



International Journal Of Scientific And University Research Publication

ISSN No **120/412**

Listed & Index with
ISSN Directory, Paris



Multi-Subject Journal



ASSOCIATIONS BETWEEN SENSITIVITY TO COLD, MENSTRUATION-RELATED SYMPTOMS AND HANDGRIP STRENGTH IN FEMALE UNIVERSITY STUDENTS IN JAPAN

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Sensitivity to cold, which is a popular symptom in Japanese women, is associated with various symptoms such as shoulder stiffness and general fatigue. However, an association of

sensitivity to cold with muscle strength has not been reported. The aim of the study was to clarify the associations of sensitivity to cold with handgrip strength and with menstruation-related symptoms in female university students in Japan. We recruited 278 female university students in Japan. Sensitivity to cold and menstruation-related symptoms including physical and psychological symptoms were assessed by using a self-administered questionnaire that we designed. Handgrip strength was measured by using a handgrip strength dynamometer. We received responses from 269 students. The prevalence rate of sensitivity to cold in the subjects was 54.3%. The students who had sensitivity to cold had a lower handgrip strength level (25.5 ± 3.8 kg) than did the students who did not have sensitivity to cold (26.7 ± 3.9 kg) ($p = 0.017$). Sensitivity to cold was associated with low body mass index. In addition, the students who had sensitivity to cold tended to have low back pain and constipation during menstruation. In conclusion, sensitivity to cold is an important symptom associated with muscle strength as well as menstruation-related symptoms for young women.

Sensitivity to Cold, Menstruation-Related Symptoms, Handgrip

مقدمة

We aimed to clarify the associations of sensitivity to cold with handgrip strength and with menstruation-related symptoms in female university students in Japan.

2. Methods

This study was designed as a cross-sectional study.

2.1. Procedure

First, we conducted a preliminary study in July 2019 to determine whether there are differences in the proportion of the subjects with sensitivity to cold and in levels of handgrip strength depending on the three phases of the menstrual cycle: luteal phase, menstrual phase and follicular phase. For preliminary study, the students completed a questionnaire for assessment of sensitivity to cold and measured their handgrip strength in the three menstrual phases over a period of one month. Among 19 female nursing students in Japan recruited, data for 8 students were eligible for analysis. It was found that the proportion of the subjects with sensitivity to cold and the levels of handgrip strength in these students were not significantly different depending on the menstrual cycle phase. Therefore, we decided to recruit subjects regardless of the phase of the menstrual cycle. We recruited 278 female university students from July to August in 2019. At the end of a lecture, we asked the students to complete a questionnaire and to measure their handgrip strength with guidance from researchers. The questionnaires were collected on the same day. Informed consent was obtained prior to participation in the study and the preliminary study. The study received approval from the Ethics Committee of Tokushima University Hospital (approval number: 3483).

2.2. Questionnaire

A self-administered questionnaire was designed by the researchers and it took about 10 minutes to complete. The first part consisted of questions about age, body height and weight, length and present phase of the menstrual cycle. Phases of the menstrual cycle include the luteal phase (21 to 25 days after the start of the last menstruation), menstrual phase (during menstruation) and follicular phase (2 to 4 days after the start of the last menstruation). The second part of the questionnaire consisted of questions about self-assessment of menstruation-related symptoms during menstruation including physical symptoms such as abdominal pain, headache, low back pain,

Autonomic thermoregulation in response to cold exposure differs in healthy individuals [1]. It has been suggested that cold hypersensitivity in the hands and feet is a symptom of sensation of cold in the extremities under conditions that would not typically evoke such a sensation [2]. In Japan, sensitivity to cold is defined as a state in which there exists a temperature range from core temperature to temperature of the extremities and there is slow recovery of the tip body temperature in a warm environment with the person usually having an awareness of cold sensation [3]. It has been reported that cold hypersensitivity in the hands and feet is common in East Asians, especially women [4]. Traditional herbal medicine has been used as an alternative approach for treatment of peripheral coldness, and improvement in peripheral coldness has been reported [5]. Peripheral coldness is thought to be a result of circulation failure caused by constriction of peripheral blood vessels. Various symptoms associated with sensitivity to cold, including shoulder stiffness, fatigue, neck stiffness, eyestrain, depressed mood and menstrual pain, have been reported [6]. Several studies have demonstrated that perceived sensitivity to cold in young students was associated with premenstrual symptoms [7] [8] and premenstrual dysphoric disorder [9]. Menstruation-related symptoms include not only physical symptoms but also psychological symptoms before and during menstruation. However, there have been few studies on the -association of sensitivity to cold in young women with menstruation related symptoms including physical and psychological symptoms during menstruation.

