

REVIEW | Exploiting Environmental Factors to Improve Health and Performance

Effects of heat and cold on health, with special reference to Finnish sauna bathing

Ilkka Heinonen^{1,2,3} and Jari A. Laukkanen^{4,5,6}

¹Turku PET Centre, University of Turku, Turku, Finland; ²Department of Clinical Physiology and Nuclear Medicine, University of Turku, Turku, Finland; ³Division of Experimental Cardiology, Thoraxcenter, Erasmus Medical Center, University Medical Center Rotterdam, Rotterdam, The Netherlands; ⁴Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland; ⁵Central Finland Health Care District, Jyväskylä, Finland; and ⁶Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland

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Heinonen I, Laukkanen JA. Effects of heat and cold on health, with special reference to Finnish sauna bathing. *Am J Physiol Regul Integr Comp Physiol* 314: R629–R638, 2018. First published December 20, 2017; doi:10.1152/ajpregu.00115.2017.—Environmental stress such as extremely warm or cold temperature is often considered a challenge to human health and body homeostasis. However, the human body can adapt relatively well to heat and cold environments, and recent studies have also elucidated that particularly heat stress might be even highly beneficial for human health. Consequently, the aim of the present brief review is first to discuss general cardiovascular and other responses to acute heat stress, followed by a review of beneficial effects of Finnish sauna bathing on general and cardiovascular health and mortality as well as dementia and Alzheimer's disease risk. Plausible mechanisms included are improved endothelial and microvascular function, reduced blood pressure and arterial stiffness, and possibly increased angiogenesis in humans, which are likely to mediate the health benefits of sauna bathing. In addition to heat exposure with physiological adaptations, cold stress-induced physiological responses and brown fat activation on health are also discussed. This is important to take into consideration, as sauna bathing is frequently associated with cooling periods in cold(er) environments, but their combination remains poorly investigated. We finally propose, therefore, that possible additive effects of heat- and cold-stress-induced adaptations and effects on health would be worthy of further investigation.

INTRODUCTION

Environmental stress such as warm or cold temperature is often considered a challenge to human health and homeostasis, but the human body also physiologically adapts to heat and cold environments at least to some extent. Furthermore, recent studies have also elucidated that particularly heat stress may even be beneficial for human health, independently of other lifestyle factors. Consequently, after a brief review of general acute cardiovascular responses and long-term adaptations in response to heat stress, we will discuss recent results of a long-term prospective study that indicates that frequency and duration of Finnish sauna bathing plays a role in preventing cardiovascular and all-cause mortality, sudden cardiac death (SCD), dementia, and Alzheimer's disease (72, 73). While other types of heat stress studies such as warm water immersion studies have revealed some plausible mechanisms that

might mediate health effects of repetitive heat stress, it is also emphasized that unique features of the Finnish sauna environment with its typical sauna tradition may not be directly comparable with other heat therapy means. A typical sauna includes relatively high temperatures (80–100°C) with dry air, which also circulates well in a Finnish sauna, making it easier to tolerate and even enjoy high sauna temperature. Another important feature is that the protective effects of the Finnish sauna may reflect life-long habits, which usually begin very early in the childhood, as children of only 0.5–1 yr old are gradually introduced to the sauna, meaning that benefits in disease end points may not be obtained by short-term or temporal heat stress activities. Sauna bathing is a tradition embedded in the culture in Finland, and it is accessible basically to everyone. As a result of this, a typical Finn takes sauna baths at least once a week, the average being about twice a week (72). A typical duration of sauna bathing can vary between 5 and 20 min (or even 30 min) and is often intermittent, including short periods in colder environment(s). These are the typical Finnish sauna features that are important to bear in mind with regard to the aims of the present review with its

Address for reprint requests and other correspondence: I. Heinonen, Turku PET Centre, PO Box 52, FI-20521 Turku, Finland (e-mail: ilkka.heinonen@utu.fi).

results and discussion. Another tradition that is often combined with sauna bathing is intermittent cooling periods between sauna bathing sessions, sometimes including a hot sauna with a short stay in ice-cold water. In this review, we will therefore also briefly discuss possible health effects of a cold environment with respect to brown fat activation and its potential to combat body adiposity and related cardiovascular and metabolic disorders.

