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Physiological characteristics of women's cold constitution and the effects of exercise

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Running title: Cold constitution and exercise

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Abstract About half of young Japanese women have a cold constitution, which heightens susceptibility to cold syndrome. In recent years, new findings on the physiological features of a cold constitution have increased. Cold constitution lowers the quality of daily life, so coldness and the related complaints need to be alleviated. Single dynamic exercise transiently relieves coldness via the warm-up effect. Exercise training decreases sensitivity to cold under normal temperature conditions and enhances peripheral cutaneous vasodilatory responses in young women with a cold constitution. This review provides an overview of the physiological characteristics of women's cold constitution and the acute and chronic effects of physical exercise as a countermeasure.

Keywords: aerobic exercise, cold sensitivity, thermal discomfort, skin temperature

タイトル： 女性の冷え性の生理学的特徴と運動の効果

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抄録： 日本人の若年女性の約半数は，体調不良に陥りやすい冷え性であるとされる．近年，冷え性の生理学特徴に関する新たな知見が増加しつつある．冷え性は日常生活の質を低下させるため，冷えとそれに伴う不定愁訴の緩和が必要である．単回の動的運動は，ウォームアップ効果により一過性に冷えを緩和する．運動トレーニングは，冷え性の若年女性において，常温環境下での寒冷に対する感受性を低下させ，末梢の皮膚血管拡張反応を亢進させる．本総説では，女性の冷え性の生理学的特徴とその対策としての身体運動の急性および慢性の効果について概説する．

Introduction

Cold-induced physiological responses usually exhibit inter-individual differences, even among healthy people. Even at times when most people do not feel cool under temperate thermal conditions, women may experience severe coldness of the body, especially the lower extremities[1-6]. A cold constitution with higher sensitivity to cold is called "hi-e-sho" in Japanese, which is more common in women than in men[1,2,5]. Prior studies have reported that about half of young Japanese women have an aware of cold constitution[5,7,8]. Women with a cold constitution often feel discomfort due to a severe cold sensation in cool environments, have general malaise (such as sleeplessness, weariness, and lowered power of concentration), and a tendency to fall ill[9,10]. Thus, a cold constitution lowers the quality of life and heightens susceptibility to cold syndrome.

Several strategies have been reported to alleviate cold symptoms: the intake of dietary supplements that have a warming effect (capsinoids, ginger, Piper longum L.)[11-13], the intake of multifunctional foods (glucosyl hesperidin, royal jelly)[14,15], foot massage[16], electro-acupuncture therapy[17], and abdominal breathing exercises[18]. In recent years, our research group has reported that physical exercise can be a strategy to improve cold symptoms. The practice of daily exercise is recommended for the prevention of lifestyle-related diseases[19,20], and the effects of exercise can include improving cold constitution.

This review first provides an overview of the physiological characteristics of women's cold constitution, for which new knowledge is increasing. Next, we discuss the currently reported effects of physical exercise on women's cold constitution.

Physiological characteristics of a cold constitution

Core temperature and metabolic rate

The resting core body temperature of people with a cold constitution is within the normal range[21,22]; thus, its physiological properties are different from hypothermia, which causes a decrease in core body temperature. However, the resting metabolic rate of people with a cold constitution is lower than normal people; thus, they have a poor ability to increase the metabolic rate during exposure to cold, because of lower nonshivering thermogenesis[21,22]. A previous study reported lower serum thyroxine (T4) levels in people with a cold constitution than in normal people; however, there were no significant differences between both groups in plasma epinephrine and cortisol levels[21]. Okada et al.[23] reported a low level of free triiodothyronine (T3) in women with a cold constitution. Low thyroid function in people with a cold constitution is responsible for the low metabolic rate during normothermia and mild cold exposure[21,23]. Prior studies demonstrated the existence of metabolically active brown adipose tissue (BAT) in adult humans, and inter-individual differences after cold exposure[24,25]. Low BAT activity in individuals with a cold constitution is suggested as a potential reason for the different metabolic responses during mild cold exposure[22]. Greater cutaneous vasoconstrictor sensitivity in individuals with a cold constitution is an adaptive characteristic for preventing possible hypothermia caused by low thermogenesis during exposure to a cold environment or almost normal temperature environment[22].

