Short- and Long-Term Exposure to Higher Temperatures is Linked to Cognitive Impairment in Taiwanese Older Adults

Wei-Peng Su
National Defense Medical Center

Yuan-Ting C. Lo
National Defense Medical Center

Shu-Hsuan Mei
National Defense Medical Center

Yu-Hung Chang
China Medical University

Han-Bin Huang (toly2000@gmail.com)
National Defense Medical Center  https://orcid.org/0000-0002-6827-7087

Research article

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Abstract

Background: Evidence on the associations between short-term and long-term air temperature exposure and cognitive function in older adults, particularly those in Asia, is limited. Therefore, we explored the relationships of short-term and long-term air temperature exposure with cognitive function in Taiwanese older adults through a repeated measures survey.

Methods: We used data from between 1996 and 2007 from the ongoing Taiwan Longitudinal Study on Aging (N = 1956), a multiple-wave nationwide survey. Participants’ cognitive function assessment was based on the Short Portable Mental Status Questionnaire. We calculated the temperature moving average (TMA) for temperature exposure windows between 1993 and 2007 using data from air quality monitoring stations, depending on the administrative zone of each participant’s residence. Generalized linear mixed models were used to examine the effects of short-term and long-term temperature changes on cognitive function.

Results: Short-term and long-term temperature exposure was significantly and positively associated with moderate-to-severe cognitive impairment, with the greatest increase in odds ratios (ORs) found for 3-year TMAs (OR = 1.247; 95% confidence interval [CI]: 1.107, 1.404). The higher the quintiles of temperature exposure were, the higher were the ORs. The strongest association found was in long-term TMA exposure (OR = 3.674; 95% CI: 2.103, 6.417) after covariates were controlled for.

Conclusions: The risk of mild cognitive impairment increased with ambient temperature in community-dwelling older adults in Taiwan.

Background

According to the Intergovernmental Panel on Climate Change, estimated annual average temperatures increased by 0.78 °C (95% confidence interval [CI]: 0.72 to 0.85 °C) between the 1850–1900 and 2003–2012 periods [1]. Although the global human health burden of climate change is not well quantified, morbidity and mortality rates related to temperatures, particularly heat effects, have been reported [2].

Older adults with mild cognitive impairment (MCI) are at an increased risk of developing Alzheimer disease or other forms of dementia [3]. An estimated 40–60% of individuals aged 58 years and over with MCI have an underlying AD pathology [4]. Thus, MCI is an intermediate stage in the trajectory from normal cognition to dementia [5, 6]. Cognitive decline in older adults is associated with poor health outcomes (e.g., falls, congestive heart failure, and mortality) and higher utilization rates of hospital and nursing homes [7–11].

In experimental studies, exposure to passive heat stress at a temperature of approximately 50 °C and passive cold stress at temperatures below 10 °C impaired cognitive function in younger or older adults [12–14]. However, several epidemiological studies have not indicated any temperature-related changes in cognitive function [14, 15]. A previous study revealed a U-shaped association at lag 1 day between residential air temperature and poor cognitive function among older adults in the United States [16]. However, whether this pattern or association exists in Asian older adults is unclear, as is the association of cognitive function with temperature, particularly different exposure windows for temperature. Thus, we investigated the associations of short-term and long-term air temperature exposure with cognitive function in community-dwelling older adults in Taiwan.

Methods
Study participants

The Taiwan Longitudinal Study on Aging (TLSA), an ongoing prospective longitudinal study with a nationally representative sample of 4049 participants aged 60 years or over, was established in 1989 by the Health Promotion Administration of the Ministry of Health and Welfare. It has a three-stage equal probability sampling design, and the initial sample had a survey response rate of 92% [17]. Participants were administered questionnaires by trained interviewers at baseline as well as in follow-up surveys in 1996, 1999, 2003, and 2007, for which the response rates were 92%, 91%, 89%, 90%, and 91%, respectively [17]. Participants provided verbal consent in all survey years before 2007, and the Health Promotion Administration obtained written consent in 2007. We used TLSA data between 1996 and 2007. The inclusion criteria were as follows: being aged 65 years or older, having completed a cognitive test, having no cognitive impairment, having no history of stroke, and not moving house during the study period. Participant numbers in 1996, 1999, 2003, and 2007 were 1956, 1700, 1248, and 876, respectively. This study was approved by the Institutional Review Board of the Tri-Service General Hospital (No. 2-104-05-153).