GENERAL CARDIOVASCULAR RESPONSES TO ACUTE HEAT STRESS

As comprehensively discussed previously (23), heat challenges the human body, which is however normally capable of responding to heat to maintain normal internal temperature that is critical for normal internal organs to function. This is obtained by directing the blood, and thus heat, to the skin, where heat is released by sweating allowed by nervous innervation and control of skin blood flow. Skin blood flow and sweating can increase even up to 7–8 l/min and 2–4 l/h, respectively, in response to acute heat stress, particularly when exposure is combined with physical activity (28, 99). This is accompanied by reduced blood pressure and increased heart rate, whereas stroke volume is largely maintained even if blood is moved away from the thorax region (24) to the periphery, which decreases venous return, particularly if a subject is at rest and venous return is not facilitated by muscle pump either. Stroke volume is maintained or is even slightly increased as systolic function and ejection fraction increase during heat stress in healthy subjects (11, 24). During prolonged heat stress, ventilation is also increased, which contributes to decreased brain blood flow in the heat as more carbon dioxide is exhaled (3), a condition that may lead to unconsciousness if this condition becomes too severe.

For many years, it was believed that as blood is directed to the periphery, it goes almost solely to skin, and muscle blood flow is not altered. However, it has now been shown that muscle blood flow also increases to some extent in response to local heat stress (44, 90). Increase in blood flow is not actually limited only to skeletal muscle, as bone marrow blood flow is also increased (44). Acute beneficial effects of hot water immersion-induced therapy in peripheral artery disease patients (82, 112) and aging (98) are likely to be mediated by increased heat-induced muscle perfusion in addition to the vasodilation in the skin. Interestingly, leg heating is also able to eliminate the detrimental effects of prolonged sitting (97), the effect that is also most likely mediated by increased skin and muscle blood flow. Increased muscle blood flow by hot water heat stress was also suggested to be the mechanism for the improved glucose balance in type 2 diabetic patients as a result of heat stress intervention (54).

HEAT-INDUCED PHYSIOLOGICAL ADAPTATIONS

Human thermoregulatory adaptations to heat have recently been comprehensively reviewed (109). It is evident that not only the cardiovascular system but also body metabolism is activated due to heat stress adaptations (see online Supplementary Table 1). The beneficial changes of heat therapy could include some similar target organs and functional adaptations, although not so well characterized, as it is documented to occur in response to long-term exercise training (45). Indeed, com-

parable with exercise-induced adaptations, repetitive heat stress could improve endothelial function and arterial stiffness and might lower resting blood pressure in sedentary humans (13). Because of strongly increased skin blood flow under heat stress conditions, cutaneous microvascular and conduit artery function and blood flow are also improved by passive, repeated heat therapy (12, 16, 17, 41, 81), although improved cutaneous vascular function by heat stress intervention has not been repeated in all studies (35). Perhaps the strongest adaptation together with enhanced sweating capacity and its sensitivity is, however, lowered core temperature (88) as a response to repetitive heat sessions, which further increases body heat tolerance, as maximal tolerable temperature cannot be increased due to fundamental effects of heat on protein folding. Blood volume, particularly plasma volume, may also increase, which is related to improved heat tolerance.

Although sauna bathing cannot induce a similar increase in muscular perfusion to exercise training (47, 49, 51), increased skeletal muscle blood flow during heat stress (44) is likely closely coupled with increased skeletal muscle gene expression of angiogenic factors due to heat therapy (66). If this response occurs also in cardiac muscle, as has been suggested from some experimental studies focusing on healthy (40), hypertensive (57), and infarcted (106) myocardium, it would be interesting to investigate whether repeated heat stress exposure could lead to favorable exercise training-linked adaptations in the human heart muscle (48, 50) and improve myocardial blood flow reserve and even build up new cardiac collateralization. Heat stress-induced myocardial metabolic adaptations are also largely unexplored to the best of our knowledge, but it can be speculated that repetitive heat stress sessions might lead to comparable adaptations that have been observed in exercise training (32, 48, 50, 53). Heat stress improves skeletal muscle contractility (95), but it remains to be shown whether contractility is improved also in heart.

