. This could result from lasting effect of increased response to 40 and 30 °C stimulations. In turn, the sudden cooling at 20 °C in the TI trial did not decrease the nasal SkBF than the baseline value. Thus, nose cutaneous vessels may not induce constriction against local vasoconstrictor cold stimulation, while that easily dilates against local vasodilator stimulation.

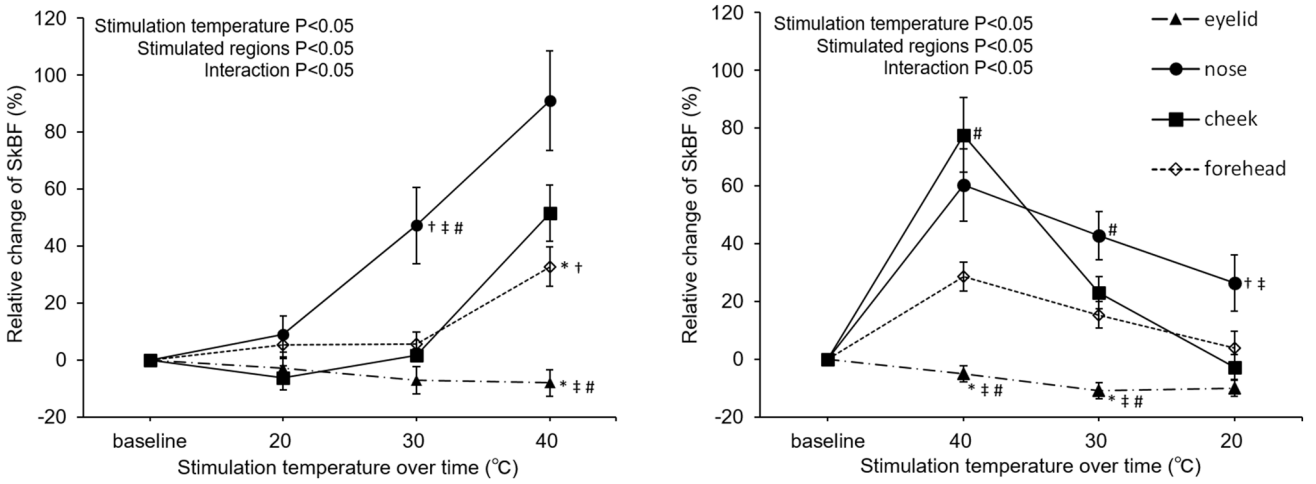



**Fig. 4** Changes in skin blood flow in the measurement regions associated with changes in the stimulation temperature. Baseline values were obtained at rest before each trial. Left panel shows the temperature-increase trial and right panel shows the temperature-decrease trial. $^{*}P<0.05$, vs. nose, $^{\dagger}P<0.05$, vs. eyelid, $^{\ddagger}P<0.05$ vs. cheek, $^{\#}P<0.05$ vs. forehead

Nasal cutaneous vasomotion is influenced by the activation of sympathetic nerves in humans and other animals (Zenju et al. 2004; Nakayama et al. 2005; Nozawa and Tacano 2009; Kuraoka and Nakamura 2011). We previously reported that vasoconstriction in the facial cutaneous vessels occurred solely in the nose as a pressor response to the cold pressor test and hand grip exercise (Kashima et al. 2013). Together these findings indicate that nose vasoconstriction is induced by sympathetic activity. The nose vasoconstriction observed in previous study (Kashima and Hayashi 2011, 2013; Kashima et al. 2013, 2014) can be induced by sympathetic vasoconstriction.

The present results imply that local control of vasomotion plays a role in facial SkBF responses, with the exception of some such responses observed in the eyelid and nose. No studies have examined a role of autonomic activity on hemodynamics within the eyelid. The experimental use of pharmacological agents on the human face is ethically questionable, and the skin structure and innervation could differ in animals since they have nonglabrous skin around the eyelid. These make it very difficult to directly establish the mechanism relevant to SkBF in the eyelid. As an alternative, we implied the role of autonomic activity in eyelid vessels since vasomotion itself related to thermal stimulation did not increase eyelid blood flow.

We can deny the possibility that facial SkBF changes induced by a local thermal stimulus are affected by the pleasant or unpleasant sensations evoked by the stimulus. While the hedonic score to local thermal stimuli was not assessed in this study, the results deny this possibility. If the emotional state and/or autonomic nervous activity was changed by local thermal stimuli, the SkBF in the eyelid and/or nose should have changed in association with the emotional state (Kashima and Hayashi 2011, 2013), and we found no such changes. Additionally, the magnitudes of the MAP responses and those of SkBFs in the eyelid and nose to thermal stimulation were very small or nonexistent, in contrast to the larger responses induced by taste stimulation. Thus, the local thermal stimuli used in this study did not change the emotional state of the subjects. The present experimental setting successfully minimized autonomic nervous and emotional responses.