(Insert Fig.1)

Temperature sensory function

The Fig. 1 shows the main physiological features of people with a cold constitution and signaling pathways for cold sensation and cutaneous vasoconstriction response. Cool stimulation of the skin is transmitted by cutaneous cold receptors in sensory nerve endings to the cerebral cortex, and the limbic system, resulting in cold sensation and discomfort, respectively[26,27]. People with a cold constitution have a strong sensation of cold and skin vasoconstriction due to the high sensitivity of these signaling pathways[22]. The higher thermal sensitivity to cold in people with a cold constitution is mainly due to: 1) greater activity in somatosensory neurons in the cerebral cortex at a given peripheral thermosensitive input, 2) greater thermosensitive neural activity in the afferent pathways from skin to cerebral cortex and limbic system, or 3) greater thermoreceptor excitation in the cutaneous endings of somatosensory neurons at a similar temperature[22]. A previous study reported that the number of cold and warm spots of the skin of the dorsal foot were not significantly different between a cold constitution group and a normal group[28]; thus, higher receptor density in the skin may be not responsible for the higher thermal sensitivity to cold. Cold receptors in the skin express TRPM8 (melastatin 8) cation channels, which generate receptor potentials upon cooling stimuli or menthol[29]. Non-cold-sensitive individuals experience increased cold sensitivity to menthol administration to the skin of the lower extremities, but this is less likely to occur in cold-sensitive individuals, suggesting paradoxical desensitization to cold receptor function[30]. Individuals with a cold constitution, characterized by often cold peripheral extremities, may adapt their temperature sensory function at the cold receptor level to reduce daily thermal discomfort.

Brain activity

Electroencephalography (EEG) is a noninvasive method of assessing brain function. EEG recordings with closed eyes during whole-body cooling have shown that brain activity is more enhanced in cold sensitive individuals[31-33]. That is, the cold sensitive individuals showed fewer 8-10 Hz EEGs (low-frequency alpha waves) and more 13-30 Hz EEGs (beta waves) than non-cold sensitive individuals; however, this was not found with open eyes[31-33]. It is thought that higher frequencies of EEG manifest discomfort symptoms in response to cold[32,33]. These brain activity characteristics also represent physiological characteristics of sensitivity to cold. There is limited information on the brain function for individuals with a cold constitution; therefore, further study is warranted for elucidating the characteristics.

Blood flow and temperature in skin

In general, cutaneous vasoconstriction occurs via reflexes and local controlling mechanisms to decrease heat dissipation from the skin when exposed to cold environments (Fig. 1). In women with a cold constitution, peripheral skin vasoconstriction occurs even under normal temperature conditions[34]. In previous studies, when the room temperature was gradually decreased from a somewhat warm temperature

(29.5°C) to a cool temperature (23.5°C), vasoconstrictor sensitivity in the dorsal foot, but not in the forearm and calf, was greater in cold sensitive subjects than in normal control subjects[21,22]. The cold sensitive subjects also showed greater vasoconstrictor responses in the dorsal foot[22,34], but not in the calf[22] during local skin cooling and the iontophoretic application of norepinephrine. These findings suggest that cold sensitive subjects possess a specific blood flow-controlling system in the peripheral pathway that is characterized by higher adrenergic sensitivity for greater cutaneous vasoconstriction in the distal portion of the lower extremities during cold exposure. Differences in the sensitivity of these receptors also cause site differences, with stronger vasoconstrictive responses occurring in the peripheral regions of the extremities[22]. Previous studies reported that increased thermal sensitivity of the body to cold and decreased skin temperature in peripheral extremities, such as the feet and fingers, during cold exposure contribute to the severe cold sensation in women with a cold constitution[21,22].

The main physiological characteristics of people with a cold constitution are summarized in Fig. 1.

