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Economical Sweating Function in Africans: Quantitative Sudomotor Axon Reflex Test

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People in tropics have the ability to tolerate heat by residential permanence in the tropics. Previously, we have shown that African and Thai subjects who lived for whole their lives in only their respective countries sweat less under hot conditions than South Koreans who also lived whole their lives in Korea. The difference in sweating responses was attributed to the dissimilar central and peripheral sweating mechanisms operating in people from both groups. In the present study, acetylcholine (ACh), the primary transmitter for the sudomotor functions, was iontophoretically administered to South Koreans and Africans to determine the characteristic sudorific responses of their acclimatized biologic make-up to their respective environments. Using quantitative sudomotor axon reflex test (QSART), direct (DIR) and axon reflex (AXR) responses were evaluated. The findings revealed that the sweat onset-time among South Koreans was 0.91 min earlier than among Africans ($P<0.01$). The axon reflex sweat volume of nicotine receptor activity AXR(1) and sweat volume of muscarinic receptor activity DIR(2) among South Koreans were 79% and 53% greater ($P<0.01$), respectively. These results indicate that the reduced thermal sweating among Africans is at least in part attributed to the diminished sensitivity of sweat glands to ACh.

Key Words: Acclimatization, Tropical natives, Direct response, Axon reflex, Sweat onset time, Sweat Volume, QSART

INTRODUCTION

Physiological acclimatization to ambient heat provides human with life-saving effective thermoregulatory capability in extremely hot environments. Evidence suggests that when unacclimatized humans are exposed to temperatures above 30°C, their physiological capacity for thermoregulation may be compromised (Wilkerson et al, 1986). Heat acclimation increases thermal resistance by causing adaptive changes in thermoregulatory mechanisms. Transitory acclimation to heat by repeated exposures to heat and/or physical training has been intensively investigated by many researchers, and it was well accepted that, in short-term acclimation, heat-tolerance was achieved by lowering the threshold for sweating and by enhancing sweat secretion (Nadel et al, 1974; Ogawa & Sugenoya, 1993). For tropical inhabitants, it was shown that heat-tolerance was characterized by suppressed sweating (Kuno, 1956; Matsumoto et al, 1993; Ogawa & Sugenoya, 1993; Lee et al, 1997; Lee et al, 2002), which is completely distinguishable from adaptation to temporary exposure to heat (Kuno, 1956). From the viewpoint of body fluid maintenance and osmoregulation, thermotolerance with reduced sweating and enhanced dry heat loss predominates in responses seen in short-term acclimation (Lee et al, 1997; Matsumoto et al, 1997; Lee et al, 2002). It seems probable that human beings acclimatize with less sweating beyond the limits of rational heat regulation, however, the underlying mechanism need to be elucidated. As a continuum of temporally varying process, acclimation is accomplished by both the central nervous system and the peripheral effectors (Horowitz, 1989). Sweating, in human beings one of its most important components, subserves as the major influence to losing body heat in hot conditions, and it is centrally regulated by preoptic area and anterior hypothalamus (PO/AH), and peripherally by sympathetic postganglionic innervation.

Acetylcholine (ACh) is the primary neurograndular transmitter of sweating. Each individual has own temperature threshold setting; when this threshold is reached, ACh is called to function and sweat begins to be secreted. A shift in this point, however, occurs, when a person becomes acclimatized to different environmental conditions. Among tropical people, a decrease in the ACh-sensitivity of sweat glands was noted (Lee et al, 1997; Matsumoto et al, 1997; Lee et al, 2002), suggesting both central and peripheral down-regulation of the sudomotor mechanisms. ACh applied to human skin is known to elicit a sweat response, which consists of a direct muscarinergic activation of sweat

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ABBREVIATIONS: ACh, acetylcholine; QSART, quantitative sudomotor axon reflex test; DIR, direct; AXR, axon reflex.

glands and an indirect nicotinic axon reflex response from sudomotor terminals, as shown schematically in Fig. 1. The applied ACh, therefore, directly stimulates the underlying sweat glands (termed as DIR sweating), and the glands of the skin in the central compartment are activated indirectly via axon reflex (termed as AXR sweating). In this study, local sweating responses to ACh iontophoresis and sweat gland density between the natives of the tropical Africa and South Korea were compared under thermoneutral condition.