Cognitive function assessment

Participant cognitive function was assessed using the Short Portable Mental Status Questionnaire (SPMSQ), which was validated by a Chinese version of the Mini-Mental State Examination [18] and has been used elsewhere [19–21]. The Cronbach’s alpha value of the SPMSQ was 0.63. Participants were asked five questions: (1) “What is today’s date (month, day, and year)?” (2) “What is the day of the week?” (3) “What is your home address?” (4) “Where are you?” and (5) “How old are you?” In addition, they were asked to subtract 3 from 20 over four consecutive repetitions. One point was given for each correct answer, and the total score ranged from 0 to 5. In consideration of the ceiling effect of the SPMSQ, we dichotomized the SPMSQ scores for the analysis of cognitive impairment risk. An SPMSQ score of < 3 was used to identify individuals with moderate-to-severe cognitive impairment [19, 22].

Environmental assessment of air temperature

Hourly temperature data (in °C) were obtained from 75 monitoring stations on Taiwan's main island, which were established by the Taiwan Environmental Protection Administration (TEPA) in or after 1993 [23]. The data were subjected to rigorous quality assurance and control procedures through independent projects. The TEPA authorized an independent private sector organization to perform annual performance audits and regular performance checks of monitoring instruments. The daily mean temperature obtained from each station was included for analysis. The daily mean temperatures from monitoring stations within the same city or county were assigned to participants living in the same city or county [24]. If a city or county had more than one monitoring station, the data were averaged. We calculated the temperature moving averages (TMAs) over periods of 7, 14, 21, 30, 60, and 90 days and 3 years prior to each participant’s interview date.

Statistical analysis

We summarized the participant characteristics by survey year and the ambient temperature distribution during the study period. In consideration of the ceiling effect of SPMSQ, we dichotomized the SPMSQ scores for the analysis of cognitive impairment risk. An SPMSQ score of < 3 was used to identify individuals with moderate-to-severe
cognitive impairment, as described previously [19, 22]. We applied generalized linear mixed models fitted using the PROC GLIMMIX procedure in SAS software (SAS Institute Inc., Cary, NC, USA) to accomplish two goals: to explore the relationship between cognitive function and exposure to temperature, which was modeled as a binary outcome (on the basis of SPMSQ scores of < 3 for moderate-to-severe cognitive impairment), and to account for random effects of repeated measures. We examined temperature exposure windows between 7 days and 3 years prior to the participants’ interview dates to assess the effect of short-term and long-term temperature exposure on cognitive function.

Furthermore, we adjusted for the following covariates measured at each visit: age, sex, educational level, marital status, (self-reported) current financial status, smoking, alcohol consumption, physical activity, scores for instrumental activities of daily living (IADLs), and season (spring: March through May, summer: June through August, fall: September through October, winter: December through February). Covariate selection was based on the following criteria: (1) being associated with exposure and outcome and not being intermediate variables between exposure and outcome [25], and (2) having a change-in-estimate criterion of ≥ 10% [26]. To examine nonlinear associations between ambient temperature and cognitive function, we divided ambient temperature into quintiles. To adjust for additional variables, namely hypertension, diabetes, air conditioning, and air pollutant exposure (e.g., PM$_{10}$ and O$_3$ levels), we conducted a sensitivity analysis. All analyses were performed using SAS software version 9.3 of the SAS System for Unix (SAS Institute Inc.), and the level of significance was set at $p < 0.05$.