It was found that, in addition to increased muscle blood flow, bone marrow blood flow may also increase in response to heat stress (44). Bone marrow blood flow also increases in response to acute exercise (46), which may be coupled to exercise-induced stem cell release (83). Consequently, exercise-like increases in bone marrow perfusion during heat stress may also stimulate the release of stem cells such as endothelial progenitor cells, which could have a wide range of tissue repair and health effects; to the best of our knowledge, however, this remains to be directly shown experimentally. Although the source of the cells has not been investigated previously, repeated heat stress treatment by sauna bathing has been shown to increase CD34-positive cells in the circulation (86), supporting the idea of heat therapy also as a possible stem cell stimulation therapy. Furthermore, reduced circulating endothelial and platelet microparticles may be contributing to the health benefits of heat exposure (2).

EFFECTS OF FINNISH SAUNA BATHING ON HUMAN HEALTH

Sauna bathing, a form of passive heat therapy, is an activity that is a tradition, especially in Finland, and is commonly used mainly for relaxation and pleasure purposes and is becoming increasingly popular in many other countries and cultures (91, 113). Unique features of Finnish sauna include hot temperature and dry air conditions with good ventilation. Temperature and

humidity can be temporarily increased by throwing water on the hot rocks of the sauna heater, which is the heating source of the 80–100°C temperature in a sauna. A typical Finnish sauna differs from far-infrared sauna bathing, which has been tested in Japanese studies using a far infrared-ray dry sauna (111). In these studies with dry sauna (58, 64, 65, 111), patients underwent regular sauna therapy at 60°C for 15 min and were then kept supine on a bed outside the bath room for 30 min with sufficient warmth provided by blankets.

Previous studies have suggested important positive effects of sauna bathing on cardiovascular health. Indeed, recent observations demonstrate that sauna bathing of only 5–20 min duration a few times per week would be associated with a decreased risk of SCD, cardiovascular and all-cause mortality (72). In a prospective population-based study, it has been reported that sauna bathing is associated with a significantly lowered risk of fatal cardiovascular disease (CVD) events and all-cause mortality (72). The higher frequency of the sauna bathing (4–7 times/wk) was related to a considerably decreased risk of SCD, fatal coronary heart disease (CHD), and CVD events and all-cause mortality independently of conventional risk factors as shown in Fig. 1. Cardiovascular risk reduction was strongest in participants with the highest duration and frequency of sauna bathing, but shorter and less frequent sauna bathing sessions also provided some cardiovascular benefits. Furthermore, a follow-up study of this cohort has also shown that sauna bathing lowers the risk of neurodegenerative diseases, dementia, and Alzheimer's disease (73). The risk reductions also in regard to these brain disorders were substantial; there is a risk reduction of 66% of dementia and a 65% risk reduction of Alzheimer's disease when sauna bathing four to seven times a week is compared with subjects having only one sauna session per week (73).

Heart rate can increase close to 100 beats per minute during moderate-temperature sauna bathing sessions and even to higher levels (~150 beats/min) during much hotter sauna bathing (43, 67). Heart rate response corresponds to low- and moderate-intensity physical activity. Although there are no

active contractions of skeletal muscles during the sauna bathing, sauna bathing may also increase the general metabolic rate (75). This is in contrast to the training response experienced during physical activity, although increased heart rate also increases myocardial oxygen demand similarly to physical exercise, which is likely to account for cardiac-specific health effects, while increased blood flow stimulates arterial health by shear stress and other mechanisms. It has been documented that cardiac output is increased mainly due to the increase in heart rate during sauna bathing. A typical Finnish sauna can positively modulate the autonomic nervous system (heart rate variability), which may contribute to the strong reduction in SCD. In the typical Finnish sauna bath session, skin blood flow increases, which leads to the higher cardiac output, whereas blood flow to internal organs decreases with an increased body temperature (63). Rectal temperature increases by ~1°C at 80°C sauna heat (75), and sweat is secreted at a rate of 0.6 to 1.0 kg/h during a hot sauna bath, with an average total secretion of 0.5 kg during a typical sauna bathing session of 15–30 min duration (116), which has effects in body fluid balance during and after sauna.