METHODS

Subjects

Forty healthy males including 17 South Koreans and 23 Africans [Nigerian (n=5), Tanzanian (n=6), Senegalese (n=7), Ghanaian (n=2) and Kenyan (n=3)], who were all students at Nagasaki University, were enrolled in this study. Africais located (from 20°00' N to 20°00' S and from 20°00' W to 40°00' E) in the tropical zone, with dry and wet-seasons and minimal seasonal variations, and its mean annual ambient temperature is 27.0°C and 80.0% relative humidity. South Korea is located in the deep south (126° 52' N, 33.38' E) and the deep north (130°4' N, 43.0' E), and its mean annual ambient temperature is 12.2°C and 66.8% relative humidity.

Their physical characteristics were as follows: South Koreans; 173.6±5.1 cm in height, 63.40±5.74 kg in weight, 29.9±3.8 years old, and Africans; 174.0±4.9 cm in height, 72.40±8.55 kg in weight, 30.4±4.6 years old. Experiment on Africans and South Koreans were conducted within 3~4 weeks upon arrival in Japan. With South Koreans who live under the same environmental conditions as in Japan, the test was done whenever they were available. The subjects gave consent after having been acquainted with the potential risks associated with experimental procedures, which were performed in accordance with Helsinki Declaration of 1975.

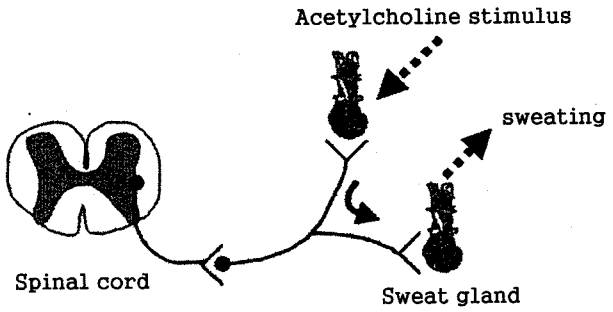

Fig. 1. Diagram of the sudomotor axon reflex. When the sympathetic postaganglionic neurons are stimulated by a neurotransmitter, sweating is caused by a sudomotor axon reflex in regions that are not directly stimulated.

Methods

The experiment was carried out under controlled climatic conditions (24±0.5°C, relative humidity 40±3% and less than 1 m/sec air velocity). Prior to the test, subjects were dressed lightly and were rested in the climatic chamber for 60 min QSART (Low et al, 1983; Chemali et al, 2001; Lee et al, 2002), which quantitatively evaluates glandular ACh-sensitivity, was employed. A sweat capsule, which consisted of three concentric compartments, was used for ACh iontophoresis and also for measuring DIR and AXR (Lee et al, 1997; Eishi et al, 2002; Lee et al, 2002), as shown in Figs. 1 and 2. The outermost compartment of the sweat capsule was filled with shredded cotton soaked in 10% ACh (Ovisot, Daiichi Pharmaceutical Co., Ltd., Japan) solution, and the innermost was where AXR was measured. Nitrogen gas, maintained at the rate of 0.3 l/min, was introduced into the compartments through a cannula. It converted the

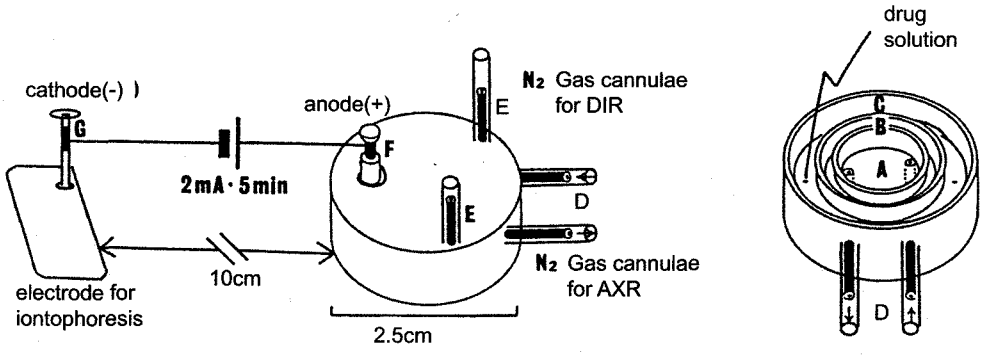

Fig. 2. The multicompartmental sweat capsule showing top (middle) and bottom (right) views and the iontophoretic cathode electrode (left) modified from Harati, Y., and Low, P.A. Autonomic peripheral neuropathies: diagnosis and clinical presentation. In: Apple, S.H. (Ed.), Current Neurology Vol. 10. Chicago: Year Book Medical Publishers, 1990, pp. 105-176. The direct compartment (C) used to load (via cannula E) the drug solution. The stimulus is administered to the drug solution via anode (F) connected with cathode (G) using a constant current generator (2 mA x 5 min). Drug solution is loaded through (E) and iontophoresed via the anode (F) connected to the stimulus compartment (C). The axon reflex-mediated sweat response is recorded from (A), the indirect compartment of an air gap (B). N_2 gas flows through cannula (D). The width of compartments (A), (B), and (C) were 1.0, 0.2 and 0.4 cm, respectively (for details see text).