Effects of exercise on a cold constitution

Acute effects

Exercise is a means of both behavioral and autonomic thermoregulation to keep the body warm in a normal air temperature condition. In order to clarify the acute effects of dynamic exercise on the temperature sensory function of cold-sensitive women, young adult females with an awareness of a cold constitution were divided into two groups: an exercise condition in which cycle exercise with a light-to-moderate intensity for 15 min was performed, and a control condition in which rest without exercise was maintained[35]. Cooling tests in which the hand was immersed in cool water at 15°C were carried out before exercise, immediately after exercise, and 30 min after exercise. The sensitivity of the cold sensory function was evaluated based on changes in skin temperature, thermal sensation, and comfort in the hand. Cold sensation and thermal discomfort during hand cooling were reduced by the significant increase in core body temperature after exercise.

The exercise condition did not alter the sensitivity of cold sensation but reduced the sensitivity of thermal discomfort. A warm feeling increased in the trunk portion immediately after exercise; however, cold feeling in the foot was decreased 30 min after exercise. These findings suggest that thermal sensation is site-dependent and influenced by increases in core and skin temperatures after exercise (Fig. 2). Furthermore, the sensitivity to cold-induced discomfort is temporarily suppressed without affecting the sensitivity to cold sensation.

(Insert Fig. 2)

Next, we determined the acute effects of exercise on EEG activity in women with a cold constitution[36)]. Cold-sensitive and normal young women performed cycle exercise with a light-to-moderate intensity for 15 min with the eye closure at a room temperature of 25°C. Before initiating exercise, cold sensation in the extremities of limbs was higher in cold sensitive subjects than control subjects. Significant increases in core and skin temperatures immediately after exercise were found in participants with reduced cold sensation. EEG alpha wave power was consistently lower in the cold-sensitive subjects than the control subjects throughout the experiments; however, no changes in spectral power by performing exercise were found. Beta wave power was increased during exercise at moderate intensity (~60% of maximum), which promptly returned to pre-exercise levels after exercise. These findings suggest that performing a single dynamic exercise transiently inhibits cold sensation due to thermal effects of exercise without altering alpha wave and beta wave power during rest under normal temperature conditions. Thus, the lower alpha wave power in the cold-sensitive women was independent of cold sensation itself.

Chronic effects

To investigate the relationship between a cold constitution and exercise habits, earlier studies[37,38)] compared the percentage of persons with symptoms of a cold constitution in subjects with and without exercise habits. In a questionnaire survey using the Internet of 6,729 patients, many subjects with an awareness of a cold constitution did little exercise[37]. Tsuyushige et al.[38] reported that symptoms of a cold constitution were milder in subjects performing intense physical exercise on a daily basis compared to subjects without an exercise habit in a survey involving healthy female university students.

A longitudinal study reported that the chronic effects of dynamic exercise, consisting of a light combination exercise training (aerobic and resistance training) for 3 months, were negation of symptoms related to coldness of the body with increased muscle strength in the trunk and lower limbs[39]. A walking exercise intervention for 4 weeks mitigated coldness in the distal portion of the extremities via a reduction in cold sensation at normal body temperature in young women who had a cold constitution[40]. Thus, the elevation of body temperature and skin vasodilation of the distal portions of the extremities that occurs during daily aerobic exercise may contribute to reduced cold sensitivity. Moreover, a shorter term (2 weeks) aerobic exercise intervention increased overall and foot warmth and comfort in cold-sensitive young women (Fig. 3)[41]. The alleviations of cold sensitivity symptoms were associated with greater pre-sleep alpha wave power and improved subjective sleep quality with a shorter mid-awake time and a longer deep sleep time[41]. The habitual exercise-induced increase in alpha wave power at rest may reflect reduced sensitivity to cold sensation and/or thermal discomfort in the brain.

(Insert Fig. 3)

To summarize the effects of exercise on women's cold constitution: 1) coldness was transiently alleviated in a body site-dependent and time-dependent manner due to the thermogenic effects of exercise, and 2) cold symptoms in the peripheral extremities at rest were improved after at least 2 weeks of aerobic exercise training.

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Conflict of Interests

The authors declare that they have no conflict of interests.

References

1) Miura T, Katano Y, Sumimoto K and Kanayama N. 2001. Study on chilliness and lifestyle in young women. *Jpn J Maternal Health* 42: 784-789.

2) Sadakata M, Satoh E and Sayama M. 2007. The skin surface temperature in the women with excessive sensitivity to cold (HIESHO) in the neutral-temperature environment. - The study of the measurement-part helping to make the judging guideline and characteristic of the skin surface temperature -. *Biomed Thermol* 27: 1-7.