A decrease in heat production due to a loss of muscle volume and/or decrease in basal metabolism is considered to be one of the causes of sensitivity to cold [6]. It has been reported that sensitivity to cold was negatively correlated with amount of exercise and that amount of exercise had a positive correlation with handgrip strength level for children [10]. On the other hand, many studies have shown that handgrip strength level was associated with various diseases such as cardiovascular diseases, respiratory diseases and cancer [11] [12]. It has also been reported that lower handgrip strength was associated with psychological symptoms such as depression and anxiety [13] [14]. In a previous study, we showed that handgrip strength was associated with degree of depression and anxiety during menstruation in female university students in Japan [15]. However, the relationship between sensitivity to cold and handgrip strength has not been elucidated. Sensitivity to cold in young women may be associated with handgrip strength, which is one of the factors in the criteria for diagnosis of sarcopenia.

3. Results

The questionnaire was distributed to 278 students, and we received responses from 269 students (96.8%), which were used for analysis. The mean age ($\pm$ standard deviation: SD) of the participants was 20.0 (± 2.7) years.

3.1. Background Characteristics of the Subjects According to the Presence of Sensitivity to Cold

Among the 269 students, the proportion of students who had sensitivity to cold (sensitivity to cold group) and the proportion of students who did not have sensitivity to cold (non-sensitivity to cold group) were 146 (54.3%) and 123 (45.7%), respectively. As shown in Table 1, there were significant differences between the two groups in body weight ($p = 0.003$) and BMI ($p < 0.001$). There was a significant difference in the proportions of women with and those without sensitivity to cold among the three groups ($p = 0.024$) according to BMI (< 18.5 , $18.5 - 24.9$, ≥ 25). There was no association of sensitivity to cold with the menstrual cycle length or menstrual cycle phase.

3.2. Difference in Handgrip Strength between the Sensitivity to Cold Group and Non-Sensitivity to Cold Group

Mean ($\pm$ SD) handgrip strength in the sensitivity to cold group was 25.5 (± 3.8)

nausea, abdominal distension, constipation, diarrhea, getting tired easily, edema, sleepiness, rough skin, thirst and psychological symptoms such as increase in appetite, irritation, depression, loss of motivation and anxiety. The severity of each symptom was assessed using the following five degrees: no symptom, unrecognizable, bearable, unrecognizable if taking medication and affecting daily life. -The third part of the questionnaire consisted of questions on self assessment of sensitivity to cold. Based on Sakaguchi's criteria of sensitivity to cold [16] in a 24-item questionnaire, we used the following 22 statements: 1) I do not think that I am sensitive to cold, 2) I tend to be more sensitive than other people to cold, 3) I sometimes suffer because my entire body is cold, 4) I suffer because my back, hands and feet or some part of my body is cold, 5) I wear thick socks even in summer because my feet are cold, 6) Due to cold weather in winter, I always use an electric blanket, mattress or pocket warmer, 7) I suffer in air-conditioned rooms because my body feels cold, 8) I have been suffering from the cold for the last several years, 9) In winter, I use an electric blanket or mattress, 10) I do not like air conditioning, 11) Compared to others, my hands and feet are cold, 12) Even in summer, I prefer wearing thick socks, 13) I like to dress warmly, 14) Especially in winter, I tend to sleep curled up, 15) In winter and on cold days, I urinate more frequently, 16) Even in summer, I like hot drinks, 17) Compared to others, my face is more pale, 18) My body temperature does not normally go above 36°C, 19) On cold days, my joints become stiff or painful, 20) Even in summer, my hands and feet get cold, 21) My body sometimes suddenly becomes too warm or cold, and 22) My hands and feet always feel cold. A response of "Yes" or "No" was given to each of them. Participants were "sensitive to cold" if they answered "Yes" to more than two statements from the five important statements 2), 4), 7), 11), and 20) or if they answered "Yes" to one of the important statements and to more than two of the 7 reference statements 3), 5), 6), 8), 15), 17), and 22).