sweat into gaseous form, which was quantified by a sudorometer. Two mA of direct current was applied for 5 min to the ACh cell (anode) of the capsule and to the flexible plate-electrode (HV-BIGPAD, Omron, Kyoto, Japan) (cathode) attached on the forearm skin just proximal to the wrist joint. The central compartment of the ACh capsule served as the site for sudomotor axon reflex, AXR(1), measurement during the 5 min of iontophoresis. Immediately after the cessation of the current loading, sweat capsules were detached, the skin covered with ACh capsule was wiped up, and the two capsules positions were then exchanged. This procedure took less than 20 sec. The data were collected for another 5 min to permit the simultaneous observation of DIR(2) and AXR(2) sweating (Lee et al, 2002). Sweat onset-time (SOT) after current loading and sweat volume for 5 min under the sweating curve, and 0-5 min for AXR(1) and 6-11 min for AXR(2) and DIR(2) were used for analysis. Oral (sublingual) and skin temperatures around the

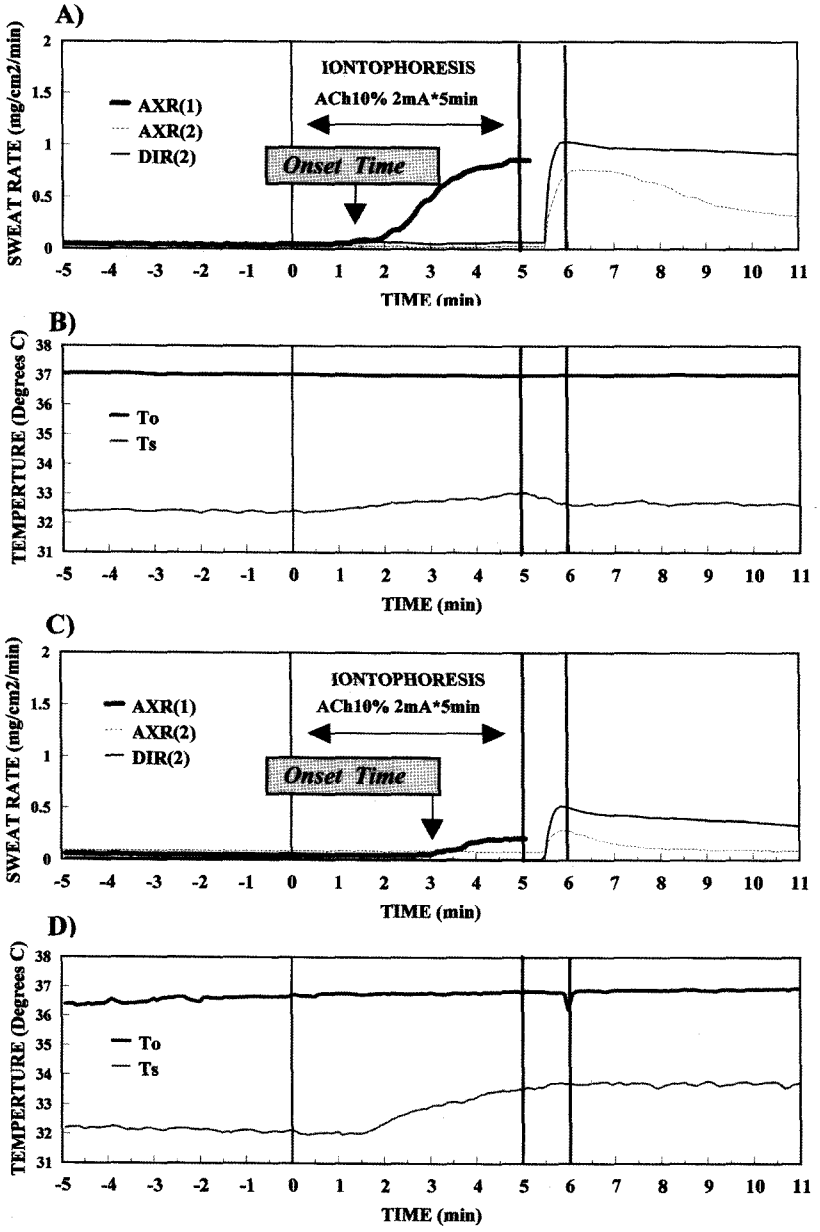

Fig. 3. Typical recording of sweating and temperature (oral and skin) in South Korean (A, B) and tropical African (C, D). The each figure shows directly activated and reflex-mediated sweating and temperature of oral and skin. A and C show AXR(1), axon reflex-mediated sweating during 5 min iontophoresis, AXR(2), axon reflex-mediated sweating during 5 min post-iontophoresis, and DIR(2), directly activated sweating during 5 min post-iontophoresis. B and D show variation of oral temperature (To) and skin temperature just beside ACh capsule (Ts).

capsule were monitored by using thermistors (PXK-67, Technol Seven, Yokohama, Japan).

Statistical analysis

Values were expressed as means±SD. Statistical significance was determined by unpaired Student's t-test for comparison between the South Koreans and the Africans, and also by one-way ANOVA for repeated measures at the assumed level of 0.05.

RESULTS

With iontophoresis, AXR(1) occurred within 1 min and 30 sec (SOT). After 30 sec, it reached a plateau, which lasted for 3 min (Fig. 3). DIR(2) appeared following AXR(1) and sustained for 5 min, which was the end of measurement period. AXR(2) declined to baseline level at about the time when DIR(2) was at its initial peak. Preliminary oral and skin temperatures were higher in South Koreans than in Africans ($P<0.01$), and both showed slight elevation throughout the recording period. At the end of iontophoresis, the skin