3) Tanaka H and Shikimi T. 2005. Thermal adjustment to mild-cold or mild-hot water immersion test in young women with cold constitution. J*pn Red Cross Med J* 56: 507-511.

4) Yamada N, Bekku N and Yoshimura H. 2007. Determinants for discriminating young woman with and without chilliness. *Jpn J Neuropsychopharmacol* 27: 191-199.

5) Yamada N and Yoshimura H. 2009. Determinants of chilliness among young women and their application to psychopharmacological trials. *Jpn J Neuropsychopharmacol* 29: 171-179.

6) Yamato T and Aomine M. 2002. Physical characteristics and living environment in female students with cold constitution. *HEP* 29: 878-884.

7) Imai M, Akasofu K and Fukunishi H. 2007. Subjective chills and their related factors in adult women. *Ishikawa J Nurs* 4: 55-64 (in Japanese).

8) Shibahara N and Ito T. 1999. Hiesho and peripheral circulatory disorder. *Kampo and the Newest Therapy* 8: 313-323 (in Japanese).

9) Ikeda T, Suzuki Y and Maeda T. 2013. Relationships between menstrual symptoms, lifestyle, habit, and cold sensitivity in high school students. *Jpn J Maternal Health* 53: 487-496.

10) Nakamura S. 2010. “Sensitivity to cold”: a concept analysis. *J Jpn Acad Nurs Sci* 30: 62-71.

11) UnnoT, Akashi N, Makino S, Ohira T and Kayahara T. 2012. Effects of Capsinoids-containing dietary supplements on sensation of cold constitution and physical and psychological complaints in female students. *Jpn Pharmacol Ther* 40: 1011-1018.

12) Natsuno T and Hirayanagi K. 2009. The Effect of ginger extract intake on energy consumption in young women with the feeling of chilliness. *Ergonomics* 45: 236-241.

13) Yamada N, Nishihara C, Yoshimura H, Yamaguchi Y and Takagaki R. 2009. Effects of Piper longum L. on chills in Japanese young women: Time-dependent changes in skin surface temperature and its recovery rate following the exposure to mild cold stress. *Jpn J Psychopharmacol* 29: 7-15.

14) Yamashita-Yasuda A, Sadakiyo T, Mitsuzumi H and Kubota M. 2010. Improvement of cold symptom and other disorders by glucosyl hesperidin oral administration. *J Jpn Mibyou Assoc* 16: 6-16.

15) Yamada N and Yoshimura H. 2010. Effect of royal jelly on chills in Japanese young women. *J Jpn Soc Nutr Food Sci* 63: 271-278.

16) Tanasaki Y and Fukai K. 2016. Effectiveness of foot massage in alleviating the symptoms of elderly individuals with sensitivity to cold. *Jpn J Nurs Art Sci* 15: 124-134.

17) Takeda T, Sakaguchi S, Kuge H, Miyazaki J, Kojima Y, Sasaki K and Mori H. 2012. Effects of electro-acupuncture therapy to lower limbs on chilly constitution ('hie' symptoms) -Comparison by the presence or absence of vasomotor dysfunction-. *J Jpn Soc Balneol Climatol Phys Med* T75: 124-137.

18) Iio Y, Mizuno-Matsumoto Y, Yamana K and Suzui E. 2017. The improvement of cold sensitivity in young women through the use of breathing exercises. Jpn J Matern Health 58: 403-411.

19) Chomistek AK, Manson JE, Stefanick ML, Lu B, Sands-Lincoln M, Going SB, Garcia L, Allison MA, Sims ST, LaMonte MJ, Johnson KC, Eaton CB. 2013. The Relationship of sedentary behavior and physical activity to incident cardiovascular disease: results from the women's health initiative. J Am Coll Cardiol 61: 2346-2354.