Background characteristics and handgrip strength of Table 1 the subjects according to the presence of sensitivity to cold.

Numbers are means $\pm$ standard deviation, and the Mann-Whitney U^a Number (%), statistical analysis^b test was used for statistical analysis. by the chi-square test.

kg and that in the non-sensitivity to cold group was 26.7 (± 3.9) (Table 1). The handgrip strength level in the sensitivity to cold kg group was significantly lower than that in the non-sensitivity to cold group ($p = 0.017$).

-3.3. Associations of Sensitivity to Cold with Menstruation Related Symptoms

There were significant associations between sensitivity to cold and physical menstruation-related symptoms including constipation ($p = 0.021$) and low back pain ($p = 0.004$), and there was a tendency for an association between sensitivity to cold and abdominal pain ($p =$ (Table 2). Regarding psychological symptoms, only anxiety 0.057) (Table 3).tended to be associated with sensitivity to cold ($p = 0.085$)

Instrument for Measuring Handgrip Strength

Handgrip strength dynamometer (GRIP-D, Takei K.K., Japan, Product No. T.K.K.5401) for handgrip strength according to the instructions for measurements were performed twice each with the left and right hands alternately. The mean value of the highest values of the forces of both hands was indicated on the display of the handgrip strength dynamometer.

2.4. Statistical Analysis

By using the criteria of sensitivity to cold that was based on the previous report [16], the subjects were divided into a sensitivity to cold group and a non-sensitivity group. Background characteristics of the participants including age, height, weight, body mass index (BMI) and handgrip strength were expressed as means and standard deviation (SD). Each categorized variable is expressed as number -with percentage. The answers for self-assessment of menstruation related symptoms during menstruation were divided into three groups depending on the degree of each symptom: no symptoms, mild symptoms (unrecognizable and bearable) and severe symptoms (unrecognizable if taking medication and affecting daily life). The Mann-Whitney U test was used for analysis of differences in age, height, weight, BMI and handgrip strength between the two groups (sensitivity to cold group and non-sensitivity to cold group). Comparisons of menstrual cycle, present phases of the menstrual cycle and intensity of each menstruation-related symptom between the two groups were performed by the chi-square test. All p values less than 0.05 were considered statistically significant. Statistical analyses were conducted using SPSS version 24 for Windows.

human body [20]. In skeletal muscle, detection of 10 different TRP channels has been reported [21]. Further study regarding the association of sensitivity of TRP channels for sensitivity to cold with skeletal muscle strength may be needed.

We showed that BMI and body weight, but not body height, in students with sensitivity to cold were lower than those in students without sensitivity to cold. Our results are consistent with the results of a previous study in young women in Japan [18]. Decrease in body weight may lead to decreases in subcutaneous and perivascular adipose tissues and subsequently increase the susceptibility to vasospastic events. It has been shown that perivascular adipose tissue altered the balance between endothelium-dependent vasodilator and vasoconstrictor substances [22], which further underlies the importance of BMI in the occurrence of Raynaud's phenomenon characterized by an episodic discoloration of the extremities in response to cold exposure. Blood circulatory failure due to abnormal balance in vessels may induce sensitivity to cold. However, in healthy female Libyans, it was reported that there were no correlations of body weight and BMI with cold pressor pain responses [23]. The reason for the difference in results is not clear. It has been reported that cold hypersensitivity in the hands and feet was associated with an increase in circulating adiponectin level, which affects thermogenesis during cold stress in women [24]. Further study on adipokines including adiponectin and leptin may be important.

-In our study, sensitivity to cold was associated with menstruation related symptoms including low back pain and constipation during menstruation and tended to have an association with abdominal pain. A previous study showed that women with sensitivity to cold have menstrual pain [6], but another study showed that women with sensitivity to cold did not have menstrual pain [18]. The difference in the results might be due to different criteria for sensitivity to cold. It was reported that sensitivity to cold was associated with back pain [18] [19] and constipation [6] regardless of menstruation. Since a number of TRP channels are expressed in nociceptive sensory neurons, pain might be closely related to sensitivity to cold. Associations of TRP channels with various diseases have been reported [25]. The difference in sensitivity of TRP channels may be related to the difference in symptoms in response to cold exposure. Sensitivity to cold may be associated with constipation since bowel movement is poor due to circulating blood flow failure. Sensitivity to cold may be associated with back pain and constipation regardless of the presence of menstruation. It has been reported that senior high school students who perceived sensitivity to cold had a higher odds ratio to have anxiety during menstruation than did students who did not perceive sensitivity to cold in an irregular menstruation group [7]. The reason for the associations of sensitivity to cold with psychological symptoms is not clear.