temperature in the Africans decreased, but remained high in South Koreans. Skin temperature within the proximity of the capsule rose following sweat onset. No change was noted in areas 10 cm distal to iontophoretic site. SOT was 0.91 min ($P<0.01$) earlier in South Koreans (Fig. 4). The axon reflex sweat volume of nicotine receptor activity AXR(1) and sweat volume of muscarinic receptor activity DIR(2) were 79% and 53% ($P<0.01$), respectively, greater among South Koreans (Figs. 5 and 6).

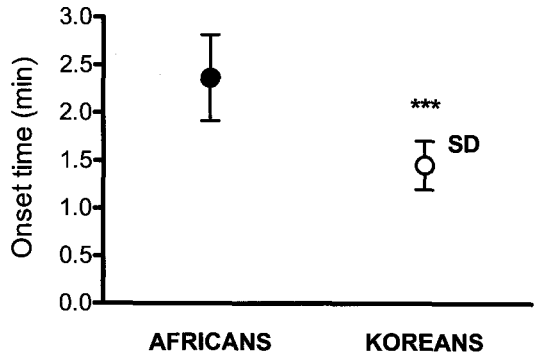

Fig. 4. Comparison of the sweat onset-time between tropical Africans (2.36±0.45 mim) and temperate South Koreans (1.45±0.25 mim). Values are expressed as means±SD.

DISCUSSION

Tropical inhabitants lose heat by radiation, convection, conduction and non- excessive sweating which are convenient mechanisms in maintaining body fluid and osmolarity (Matsumoto et al, 1997). In the present study, QSART findings revealed a longer onset-time and smaller AXR and DIR responses in the Africans than the South Koreans. These results are in support of the previous findings that the reduced sudomotor function in tropical natives is attributed to the suppression of both central sudomotor mechanism (upward threshold shift for sweating) and sweat gland sensitivity to ACh (Lee et al, 1997). Additionally, these results are in fair concordance with other reports, in which the diminished sweating among the tropical natives was attributed to acclimation of central thermoregulatory mechanisms to heat and depression of thermal sweating after repeated ACh iontophoresis was shown (Chen & Elizondo, 1974; Ogawa et al, 1993). These results also suggest that sweat glands of tropical subjects can be desensitized by repeated exposure to ACh secreted from sudomotor nerve terminals through long-term residence in tropical areas. Sweat glands may not react to certain kind of neural impulses, as indicated by some kind of subthreshold neural impulses originating from the central nervous system in the absence of visible sweating (Ogawa & Bullard, 1972). However, it is known that local heating facilitates transmitter release at the neuroglandular junction and also augments responsiveness to the transmitter (Ogawa & Asayama, 1986). It is, therefore, postulated that the skin temperature is an important factor to modulate sweating response not only as an input to the central regulatory mechanisms, but also as a local effector for sweating to proceed, and that the lower temperature