**Results**

**Demographic characteristics**

Table 1 presents the demographic characteristics of the participants between 1996 and 2007. At baseline, participants had a mean age of 73 years, and 59.9% were men. Most of the participants were married. Only 12.5% had a high school degree, and approximately 40% considered their financial status to be fair. Higher rates of regular physical activity, nonconsumption of alcohol, nonsmoking status, and absence of hypertension and diabetes were observed. In total, 4.9% of participants had SPMSQ scores of < 3, and the mean IADL score was 1.81. In 2007, the demographic characteristics were similar, but participants were older (mean age 82.29 years). The rates of hypertension and diabetes were higher in 2007 than in 1996. In total, 18.2% of participants had SPMSQ scores of < 3, and the mean IADL score was 4.13.
## Table 1
Participants’ demographic characteristics by survey year.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Year 1996 (n = 1956)</th>
<th>Year 1999 (n = 1700)</th>
<th>Year 2003 (n = 1248)</th>
<th>Year 2007 (n = 876)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1,172 (59.9)</td>
<td>998 (58.7)</td>
<td>727 (58.3)</td>
<td>464 (53.0)</td>
</tr>
<tr>
<td>Age, y, mean ± SD</td>
<td>73.44 ± 4.91</td>
<td>76.10 ± 4.69</td>
<td>78.64 ± 4.05</td>
<td>82.29 ± 3.76</td>
</tr>
<tr>
<td>Spouse, yes, n (%)</td>
<td>1,233 (63.0)</td>
<td>1,007 (59.2)</td>
<td>673 (53.9)</td>
<td>403 (46.0)</td>
</tr>
<tr>
<td>Personal education, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>664 (33.9)</td>
<td>555 (32.6)</td>
<td>379 (30.4)</td>
<td>285 (32.5)</td>
</tr>
<tr>
<td>Primary and secondary school</td>
<td>1,047 (53.5)</td>
<td>928 (54.6)</td>
<td>689 (55.2)</td>
<td>461 (52.6)</td>
</tr>
<tr>
<td>High school and above</td>
<td>245 (12.5)</td>
<td>217 (12.8)</td>
<td>180 (14.4)</td>
<td>130 (14.8)</td>
</tr>
<tr>
<td>Self-reported financial status, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>very satisfied</td>
<td>163 (8.30)</td>
<td>125 (7.40)</td>
<td>71 (5.70)</td>
<td>47 (5.40)</td>
</tr>
<tr>
<td>Satisfied</td>
<td>655 (33.5)</td>
<td>562 (33.1)</td>
<td>515 (41.3)</td>
<td>365 (41.7)</td>
</tr>
<tr>
<td>Fair</td>
<td>843 (43.1)</td>
<td>678 (39.9)</td>
<td>427 (34.2)</td>
<td>310 (35.4)</td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>243 (12.4)</td>
<td>250 (14.7)</td>
<td>180 (14.4)</td>
<td>117 (13.4)</td>
</tr>
<tr>
<td>Very dissatisfied</td>
<td>52 (2.70)</td>
<td>85 (5.00)</td>
<td>55 (4.40)</td>
<td>37 (4.20)</td>
</tr>
<tr>
<td>Physical activity, n (%)</td>
<td>1,164 (59.5)</td>
<td>1,099 (64.6)</td>
<td>844 (67.6)</td>
<td>591 (67.5)</td>
</tr>
<tr>
<td>Smoking status, n (%)</td>
<td>542 (27.7)</td>
<td>401 (23.6)</td>
<td>231 (18.5)</td>
<td>107 (12.2)</td>
</tr>
<tr>
<td>Alcohol consumption, n (%)</td>
<td>381 (19.5)</td>
<td>380 (22.4)</td>
<td>265 (21.2)</td>
<td>170 (19.4)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>512 (26.2)</td>
<td>634 (37.3)</td>
<td>540 (43.3)</td>
<td>407 (46.5)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>192 (9.80)</td>
<td>254 (14.9)</td>
<td>203 (16.3)</td>
<td>121 (13.8)</td>
</tr>
<tr>
<td>MMSE score (0–5), mean ± SD</td>
<td>4.50 ± 0.87</td>
<td>4.47 ± 0.90</td>
<td>4.23 ± 1.02</td>
<td>3.75 ± 1.33</td>
</tr>
<tr>
<td>&lt; 3, n (%)</td>
<td>95 (4.90)</td>
<td>93 (5.50)</td>
<td>93 (7.50)</td>
<td>159 (18.2)</td>
</tr>
<tr>
<td>≥ 3, n (%)</td>
<td>1,861 (95.1)</td>
<td>1,607 (94.5)</td>
<td>1,155 (92.5)</td>
<td>717 (81.8)</td>
</tr>
<tr>
<td>IADL score (0–18), mean ± SD</td>
<td>1.81 ± 3.49</td>
<td>2.27 ± 3.91</td>
<td>3.10 ± 4.42</td>
<td>4.13 ± 5.04</td>
</tr>
</tbody>
</table>