20) Kyu HH, Bachman VF, Alexander LT, Mumford JE, Afshin A, Estep K, Veerman JL, Delwiche K, Iannarone ML, Moyer ML, Cercy K, Vos T, Murray CJ, Forouzanfar MH. 2016. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ 354: i3857. https://doi.org/10.1136/bmj.i3857

21) Nagashima K, Yoda T, Yagishita T, Taniguchi A, Hosono T and Kanosue K. 2002. Thermal regulation and comfort during a mild-cold exposure in young Japanese women complaining of unusual coldness. *J Appl Physiol* 92: 1029-1035.

22) Yamazaki F. 2015. The cutaneous vasoconstrictor response in lower extremities

during whole-body and local skin cooling in young women with a cold constitution. *J Physiol Sci* 65: 397-405.
23) Okada M, Uno M, Nagano E, Nomura Y, Ohira T, Sato S and Shimamoto T. 2005. The relation of cold-water loading thermography with physical findings and lifestyle habit among women who have a cold constitution. *Biomedical Thermology* 24: 44-50.
24) Nedergaard J, Bengtsson T and Cannon B. 2007. Unexpected evidence for active brown adipose tissue in adult humans. *Am J Physiol Endocrinol Metab* 293: E444-E452.
25) Yoneshiro T, Aita S, Matsushita M, Kameya T, Nakada K, Kawai Y and Saito M. 2011. Brown adipose tissue, whole-body energy expenditure, and thermogenesis in healthy adult men. *Obesity* 19: 13-16.
26) Nakamura K and Morrison SF. 2008. Preoptic mechanism for cold-defensive responses to skin cooling. *J Physiol* 586: 2611-2620.
27) Nakamura K and Morrison SF. 2008. A thermosensory pathway that controls body temperature. *Nat Neurosci* 11: 62-71.
28) Sadakata M and Yamada Y. 2007. Perception of foot temperature in young women with cold constitution: analysis of skin temperature and warm and cold sensation thresholds. *J Physiol Anthropol* 26: 449-457.
29) Almeida MC, Hew-Butler T, Soriano RN, Rao S, Wang W, Wang J, Tamayo N, Oliveira DL, Nucci TB, Aryal P, Garami A, Bautista D, Gavva NR, and Romanovsky AA. 2012. Pharmacological blockade of the cold receptor TRPM8 attenuates autonomic and behavioral cold defenses and decreases deep body temperature. *J Neurosci* 32: 2086-2099.
30) Yamazaki F and Sone R. 2017. Desensitization of menthol-activated cold receptors in lower extremities during local cooling in young women with a cold constitution. *J Physiol Sci* 67: 331-337. https://jps.biomedcentral.com/articles/10.1007/s12576-016-0488-6
31) Yamazaki F, Date Y and Sone R. 2018. Changes in thermal sensations and electroencephalography during local skin cooling -differences between males and females and effects of a cold constitution-. *Jpn J Biometeor* 55: 9-18. https://doi.org/10.11227/seikisho.55.9
32) Yamazaki F, Iiyama H, Iwata K, Kato M. 2019. Electroencephalogram characteristics

during local and whole-body skin cooling in women with a cold constitution. *Jpn J Biometeor* 56: 25-33. https://doi.org/10.11227/seikisho.56.25

33) Yamazaki F, Suehiro K, Mishiro S and Yoshimura H. 2019. Characteristics of resting electroencephalogram in women with a cold constitution. *Academic Arch Yamaguchi Pref Univ* 12: 17-24. (in Japanese) http://ypir.lib.yamaguchi-u.ac.jp/yp/1540

34) Ogata Y, Kaneko K, Goto K, Kono K and Yamamoto M. 2017. Physiological mechanism of Hiesho -Evaluation by cardiovascular and autonomic dynamics-. *Jpn J Nurs Art Sci* 15: 227-234. (*in Japanese*).

35) Yamazaki F, Kobayashi W, Suenaga M and Tsuchimoto K. 2022. Acute influence of mild cycle exercise on the cold sensory function in young women with an awareness of a cold constitution. *J Phys Fitness Sports Med* 11: 21-28. https://doi.org/10.7600/jpfsm.11.21

36) Yamazaki F. 2023. Acute effects of mild cycle exercise on thermal sensation and brain activity in cold-sensitive young women. *Adv Exerc Sports Physiol* 29: 13-18.

