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Research Article

Personal-level exposure to environmental temperature is a superior predictor of endothelial-dependent vasodilatation than outdoor-ambient level

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Abstract

Environmental temperatures influence cardiovascular physiology. However, the majority of time is spent indoors, making outdoor-ambient temperatures inaccurate estimates of true exposures encountered by most individuals. We evaluated in 50 healthy adults the associations between previous 7-day outdoor-ambient (four occasions) and prior 24-hour personal-level (two occasions) environmental temperature exposures with blood pressure, heart rate variability, sleep parameters, and endothelial-dependent vasodilatation (brachial flow-mediated dilatation [FMD]) using generalized estimating equations. Participants (34 females; age, 32.1 ± 9.6 years) had normal blood pressures (107.8 ± 13.3/70.2 ± 9.4 mm Hg), FMD (7.4 ± 2.8%), as well as sleep and heart rate variability parameters. Mean 7-day outdoor-ambient (4.6 ± 9.7°C) differed from personal-level temperature exposures (22.0 ± 3.0°C). Colder outdoor-ambient temperatures (per −10°C) over the previous 1–6 days (rolling averages) were associated with decreases in FMD: −0.57% (95% confidence interval [CI]: −1.14% to 0.01%, $P = .055$) to −0.62% (95% CI: −1.07% to −0.18%, $P = .006$). However, a 10°C decrease in personal-level temperature during the prior 24 hours was associated with a greater decrement in FMD: −2.44% (95% CI: −4.74% to −0.13%, $P = .038$). Both were also linearly related to FMD during all seasons and without a threshold temperature. Other end points were not significantly related to either temperature level in this study. Short-term exposures to colder environmental temperatures reduced endothelial-dependent vasodilatation, supporting the epidemiologic associations with heightened cardiovascular risk. We show here for the first time that temperature exposures characterized at the personal level may be more robust predictors of endothelial function than outdoor-ambient levels. J Am Soc Hypertens 2017;■(■):1–8.

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Numerous studies conducted worldwide have demonstrated that environmental temperatures during the prior few days are associated with all-cause as well as cardiovascular morbidity and mortality.[1–4] While extreme heat is linked to adverse health effects, a large body of evidence demonstrates that colder temperatures are strongly predictive of increased cardiovascular events.[2,4] This issue is likely to become an even greater public health problem due to global climate change which not only heightens

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summer heat waves but can promote larger overall variations in temperature and more pronounced winter cold spells across temperate zones.[5,6]

Several biological mechanisms may underlie the linkage between temperature and cardiovascular risk.[1] Cold exposure causes adrenal and sympathetic nervous system activation as well as thermoregulatory vasoconstriction which may explain the well-established association with elevations in arterial blood pressure (BP).[1,7,8] In addition, a few studies have shown that temperature and season are related to changes in brachial flow-mediated dilation (FMD), an established measure of endothelial-dependent vasodilatation.[9–11] FMD is an independent predictor of cardiovascular events, and as such, temperature-induced endothelial dysfunction could be a key pathway explaining the epidemiologic associations.[12]

It is important to note that the relationship with FMD in the published literature has thus far relied on ambient (ie, prevailing regional outdoor) temperature values. However, ambient levels are known to be inaccurate metrics of "true" temperature exposures given that most individuals spend the majority (~90%) of their time indoors in regulated environments where the temperature is held relatively constant, particularly in colder regions/seasons and urban locations.[13] We and others have reported greater predictive value of arterial BP by using personal-level environmental temperature (PET) exposures compared to ambient-outdoor levels.[8,14–16] On the other hand, only one study has yet evaluated the differing associations with FMD.[14] Give that endothelial dysfunction plays a fundamental role in cardiovascular diseases,[12] we aimed to explore the impact of recent temperature exposures measured by PET versus outdoor-ambient levels on several physiological parameters with a specific focus on FMD.

Methods

This study is a post hoc exploratory analysis of results obtained from the human project component of the Great Lakes Air Center for Integrated Environmental Research at the University of Michigan. The protocol was designed and powered to evaluate the effect of personal-level $PM_{2.5}$ exposures on primary cardiometabolic health end points. The study was approved by the Institutional Review Board of the University of Michigan, and all participants signed a written informed consent document during a screening visit. Participant inclusion criteria were healthy, nonsmoking adults living in nonsmoking households aged 18–50 years without a history of cardiovascular disease or risk factors (screening visit BP $<$ 140/90 mm Hg and fasting glucose $<$ 126 mg/dL). Body mass index was calculated from height and weight measured at a screening visit. Subjects were also excluded if they were taking any medication or over-the-counter pill (eg, cholesterol or BP-lowering medication, fish oil, antioxidant) on a routine basis that might alter study outcomes.

Qualifying participants (n = 50) were enrolled into a repeated measures panel study, each fully completing the protocol within a 2- to 3-week-long period (online supplement, Figure S1). The study was conducted among individuals living in southeast Michigan within a 2-year period during the months of August through October 2014; January through May 5, 2015; November through December 2015; and January through February 2016. There were two study blocks, each consisting of 2 visit days in a row when participants came fasting $\geq$8 hours at 8 AM to a temperature-controlled (21°C–22°C) outpatient Clinical Translational Science Award research facility of the University of Michigan (Domino's Farms, Ann Arbor, MI). On visit day 1, cardiovascular outcomes were measured in the order provided in Figure S1, and afterward, participants were discharged with instructions to proceed with usual daily activities (excluding exercise and travel) while wearing a personal environmental monitor. They were also provided with a portable home sleep monitor and instructions on its usage during the upcoming night. The following morning (visit day 2), participants returned to the Clinical Translational Science Award. Cardiovascular outcomes were repeated in the same sequence as day 1. Participants were then discharged home and underwent a 6-day (minimum) to 3-week (maximum) washout period. Thereafter, each participant repeated the same process during study block 2.

Cardiovascular Outcomes

Study outcome methods were performed as detailed in our prior experiments and are only be briefly outlined here.[14,17] Seated right upper arm BP using an appropriate sized cuff was measured by an automated device (BPM-100; http://www.bptru.com/) after participants rested unattended in the examination room for 5 minutes with their arm supported at midsternal level. The average of five BP readings (2nd to 6th levels using 1-minute intervals) was defined as the BP outcome. Participants next rested supine on a patient examination bed, and continuous electrocardiogram monitoring was performed for 6 minutes using a Spacelabs evo Holter system. Time domain (standard deviation of normal-to-normal intervals), frequency domain (high and low frequencies), and heart rate variability (HRV) metrics were analyzed using the Spacelabs Pathfinder system (http://www.spacelabshealthcare.com/). Thereafter, resting basal longitudinal brachial artery diameter (BAD) images were measured at a standardized site on the right upper arm using a portable Terason ultrasound system and a 10-mHz linear array transducer (http://www.terason.com/). All images were captured by an electrocardiogram triggered on the R-wave. Digital images were analyzed using a software package employing an edge-detection system (Brachial Analyzer,