Nasal SkBF showed inconsistent response in trials; significantly increased at 40 °C in TI but not by TD. We consider that the difference is due to the difference in the duration of thermal stimulation greater than skin temperature between TI and TD. In the TI, the skin is gradually heated at temperature over skin temperature (35–40 °C), whereas in TD trial the stimulation at 40 °C was instantaneous and the temperature started decreasing, even though the duration stimulated at 40 °C is the same both in TI and TD trials. This inconsistent response was not shown in cheek and forehead; still there is a regional difference in SkBF responses.

## Conclusion

To investigate the factors causing regional differences in facial SkBF responses to a given stimulus, we observed the responses of the facial SkBF to local thermal stimulation. The SkBFs in the cheek and forehead increased significantly with the applied temperature. In contrast, the SkBF in eyelid did not change to any thermal stimulation, and that in nose did not decrease to cold stimulation at 20 °C, against our expectation. These findings indicate a large regional

variation exists in facial skin blood flow response to local heating or cooling.

**Acknowledgements** This work was supported by JSPS KAKENHI grants: number 15J11556 to A.M. and number 26560396 to N.H.

**Author contributions** AM, SH and NH designed the study, contributed to analysis and interpretation of data, and assisted in the preparation of the manuscript. AM and SH wrote the initial draft of the manuscript. SH have contributed to data collection. AM and NH have contributed to interpretation, and critically reviewed the manuscript. All authors approved the final version of the manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Compliance with ethical standards

**Conflict of interest** The authors have no financial conflict of interest.

## References

Drummond PD (1994) Sweating and vascular responses in the face: normal regulation and dysfunction in migraine, cluster headache and harlequin syndrome. Clin Auton Res 4:273–285

Drummond PD (1995) Mechanisms of physiological gustatory sweating and flushing in the face. J Auton Nerv Syst 52:117–124

Drummond PD, Lance JW (1987) Facial flushing and sweating mediated by the sympathetic nervous system. Brain 110:793–803

Hodges GJ, Zhao K, Koshiba WA, Johnson JM (2006) The involvement of nitric oxide in the cutaneous vasoconstrictor response to local cooling in humans. J Physiol 574:849–857

Izumi H, Karita K (1993) Innervation of the cat lip by two groups of parasympathetic vasodilator fibres. J Physiol 465:501–512

Johnson JM, Minson CT, Kellogg DL Jr (2014) Cutaneous vasodilator and vasoconstrictor mechanisms in temperature regulation. Compr Physiol 4:33–89

Kashima H, Hayashi N (2011) Basic taste stimuli elicit unique responses in facial skin blood flow. PLoS One 6:e28236

Kashima H, Hayashi N (2013) Facial skin blood flow responses to irritant stimuli in the oral cavity. Auton Neurosci 174:61–65

Kashima H, Ikemura T, Hayashi N (2013) Regional differences in facial skin blood flow responses to the cold pressor and static handgrip tests. Eur J Appl Physiol 113:1035–1041

Kashima H, Hamada Y, Hayashi N (2014) Palatability of tastes is associated with facial circulatory responses. Chem Senses 39:243–248

Kellogg DL Jr, Zhao JL, Wu Y (2009) Roles of nitric oxide synthase isoforms in cutaneous vasodilation induced by local warming of the skin and whole body heat stress. J Appl Physiol 107:1438–1444

Kuchiiwa S, Izumi H, Karita K, Nakagawa S (1992) Origins of parasympathetic postganglionic vasodilator fibers supplying the lips and gingivae; an WGA-HRP study in the cat. Neurosci Lett 142:237–240

Kuraoka K, Nakamura K (2011) The use of nasal skin temperature measurements in studying emotion in macaque monkeys. Physiol Behav 102:347–355

Minson CT, Berry LT, Joyner MJ (2001) Nitric oxide and neurally mediated regulation of skin blood flow during local heating. J Appl Physiol (1985) 91:1619–1626

Nakayama K, Goto S, Kuraoka K, Nakamura K (2005) Decrease in nasal temperature of rhesus monkeys (Macaca mulatta) in negative emotional state. Physiol Behav 84:783–790

Nozawa A, Tacano M (2009) Correlation analysis on alpha attenuation and nasal skin temperature. J Stat Mech P01007:1–10

Yamazaki F, Sone R, Zhao K, Alvarez GE, Koshiba WA, Johnson JM (2006) Rate dependency and role of nitric oxide in the vascular response to direct cooling in human skin. J Appl Physiol (1985) 100:42–50

Zenju H, Nozawa A, Tanaka H, Ide H (2004) Estimation of unpleasant and pleasant states by nasal thermogram. IEEJ Trans Electron Inf Syst 124:213–214