37) Kawagoe H, Takahashi K, Kawashima A and Ishikawa T. 2003. General survey of the chill. Basic data and frequency of chills according to the disease. *Diagnosis and Treatment* 91: 2293-2296 (*in Japanese*).

38) Tsuyushige Y, Hamamoto T, Fukumoto E, Lin T, Kawasaki H, Matsuura K, Yokota M, Liu W, Sonoda J, Hirotsu K, Hasegawa M and Yoshimura K. 2019. Relationship between physical activity and cold constitution in young women. *Academic Archives of Yamaguchi Pref Univ* 12: 123-129 (*in Japanese*).

39) Yamazaki F. 2020. Influence of a light exercise intervention for 3 months on coldness of the body, body composition and muscular strength in young women. *JMNE* 29: 33-37 (*in Japanese*).

40) Yamazaki F, Araki Y, Takuno S and Hamada A. 2021. Walking exercise intervention for 4 weeks mitigates cold symptoms in young women with a cold constitution. *J Phys Fitness Sports Med* 10: 255-262. https://doi.org/10.7600/jpfsm.10.255

41) Yamazaki F, Inoue K, Ohmi N and Okimoto C. 2023. A two-week exercise intervention improves cold symptoms and sleep condition in cold-sensitive women. *J Physiol Anthropol* 42: 22. https://doi.org/10.1186/s40101-023-00339-y