POSSIBLE MECHANISMS MEDIATING HEALTH-ENHANCING EFFECTS OF FINNISH SAUNA BATHING

It is important to understand the mechanism by which health benefits of sauna bathing are mediated. In addition to being a relaxing lifestyle habit, it remains a potential strategy that could be useful in improving cardiovascular function and subsequently also prevent or delay the development of neurodegenerative diseases such as dementia. The possible health-enhancing effects of sauna bathing are likely mainly those adaptations that have already been presented and discussed in the earlier section(s), including improved endothelial and microvascular function, reduced arterial stiffness and blood pressure, and increased angiogenesis in sedentary humans (see online Supplementary Table 1). However, some Finnish sauna-specific adaptations may also occur, which may not be ob-

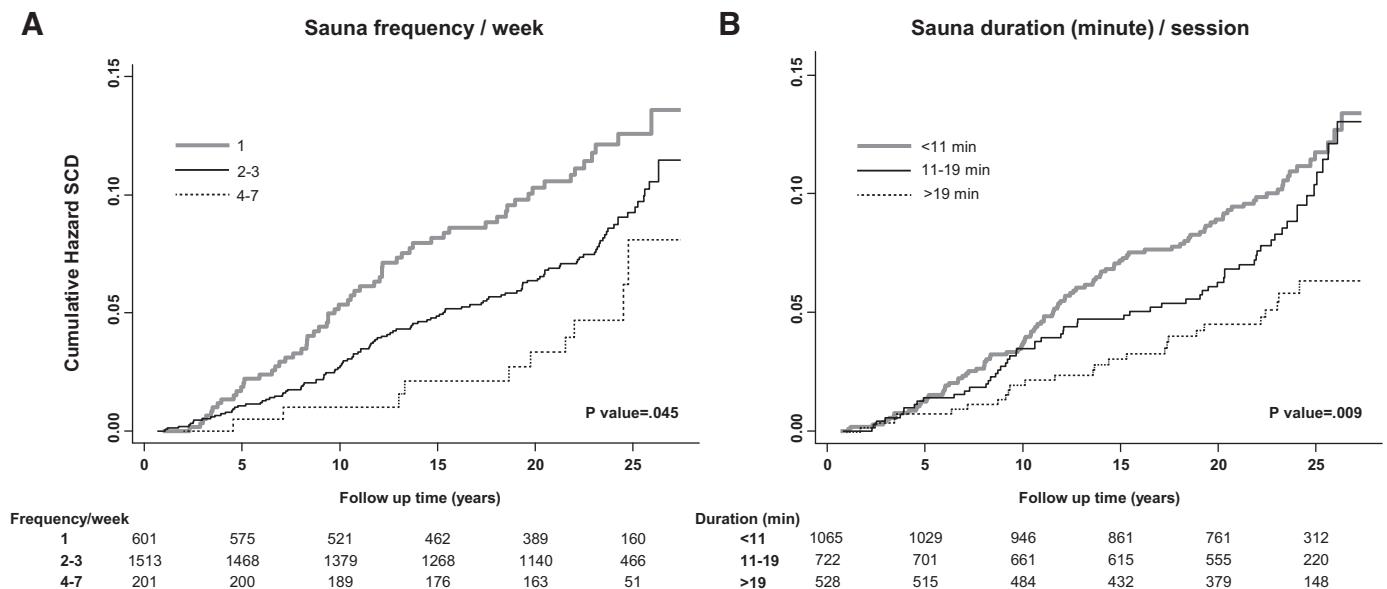


Fig. 1. Cumulative hazards of sudden cardiac death (SCD) according to frequency (A) and duration (B) of Finnish sauna bathing.

tained by other passive heat therapies such as warm water (leg) immersion, which has been applied in some studies. This is because of the relatively high (80–100°C) sauna temperatures and dry air (15–20% humidity) during Finnish sauna bathing sessions, but particularly its practicality in normal daily life as a heat stress therapy, by which mortality and neurodegenerative disease risk reductions have been described.