### Short- and long-term TMAs

Significant increasing trends in short-term mean and median temperatures between 1996 and 2007 were observed ($p < 0.001$). The 7-day TMAs in 1996 (mean 19.57 °C; median 19.31 °C) were higher than those in 2007 (mean 27.69 °C; median 27.76 °C). The 3-year TMAs (mean 22.38 °C; median 22.16 °C) in 1996 were higher than those in 2007 (mean 22.38 °C; median 21.33 °C) in 2007 (Table 2).
Table 2
Short- and long-term temperature moving averages.

<table>
<thead>
<tr>
<th>Temperature Moving Average (°C)</th>
<th>Year 1996 (n = 1,956)</th>
<th>Year 1999 (n = 1,700)</th>
<th>Year 2003 (n = 1,248)</th>
<th>Year 2007 (n = 876)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD (Q1, Q3)</td>
<td>Mean ± SD (Q1, Q3)</td>
<td>Mean ± SD (Q1, Q3)</td>
<td>Mean ± SD (Q1, Q3)</td>
<td></td>
</tr>
<tr>
<td>7 days</td>
<td>19.57 ± 0.95 (18.97, 20.49)</td>
<td>20.83 ± 1.83 (19.07, 22.11)</td>
<td>24.50 ± 2.87 (22.92, 26.83)</td>
<td>27.69 ± 2.20 (26.04, 29.25)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>14 days</td>
<td>20.55 ± 1.39 (19.46, 22.16)</td>
<td>21.50 ± 1.82 (19.79, 22.67)</td>
<td>24.87 ± 2.84 (23.32, 27.18)</td>
<td>27.41 ± 2.12 (26.09, 28.82)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>21 days</td>
<td>20.23 ± 1.67 (18.82, 22.06)</td>
<td>21.37 ± 1.99 (19.40, 22.60)</td>
<td>25.21 ± 2.81 (23.67, 27.52)</td>
<td>27.12 ± 2.23 (25.81, 28.55)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>30 days</td>
<td>19.67 ± 1.84 (18.13, 21.58)</td>
<td>20.93 ± 2.13 (18.82, 22.27)</td>
<td>25.59 ± 2.76 (23.98, 27.88)</td>
<td>26.75 ± 2.37 (25.19, 28.35)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>60 days</td>
<td>19.59 ± 1.93 (17.82, 21.32)</td>
<td>19.96 ± 1.79 (18.34, 20.96)</td>
<td>26.61 ± 2.51 (25.65, 28.35)</td>
<td>25.45 ± 2.58 (23.53, 27.39)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>90 days</td>
<td>18.39 ± 1.89 (16.60, 19.82)</td>
<td>19.14 ± 1.71 (17.68, 19.95)</td>
<td>27.40 ± 2.18 (26.63, 28.88)</td>
<td>24.23 ± 2.55 (22.25, 25.96)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3 years</td>
<td>22.38 ± 1.12 (21.33, 23.40)</td>
<td>23.04 ± 1.14 (21.95, 23.77)</td>
<td>23.75 ± 0.84 (22.92, 24.67)</td>
<td>24.23 ± 0.90 (23.58, 24.98)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Table 3
Crude and adjusted associations between temperature exposure (each 1 °C) and cognitive function (n = 5780).