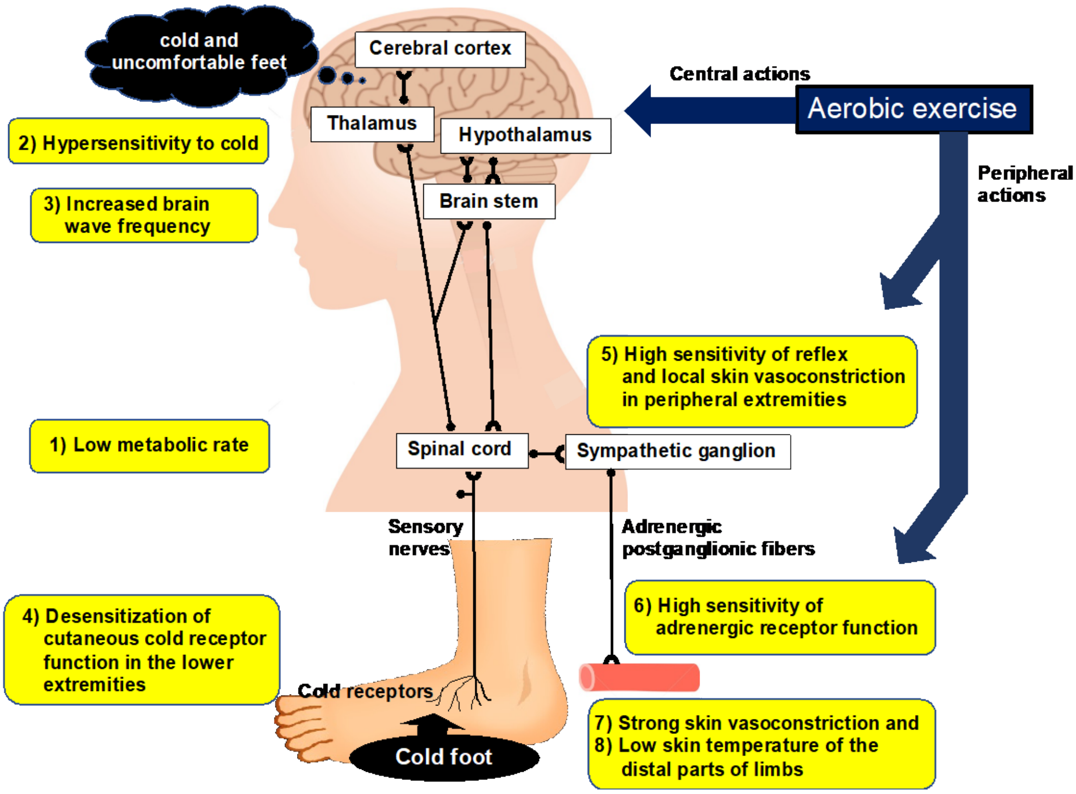

Fig. 1 Signal transduction pathways of cold sensation and cutaneous vasoconstriction and physiological characteristics of cold constitution. The main physiological characteristics of people with a cold constitution under normothermic conditions are: 1) low resting metabolic rate, 2) high sensitivity of cold sensory function, 3) high cerebral nerve activity expressed as low alpha wave power, 4) desensitization of cutaneous cold receptor function in the lower limbs, 5) high sensitivity of reflex and local skin vasoconstriction in the distal portion of the peripheral extremities, 6) high sensitivity of adrenergic receptor function in the skin of the lower limbs, 7) strong skin vasoconstriction of the distal parts of limbs, and 8) low skin temperature of the extremities. Aerobic exercise acts on the physiological mechanisms of cold constitution and alleviates cold symptoms through central and peripheral pathways.

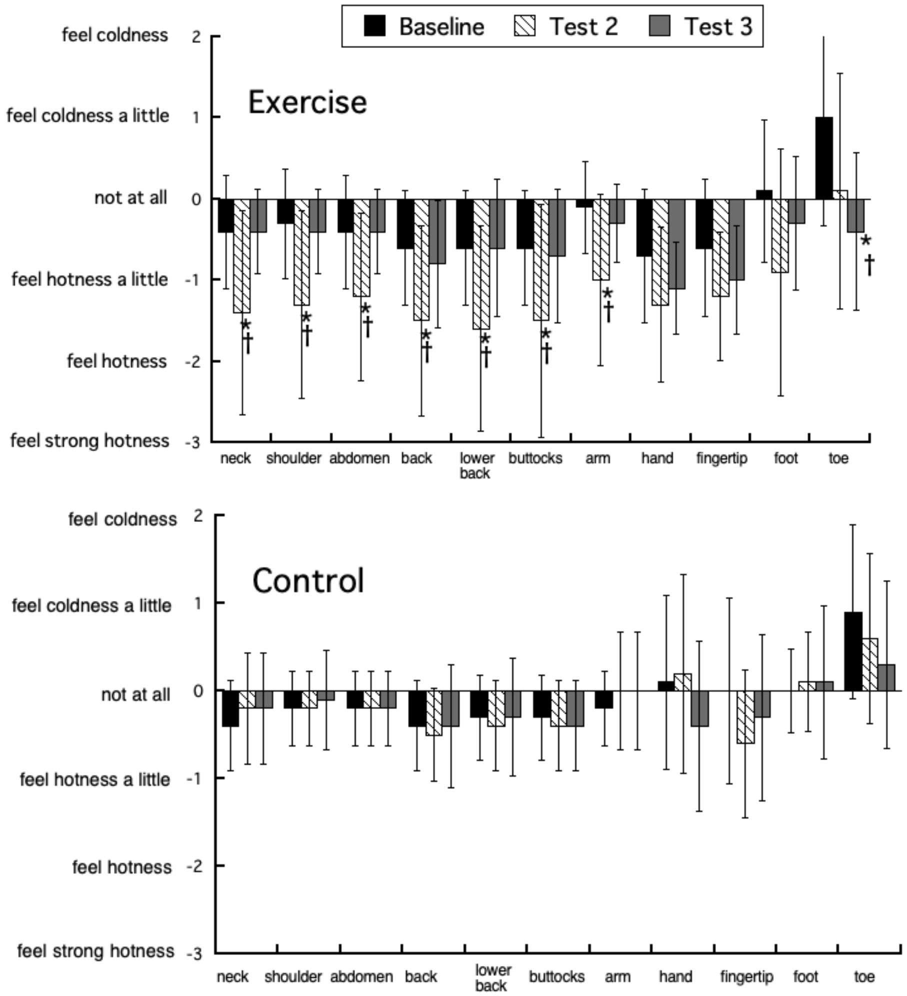

Fig. 2 Changes in thermal sensation of each body part in young women with a cold constitution[35]. In exercise experiment (upper panel), the measurements were performed 10 min before the start of cycle exercise for a total of 15 min (Baseline), immediately after exercise (Test 2), and 30 min after the end of exercise (Test 3). In control experiment (lower panel), the subjects maintained at rest without exercising. * $p < 0.05$ vs Baseline, † $p < 0.05$ vs Control condition.