Heat exposure of the sauna may improve cardiovascular function, which has been previously documented in subjects with CHD risk factors (58, 64), indicating a protective role of heat therapy on arterial stiffness (13, 74). Arterial stiffness can be modified by various underlying vessel-related factors such as elastic fiber degeneration, increased collagen content, and structural changes with vascular smooth muscle cell hypertrophy and hyperplasia (101). In addition to these long-term structural adaptations, improved arterial compliance is acutely improved through changes in hydration status as a result of sweating and thus the loss in plasma volume (14, 36). Consistent with existing evidence based on the effect of heat therapy such as sauna, there are also some findings showing that blood pressure may be decreased because of increased ambient temperature (68, 77, 117), including sauna bathing (75, 118). It has also been shown that even a short dry sauna session favorably modifies heart rate variability in patients with untreated hypertension (37). In patients with slightly elevated blood pressure, a single sauna session produced positive effects on systemic blood pressure as assessed by 24-h blood pressure levels (86), although a reduction in 24-h blood pressure is not a consistent finding (38). It has also been found that sauna exposure is associated with lower levels of cardiac propeptide concentrations with improved left ventricular function (86, 96). Repeated sauna treatment has been shown to improve endothelial function in patients with CHD risk factors and heart failure, suggesting a preventive role of thermal sauna therapy for vascular endothelium (86) as well as for myocardial perfusion in patients suffering from ischemia (105). However, additional well-controlled studies are needed to show whether regular long-term sauna bathing could produce longer-term changes in cardiovascular function.

Only a limited number of studies have reported that repeated sauna treatment or thermal therapy is associated with improvement in neurohumoral factors, which are widely used markers of prognosis in patients with CVDs (86, 110). Otori et al. (86) demonstrated that 3 wk of repeated far-infrared sauna treatment (Waon therapy) in patients with chronic heart failure was associated with lower concentrations of brain natriuretic peptide and plasma norepinephrine. In patients with heart failure who were treated with dry sauna for 2 wk, Kihara et al. demonstrated a significant decrease in concentrations of circulating brain natriuretic peptides, which are associated with better prognosis among heart failure patients (64).

The beneficial effects of sauna bathing on cardiometabolic health outcomes have been linked to its impact on circulatory and cardiovascular function. Sauna therapy may improve microvascular and endothelial dysfunction (64), which has been suggested to be involved in the pathophysiology of outcomes such as hypertension, CVDs, and diabetes (62, 89, 107). Sauna bathing has been shown to produce systemic blood pressure-lowering effects, increase cardiac output via an increase in heart rate, and decrease peripheral vascular resistance. Sauna therapy may exert its effects via changes in levels of blood-

based cardiovascular biomarkers such as markers of glucose metabolism and insulin resistance, natriuretic peptides, cardiac troponin T, and inflammatory markers such as interleukins and C-reactive protein, although data on this topic are still very limited and further studies are warranted to elucidate these potential mechanisms. However, it has been documented in both men and women that Finnish sauna has positive effects on cholesterol and lipid levels, including total cholesterol and LDL and HDL (42, 93) and transiently also triglycerides (42). There is also some evidence that Finnish sauna can boost the immune system (92), which may partly explain why hot-cold bathing reduces susceptibility to colds and prevents infections in healthy subjects (31). Furthermore, although one sauna bath session may acutely increase oxidative stress, sauna bathing may also reduce exercise-induced oxidative stress and lead to improved antioxidant capacity after repeated sauna heat exposures (94, 108). This is plausible, as antioxidative enzymes can be boosted by heat shock proteins, which will be increased as a response to heat stress and their changes correlate with heat acclimatization (79).