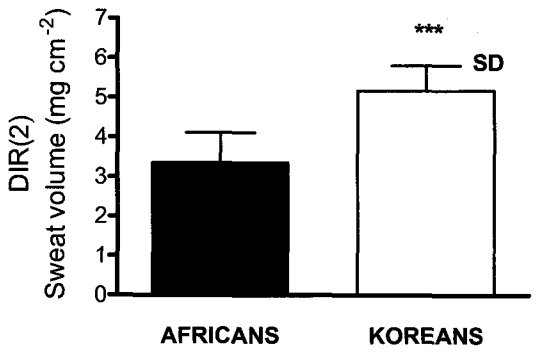

Fig. 5. Comparison of the sweat volume induced by ACh applied iontophoretically between tropical Africans (3.37±0.74 mg cm^{-2}) and temperate South Koreans (5.17±0.64 mg cm^{-2}). DIR areas under the curve for 6-11 min. Values are expressed as means±SD.

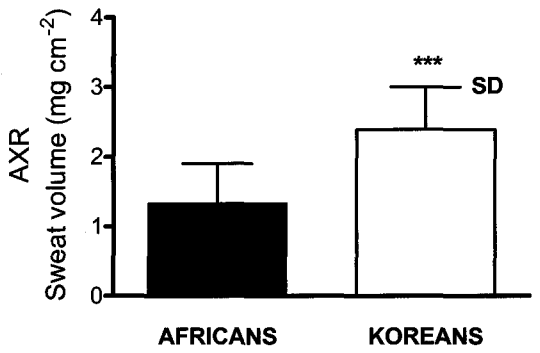

Fig. 6. Comparison of the sweat volume induced by ACh applied iontophoretically between tropical Africans (1.33±0.57 mg cm^{-2}) and temperate South Koreans (2.39±0.61 mg cm^{-2}). AXR areas under the curve for 0~5 min. Values are expressed as means±SD.

is not able to maximally stimulate sweat secretion in the Africans. These postulates can be explained by fact that DIR increased by 1.5% and AXR by 3%, when the temperature was elevated by 1°C (Low et al, 1983). In the present study, the Africans were studied upon arrival in Japan in order to minimize the influence of acclimation to cold environment, and the South Koreans were tested whenever they were available, since Korea is almost in the same geographical location as Japan (33~38 degree North latitude and 127 degree East longitude).

Total number of active sweat glands remains unchanged throughout life after about 2.5 years of age. As the body surface area enlarges, Sweat gland density decreases (Bar-Or, 1980) while sweat gland output increases (Lee et al, 1997). Based on the comparison between Filipinos and Japanese, who have fewer sweat glands than the former (Kuno, 1956), it is thought that the number of active sweat gland is dependent on the climate, where man lived during his developmental period. Additional evidence suggests that individuals who are judged to be poor sweaters have smaller gland size, low secretory activity, and decreased ACh gland sensitivity than physically fit individuals (Sato & Sato, 1983). It could be possible that, in addition to individual factors, racial differences play a big role in sweating mechanism. Although not examined in this study, it is highly possible that Africans have smaller size of sweat gland than Asians, thus resulting, in reduced sweating responses, as observed in this experiment.

In the present study, the axon reflex sweat volume of nicotine receptor activity and sweat volume of muscarinic receptor activity were found to be larger by 79% and 53%, respectively, in the South Koreans than the Africans, indicating diminished ACh sensitivity of African sweat glands in both recruitment and output.

As used in this experiment, sweat gland density indicates the percentage of sweat glands activated by ACh, which, according to Low et al (1992), is maximum 10% of the total. Iontophoretically applied to the skin, ACh induces vasodilatation (Morris & Shore, 1996), which occurs concurrently with sweat expulsions (Sugenoya et al, 1995). It has also been observed that the elevation of skin temperature accompanies sweating (Lee et al, 1997). In this study, local skin temperature rose with concomitant sweating during ACh iontophoresis. These results strongly support the idea that skin vasodilatation is accompanied with sudomotor activities. In conclusion, fewer activated sweat glands and lesser output of sweat gland to iontophoretically applied ACh were observed in the Africans, suggesting that the limited thermal sweating in the Africans is at least in partly attributed to the reduced glandular sensitivity to ACh through both recruitment of sweat glands and sweat output per gland.

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