There was no association between sensitivity to cold and length of the menstrual cycle in this study, being in agreement with the results of previous studies [18]. Circulating gonadal hormones have been reported to mediate adaptation to cold pressor pain [26]. Estrogen deficiency might be related to sensitivity to cold since menopausal status was shown to be significantly related to sensitivity to cold [27]. In young women with regular menstruation, there has been no report regarding an association between sensitivity to cold and estrogen. -Given that basal body temperature in women increases in the mid luteal phase, we speculated that the proportion of the subjects with sensitivity to cold may differ depending on the phase of the menstrual cycle. However, no difference in the proportions of subjects with sensitivity to cold was found among the three menstrual cycle phases. Sensitivity to exogenous cold exposure may be different from endogenous body temperature in the subjects.

Sensitivity to cold in young women may influence their reproductive

. Associations of sensitivity to cold with degrees of Table 2 physical symptoms in menstruation-related symptoms.

Number (%), statistical analysis by the chi-square test. *Mild: unrecognizable and bearable, Severe: unrecognizable if taking medication and affecting daily life.

Table	Association
Table 1	Table 1
Table 2	Table 2
Table 3	Table 3
Table 4	Table 4
Table 5	Table 5
Table 6	Table 6
Table 7	Table 7
Table 8	Table 8
Table 9	Table 9
Table 10	Table 10
Table 11	Table 11
Table 12	Table 12
Table 13	Table 13
Table 14	Table 14
Table 15	Table 15
Table 16	Table 16
Table 17	Table 17
Table 18	Table 18
Table 19	Table 19
Table 20	Table 20
Table 21	Table 21
Table 22	Table 22
Table 23	Table 23
Table 24	Table 24
Table 25	Table 25
Table 26	Table 26
Table 27	Table 27
Table 28	Table 28
Table 29	Table 29
Table 30	Table 30
Table 31	Table 31
Table 32	Table 32
Table 33	Table 33
Table 34	Table 34
Table 35	Table 35
Table 36	Table 36
Table 37	Table 37
Table 38	Table 38
Table 39	Table 39
Table 40	Table 40
Table 41	Table 41
Table 42	Table 42
Table 43	Table 43
Table 44	Table 44
Table 45	Table 45
Table 46	Table 46
Table 47	Table 47
Table 48	Table 48
Table 49	Table 49
Table 50	Table 50
Table 51	Table 51
Table 52	Table 52
Table 53	Table 53
Table 54	Table 54
Table 55	Table 55
Table 56	Table 56
Table 57	Table 57
Table 58	Table 58
Table 59	Table 59
Table 60	Table 60
Table 61	Table 61
Table 62	Table 62
Table 63	Table 63
Table 64	Table 64
Table 65	Table 65
Table 66	Table 66
Table 67	Table 67
Table 68	Table 68
Table 69	Table 69
Table 70	Table 70
Table 71	Table 71
Table 72	Table 72
Table 73	Table 73
Table 74	Table 74
Table 75	Table 75
Table 76	Table 76
Table 77	Table 77
Table 78	Table 78
Table 79	Table 79
Table 80	Table 80
Table 81	Table 81
Table 82	Table 82
Table 83	Table 83
Table 84	Table 84
Table 85	Table 85
Table 86	Table 86
Table 87	Table 87
Table 88	Table 88
Table 89	Table 89
Table 90	Table 90
Table 91	Table 91
Table 92	Table 92
Table 93	Table 93
Table 94	Table 94
Table 95	Table 95
Table 96	Table 96
Table 97	Table 97
Table 98	Table 98
Table 99	Table 99
Table 100	Table 100

. Associations of sensitivity to cold with degrees of Table 3 psychological symptoms in menstruation-related symptoms.

Number (%), statistical analysis by the chi-square test. *Mild: unrecognizable and bearable, Severe: unrecognizable if taking medication and affecting daily life.