With regard to tissue-specific effects of sauna bathing, it is evident that improvements in many of the “general” cardiovascular risk factors, which are underlying factors for both cardiac and neurodegenerative disorders, such as endothelial function, arterial stiffness, blood pressure, and lipid profile, are largely responsible also for these organ-specific influences. However, sauna-induced improvements in cardiovascular function may also directly translate to improvements in brain function due to important interactions between these organs (60, 61). Furthermore, it is also likely that shear stress-induced mechanisms are one of those factors that lead to improvements in brain perfusion and brain arterial health (15). Regarding changes in brain perfusion and prevention of neurodegenerative diseases by sauna bathing, it is somewhat paradoxical that heat stress is consistently shown to decrease brain blood flow acutely (3). However, to the best of our knowledge these studies are almost solely based on transcranial Doppler measurements, which can derive only blood flow velocity in one artery. Since even minimal changes in arterial diameter, which could be modified during heat stress, can lead to fairly large changes in total brain blood flow, it remains to be determined whether total blood flow is altered during heat stress and as an adaptation to long-term sauna bathing. In this regard, it is important to note that repeated warm water immersion can induce similar cerebrovascular adaptations to exercise training with moderate exercise intensity (1). In addition to total blood flow, it would also be important to determine regional distribution of brain perfusion in these experiments (34). These investigations have been performed at the level or large arteries (4, 85) but, to the best of our knowledge, not at the brain tissue perfusion level. It is also possible that there are direct influences of angiogenesis and neurogenesis in the brain (55, 102) that also contribute to explain the preventive effects of neurodegenerative diseases due to Finnish sauna bathing.

Finally, sauna bathing may improve symptoms of lung disease (22, 71) and has also been used in treating musculoskeletal pain (59, 84). It is suggested that sauna bathing increases the vital capacity, minute ventilation, and forced expiratory volume of the lungs (71), as heat stress increases minute ventilation leading to these favorable effects in regard to lung function. These effects of sauna on lung function may

explain recent findings indicating that Finnish sauna bathing is associated with a decreased risk of respiratory diseases (70).

RISKS OF SAUNA AND THE ROLE OF OTHER (DEMOGRAPHIC) CHARACTERISTICS

Most people in general can tolerate a typical warm dry Finnish sauna, which is a pleasurable activity with an additional health benefit (100). It is, however, also well known that survival and heat stroke severity are related to the severity and duration of hyperthermia (56). There are therefore some concerns that sauna bathing might have some risks, particularly in patients with particular disease conditions; the very hot sauna exposure could be potentially harmful (67). Particularly, persons with unstable coronary artery disease or ischemic heart failure should be cautious with sauna bathing, as it might cause myocardial ischemia in patients with reversible exercise-induced ischemia, although it is still relatively less than that induced by exercise (39). Furthermore, persons who are prone to orthostatic hypotension or severe valvular disease should also be cautious of hot sauna bathing because of a possible decrease in blood pressure, which typically occurs just after a hot sauna bath during the cooling down period (17, 44). However, dry common sauna bathing seems to be safe. Even patients who have recovered from myocardial infarction and patients with stable angina pectoris or heart failure can enjoy sauna bathing without any significant adverse cardiovascular effects (63), as also shown with heart failure patients who can gain substantial health benefits even if heat therapy has been started fairly late in life (65). However, it is likely that those who are not able to exercise even at a low-intensity level should be advised to apply sauna therapy cautiously.

Far infrared sauna intervention studies have been conducted in Japan to use sauna bathing as one component of the treatment of congestive heart failure. Cardiac events due to heart failure or cardiac death occurred in 68.7% of the control group but only 31.3% of the Waon therapy group after 60 mo of follow-up (65). In that study, hospitalization due to heart failure occurred in 20 patients in the sauna group and 44 patients in the control group, suggesting the beneficial effects of far infrared saunas among patient with heart failure.

In epidemiological studies, there is a lack of repeat and regular evaluations of sauna bathing habits that enable us to confirm the long-term health effects of sauna. Epidemiological evidence relies only on a questionnaire-based baseline assessment of sauna bathing habits during everyday life. These studies have used an exposure of sauna habits during a typical weekly sauna sessions (69, 70, 72, 73, 118). Second, it is possible that sauna bathing habits have changed during long-term follow-up due to possible changes in lifestyle habits or other diseases of participants occurring over a long period of time, which could have introduced some biases in the epidemiological studies. However, this is unlikely, given that sauna bathing is a tradition embedded in the culture in Finland, and even subjects with cardiovascular and metabolic diseases such as diabetes take sauna baths regularly. Given that sauna bathing is a commonly used relaxation habit in the Finnish population, it is anticipated that the correlation between measured sauna habits taken several years apart is high, and therefore analysis using baseline assessments is unlikely to considerably underestimate the associations.