<table>
<thead>
<tr>
<th>Temperature Moving Average (°C)</th>
<th>SPMSQ &lt; 3 OR (95% CI)</th>
<th>SPMSQ &lt; 3 AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 days</td>
<td>1.321 (1.255,1.390)</td>
<td>1.079 (1.038, 1.121)</td>
</tr>
<tr>
<td>14 days</td>
<td>1.352 (1.277,1.432)</td>
<td>1.082 (1.037, 1.129)</td>
</tr>
<tr>
<td>21 days</td>
<td>1.335 (1.262,1.411)</td>
<td>1.072 (1.029, 1.117)</td>
</tr>
<tr>
<td>30 days</td>
<td>1.315 (1.247,1.387)</td>
<td>1.063 (1.023, 1.105)</td>
</tr>
<tr>
<td>60 days</td>
<td>1.277 (1.215,1.343)</td>
<td>1.048 (1.010, 1.087)</td>
</tr>
<tr>
<td>90 days</td>
<td>1.228 (1.175,1.282)</td>
<td>1.033 (1.000, 1.067)</td>
</tr>
<tr>
<td>3 years</td>
<td>2.708 (2.213,3.315)</td>
<td>1.247 (1.107, 1.404)</td>
</tr>
</tbody>
</table>

AOR: adjusted odds ratios (for age, sex, educational level, marital status, current financial status, smoking, alcohol consumption, physical activity, scores for instrumental activities of daily living, and season).

Relationship of short-term and long-term temperature exposure with cognitive function

Both the crude and adjusted models revealed significant and positive associations of short-term (7-, 14-, 21-, 30-, 60-, and 90-day) and long-term (3-year) TMAs with moderate-to-severe cognitive impairment. A 1 °C-increase in TMA was significantly and positively associated with moderate-to-severe cognitive impairment after adjustment for covariates, with the greatest increase in odds found for 3-year exposure (OR = 1.247; 95% CI: 1.107, 1.404). To examine the nonlinear associations between air temperature and cognitive function, we grouped the quintiles of temperatures from different exposure windows. Compared with the that for quintile 1, the TMA for quintile 5 in the short term (over 7, 14, 21, 30, 60, and 90 days) was significantly positively associated with moderate-to-severe cognitive impairment. The strongest association observed was for long-term (3-year) exposure (OR = 3.674; 95% CI: 2.103, 6.417) after all potential covariates were controlled for (Fig. 1 and Table S1). In addition, we noted a monotonic trend of temperature over all but the 90-day exposure windows and cognitive function. In the sensitivity analysis, we further adjusted for hypertension, diabetes, and air conditioning in 1996, and exposure to air pollutants from the same exposure window (e.g., PM$_{10}$ and O$_3$), and the same patterns were observed (Table S2).

Discussion

We observed significant and positive associations between short-term and long-term temperature exposure and moderate-to-severe cognitive impairment. In particular, long-term exposure to higher-quintile temperatures was significantly associated with higher risks of cognitive impairment among older adults. The results suggest that exposure to higher temperatures may impair cognitive function among community-dwelling, free-living older adults.
In a study by [12], 16 middle-aged participants performed cognitive tests on attention and working memory in control, hot (room temperature of 50 °C), or hot head cool (hot condition with application of cold packs to the head) conditions. Compared with those in the control condition, participants in the hot condition had a significant decline in working memory. Another study indicated that young adults in non–air-conditioned buildings experienced reduction in cognitive function on working memory and selective attention or processing speed [13]. Further, another study revealed that higher-temperature environments could negatively affect productivity in participants with a mean age of 23 years [27]. Even short-term exposure to hot temperatures impaired cognitive function in participants with a mean age of 31 years [28]. Most relevant research focuses on young people rather than on older adults. In a longitudinal cohort study of older men, short-term exposure to higher air temperatures was significantly associated with low scores on the Mini-Mental State Examination [16]. Our finding of an association between short-term exposure to higher temperatures and moderate-to-severe cognitive impairment in community-dwelling older adults was consistent with those of other studies. In addition, in the present study, long-term exposure to higher temperatures affected participant cognitive function. Further large-scaled studies are required to confirm this finding.

Studies have demonstrated that short-term exposure to acute low temperature leads to a decline in cognitive function in young adults [29–31] as well as in older adults [16]. However, we did not observe this association. This may be because our study was conducted in Taiwan, where the climate is subtropical to tropical and acute low temperatures are rare.