Table	Association
Table 1	Table 1
Table 2	Table 2
Table 3	Table 3
Table 4	Table 4
Table 5	Table 5
Table 6	Table 6
Table 7	Table 7
Table 8	Table 8
Table 9	Table 9
Table 10	Table 10
Table 11	Table 11
Table 12	Table 12
Table 13	Table 13
Table 14	Table 14
Table 15	Table 15
Table 16	Table 16
Table 17	Table 17
Table 18	Table 18
Table 19	Table 19
Table 20	Table 20
Table 21	Table 21
Table 22	Table 22
Table 23	Table 23
Table 24	Table 24
Table 25	Table 25
Table 26	Table 26
Table 27	Table 27
Table 28	Table 28
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Table 30	Table 30
Table 31	Table 31
Table 32	Table 32
Table 33	Table 33
Table 34	Table 34
Table 35	Table 35
Table 36	Table 36
Table 37	Table 37
Table 38	Table 38
Table 39	Table 39
Table 40	Table 40
Table 41	Table 41
Table 42	Table 42
Table 43	Table 43
Table 44	Table 44
Table 45	Table 45
Table 46	Table 46
Table 47	Table 47
Table 48	Table 48
Table 49	Table 49
Table 50	Table 50
Table 51	Table 51
Table 52	Table 52
Table 53	Table 53
Table 54	Table 54
Table 55	Table 55
Table 56	Table 56
Table 57	Table 57
Table 58	Table 58
Table 59	Table 59
Table 60	Table 60
Table 61	Table 61
Table 62	Table 62
Table 63	Table 63
Table 64	Table 64
Table 65	Table 65
Table 66	Table 66
Table 67	Table 67
Table 68	Table 68
Table 69	Table 69
Table 70	Table 70
Table 71	Table 71
Table 72	Table 72
Table 73	Table 73
Table 74	Table 74
Table 75	Table 75
Table 76	Table 76
Table 77	Table 77
Table 78	Table 78
Table 79	Table 79
Table 80	Table 80
Table 81	Table 81
Table 82	Table 82
Table 83	Table 83
Table 84	Table 84
Table 85	Table 85
Table 86	Table 86
Table 87	Table 87
Table 88	Table 88
Table 89	Table 89
Table 90	Table 90
Table 91	Table 91
Table 92	Table 92
Table 93	Table 93
Table 94	Table 94
Table 95	Table 95
Table 96	Table 96
Table 97	Table 97
Table 98	Table 98
Table 99	Table 99
Table 100	Table 100

4. Discussion

In our survey, the prevalence rate of sensitivity to cold for female university students was 54%. The prevalence rates for female university students in previous studies were 42.3% [17], 69.1% [18] and 68.9% [8]. It has been reported that mild sensitivity to cold in hands and feet occurs in 49% and severe sensitivity occurs in 35% of Japanese women respectively [19]. Since the definition of sensitivity to cold has not been well established, there is variation in the reported prevalences.

In this study, we found that the students who have sensitivity to cold tended to have weak handgrip strength. This result is similar with the results that handgrip strength was correlated with amount of exercise and negatively correlated with sensitivity to cold [10]. Therefore, an appropriate amount of physical activity for increasing muscle strength might be needed to prevent sensitivity to cold. Transient receptor potential melastatin 8 (TRPM8) is widely distributed in the

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health in the future since female infertility [28], abnormalities of delivery [29] and menopausal symptoms [30] have been reported in women who had sensitivity to cold. Low handgrip strength related to sensitivity to cold may lead to sarcopenia and dynapenia in the future. Improvement of sensitivity to cold is important for young women to solve lifelong problems.

This study has several limitations. There was not sufficient evidence for a causal relationship since this study was a cross-sectional design. We used questions to clarify the presence of sensitivity to cold based on the criteria of Sakaguchi. Further study using objective assessment of sensitivity to cold is needed. The study subjects were limited to nursing students at a university in Japan. Thus, a future study needs to target various kinds of women at various ages.

استنتاج

More than half of the university female students in this study had sensitivity to cold, which was associated with low back pain and constipation during menstruation and with handgrip strength level. Sensitivity to cold is an important symptom associated with muscle strength as well as menstruation related symptoms for young women.

Acknowledgements

The authors would like to thank the participants in this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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