Even though socioeconomic status (SES) has been shown to influence future risk of CVD and may be associated with access to sauna bathing, previous studies have shown that adjustment for SES does not materially change the association of sauna bathing with outcomes (69, 70, 72, 73, 118) after an additional adjustment for a wide range of CVD risk factors and possible confounders, including a comprehensive panel of lifestyle and clinical factors. Thus, the associations persisted significant for SCD, fatal CHD and CVD events, suggesting the additional and independent health benefits of sauna bathing when SES was also taken into consideration. Indeed, strengths of the published follow-up studies on sauna habits and health-related outcomes (42, 43) include the rigorous measurement of other risk factors, the large community-based study sample (2,315 participants), and the long-term of follow-up with data on major health outcomes. Based on the available evidence, sauna bathing can be considered a recommended habit as part of a healthy lifestyle for the prevention strategies of CVDs.

EFFECT OF MODERATE COLD STRESS ON HUMAN HEALTH AND ITS IMPLICATIONS

In addition to heat stress induced by sauna bathing, intermittent heat and cold exposures are a quite common practice, for instance in Finland and other Nordic countries, when sauna bathing. They are normally practiced by going outside in a cold environment between sauna sessions. Other common ways are to sit or roll in snow or simply take a cold shower for several minutes. In an extreme form, they can also be practiced by dipping in ice-cold water three to five times from five seconds to a few minutes between sauna bathing sessions of 5–15 min, but it is currently not well known whether this kind of extreme activity promotes positive health effects even better than a single hot sauna bathing session alone. In addition to the effects of heat exposure on the human body and the common utilization of cold exposure between sauna bathing sessions, it is thus also important to consider the possible effects of cold temperatures in health.

As with acute exercise, heat stress, and hypoxia, cold stress also challenges physiological systems and may be detrimental to human health acutely (18). When entering a cool environment, the human body will adjust to maintain heat balance. Heat balance can be restored by reducing heat loss and/or increasing heat production. Heat loss is minimized by cutaneous vasoconstriction, induced by reflex and local mechanisms (19), which decrease heat transfer from the core to the skin and other distal parts of the body. On the other hand, heat production can be increased by nonshivering and shivering thermogenesis. Shivering especially is a very efficient way to produce heat. Although not commonly practiced as a part of body weight management, its efficiency in energy production and consumption is highlighted by the fact that peak shivering intensity can increase heat production close to five times over basal metabolic rate (33).

The physiological and health effects of cold exposures such as winter swimming in ice-cold water have been investigated in many studies (30, 76, 103, 104). They indicate that they are generally not harmful for health when, for instance, antioxidant capacity or hormonal function is considered (30, 76, 103), but they can lead to reduction in skinfold thickness (104), meaning that cold exposures can be beneficial in reducing body adipos-

ity. They are also well tolerated as thermal sensation and comfort is increased after first exposure to cold, meaning that subjects become habituated to cold (104). Numerous hormonal and nervous system adaptations contribute to this adaptation to cold (21, 27, 78). From the cardiovascular health point of view, one of these mechanisms can be called cold-induced vasodilation, which means that, after initial exposure to cold and resulting vasoconstriction in limbs, a period of vasodilation is observed that enables the return of warm blood to the fingers and other distal body parts (20, 21, 26). It is known that this periodic cold-induced vasodilation reflects a vasodilation in both muscle and cutaneous vasculature (29). It is likely to stimulate shear stress-mediated improvements in vascular function leading to better health of the peripheral circulation. It is also likely that repeated extreme temperature variations such as sauna bathing and ice-cold swimming are particularly strong mediators of this effect. When an individual returns to the sauna after a swim in ice-cold water, this effect is evidenced by a feeling of swollen hands and legs together with strong pulsation sensations as blood flow is strongly stimulated by these extreme variations in temperature.