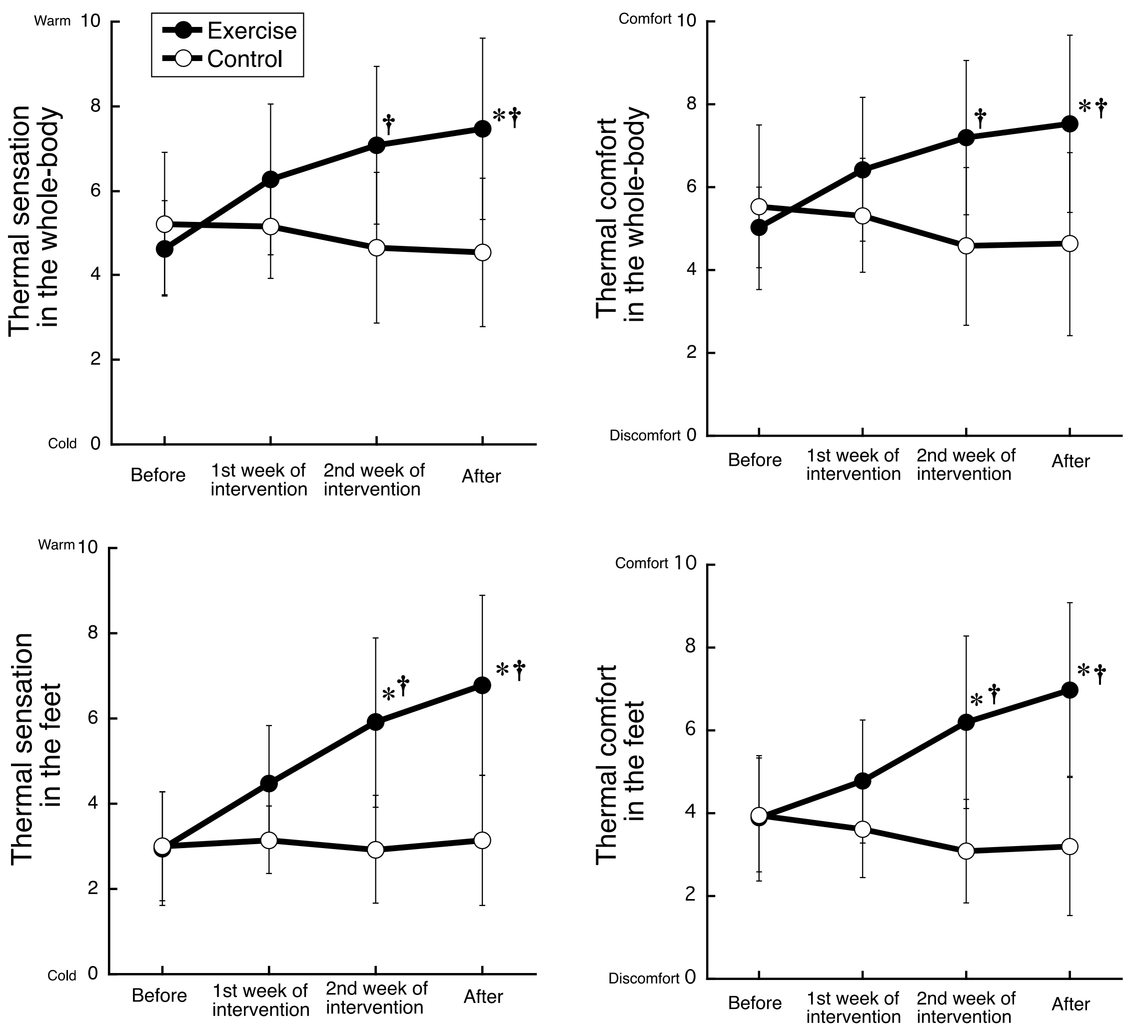

Fig. 3 Changes in thermal sensation and thermal comfort in the whole-body and feet with 2-week exercise or time-controlled interventions in young women with a cold constitution[41)]. The measurements were performed during rest in a room at 18°C. * $p < 0.05$ vs Before, † $p < 0.05$ vs. Control