Several possible mechanistic and observational theories may explain cognitive alterations induced by high air temperatures. A study reported an association between warmer outdoor temperatures and worse cognitive status in patients with multiple sclerosis [32]. In another study by [33], functional magnetic resonance imaging revealed greater blood-oxygen-level-dependent activation within frontal/dorsolateral prefrontal and parietal regions of the brains of patients with multiple sclerosis, indicating reduced neurological function. This was not found in healthy controls. Human body temperature also affects the function of the hippocampal gyrus, which plays an essential role in brain functions such as learning and memory. Warm temperatures activate transient receptor potential vanilloid 4, a temperature-sensitive channel. Increased physiological temperature activates and controls the activity of hippocampal neurons [34, 35]. This channel parallels the behavior of the corresponding afferent sensory fibers [36]. A plausible explanation for the negative association of heat stress with cognitive function is that it increases levels of plasma serotonin, which inhibits the production of dopamine, a neurotransmitter involved in complex task performance [14].

Our study had several limitations. First, the air temperatures in the study setting are much higher than those in relevant studies; therefore, observing whether lower air temperatures negatively affect cognitive function was challenging. Second, data on exact air temperatures from participants’ specific locations could not be collected. The air temperatures we used were outdoor air temperatures recorded by monitoring stations that were matched to each participant’s city or county. This could have caused misclassification in temperature exposure. However, this likely had a limited impact on our results because our estimations of individual exposures to air temperature from monitoring station data were equivalent to those from spatiotemporal modeling [37]. Third, as in all longitudinal studies of aging, our sample size diminished because of participants’ development of diseases and mortality at older ages, potentially affecting the results [38]. Fourth, several exposure variables, such as noise, were not considered; this could also have influenced the results.
Fifth, the fact that the SPMSQ, rather than clinical diagnosis, was used for the cognitive function assessment could restrict our findings. Although is the SPMSQ a valid and reliable instrument for identifying cognitive impairment, it is unlikely to identify subtle deficits [39]. Nevertheless, the measures we used evaluated working memory and orientation, for which deficits may reflect cognitive loss [20, 40, 41].

The principal strengths of our study were that the sample was nationally representative [42], and that potential confounders were accounted for in assessing the association between short- and long-term temperature exposure and cognitive function.

**Conclusions**

In a nationally representative sample of Taiwanese older adults, short-term and long-term exposure to higher ambient temperatures were associated with risks of MCI. Moreover, a monotonic trend of air temperature exposure and cognitive function was observed. Thus, mitigating the effects of high temperature stress on the health of vulnerable populations such as older adults is advised.

**Declarations**

**Acknowledgements**

We are grateful for the data provided by the Health and Welfare Data Science Center (HWDC) and the Survey Research Data Archive, Academia Sinica.

**Declaration of Sources of Funding**

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**Availability of data and materials**

The data were used under license from the Health and Welfare Data Science Center (HWDC) and the Survey Research Data Archive, Academia Sinica, Taiwan and under their rules of data protection for the current study, and thus not publicly available.

**Ethics approval and consent to participate**

This study was approved by the Institutional Review Board of the Tri-Service General Hospital (No. 2-104-05-153). Participants provided verbal consent in all survey years before 2007, and the Health Promotion Administration (Taiwan) obtained written consent in 2007.

**Author Contribution**

Conceived and designed the experiments: HBH. Analyzed the data: WPS, YTCL, SHM, HBH. Wrote the paper: YTCL, WPS, HBH. Contributed to critical revision of the manuscript: YTCL, YHC, HBH. All authors read and approved the final manuscript.

**Consent for publication**
Not applicable.

**Competing Interests**

The authors declare no competing interests.

**References**

   *Climate change 2013: The physical science basis*, vol. 1535. Cambridge, UK: Cambridge University Press; 2013.


17. Taiwan Longitudinal Study on Aging (TLSA)._Response Rate [https://www.hpa.gov.tw/EngPages/Detail.aspx?nodeid=1077&pid=6197]


35. Shibasaki K: **TRPV4 activation by thermal and mechanical stimuli in disease progression.** *Laboratory investigation; a journal of technical methods and pathology* 2020, 100(2):218-223.