Furthermore, with respect to cold stress it is important to consider that two types of adipose tissue exist in humans, white and brown adipose tissue. White adipose tissue is distributed mainly subcutaneously throughout the body, and in most of the subjects, it has the capacity to expand substantially when energy intake has been excessive and consumption minimal. In contrast to white adipose tissue, brown adipose tissue is localized only in special small depots, mostly in the neck area, and is activated by cold exposure (115). In contrast to white fat, which stores fat, brown fat mainly burns energy, which is released as heat. Brown fat is activated by cold, and colder environment relates to higher cold fat activation and lower body weight (25, 114). Although skeletal muscles are also very important contributors (8), brown adipose tissue plays a role in energy expenditure in response to acute cold exposure (87). Brown adipose tissue oxidative capacity and activity increase in response to repeated cold exposure (5, 9), leading to changes in lipid metabolism (6, 10). These effects on metabolism may contribute to human health, although glucose metabolism also plays a role, as that has been shown to be impaired in brown adipose tissue of type 2 diabetic patients (7). Therefore, as activation of brown fat may prevent body adiposity and related metabolic and cardiovascular disorders, repeated cold exposure may also be beneficial for health. However, in this respect it is noteworthy that as actual brown fat depots are only a few grams, browning of white fat, and that to a substantial extent, would be needed to show physiologically relevant effects on whole body metabolism, as an investigation in humans has shown that purely brown fat thermogenesis can only account for energy consumption of less than 20 kcal/day (80). This amount of energy consumption can be obtained by doing moderate-intensity physical activity, such as brisk walking or moderate-intensity running for only 2 min (80). This emphasizes the importance and potential of physical activity in the prevention and treatment of excessive body adiposity and related cardiometabolic disorders, although activation of brown fat by cold could certainly be applied as an adjunct therapy. Moreover, the combined and possibly additive effects of alternating heat and cold exposures, such as sauna plus cold

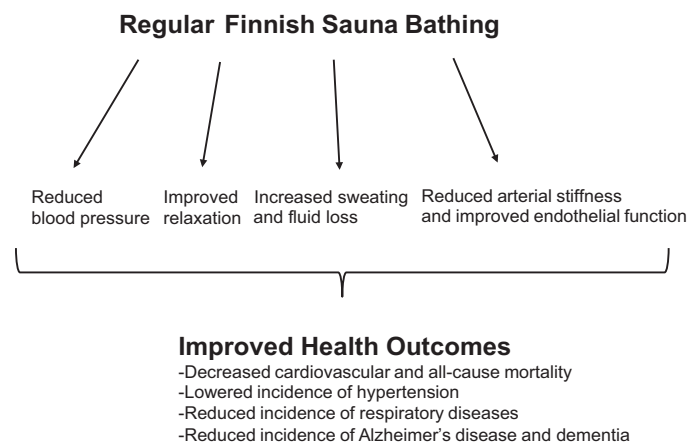


Fig. 2. Plausible mechanisms that mediate the documented (70, 72, 73, 118) health effects of regular Finnish sauna bathing.

water immersion, on human health are currently not well known but should be investigated in the future.

CONCLUSIONS

In conclusion, although acute warm and hot temperatures are stressful for humans, the human body also adapts physiologically to repetitive heat sessions, leading to improved heat tolerance and ultimately also decreased mortality and reduced risks for brain disorders such as dementia and Alzheimer's disease (Fig. 2). Therefore, similarly to hypoxia or altitude (52), heat or cold stress could also be applied as an independent or adjunct therapy to exercise and physical activity to maintain or improve human health, particularly among those people who do not want to or cannot exercise. It seems that the best benefits in cardiovascular and all-cause mortality will, however, be obtained by increasing physical fitness combined with sauna bathing (69), highlighting the fact that several lifestyle habits affect human health.

Perspectives and Significance

Although environmental stressors such as extremely warm or cold temperature are often considered a challenge to human health and body homeostasis, the human body can adapt relatively well to heat and cold environments. Furthermore, recent studies have elucidated that heat stress in particular might even be highly beneficial for human health. Indeed, heat stress particularly in the form of Finnish sauna bathing has been shown to improve general and cardiovascular health and mortality as well as preventing against dementia and Alzheimer's disease risks. Therefore, sauna bathing or other heat stress activities are recommended habits for the improvement of population health.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

I.H. and J.A.L. conceived and designed research; I.H. and J.A.L. interpreted results of experiments; I.H. and J.A.L. prepared figures; I.H. drafted manuscript; I.H. and J.A.L. edited and revised manuscript; I.H. and J.A.L. approved final version of manuscript.

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