Human ACE I/D polymorphism is associated with individual differences in exercise heat tolerance

Yuval Heled, Daniel S Moran, Liran Mendel, Arie Laor, Elon Pras, Yair Shapiro

Heller Institute of Medical Research, and the Danek Gartner Institute of Human Genetics, Tel Aviv University, Sheba Medical Center, Tel Hashomer, Israel

Key words: ACE polymorphism, Thermoregulation, Exercise, Heat Stress, Genetics

Corresponding Author:
Yuval Heled PhD
Heller Institute of Medical Research
Sheba Medical Center, Tel Hashomer
Tel: 972-3-5303564
Fax: 972-3-7377002
E mail: yheled@sheba.health.gov.il

Copyright (c) 2004 by the American Physiological Society.
Abstract

We hypothesized that there is an association between the ACE I/D polymorphism with the variability in exercise heat tolerance in humans. 58 Caucasian males were exposed to a 2h exercise heat tolerance test. We analyzed the association between their heat tolerance levels with the ACE DD (N=25) and I+ (N=33) genotypes and with various anthropometrical parameters and aerobic fitness. It was found that the relative changes in body core temperature, heart rate and heat storage during the 120 min exposure to exercise heat stress was consistently lower in the I+ genotype group compared to the DD genotype group (0.8±0.2°C vs. 1±0.1°C; p<0.05, 17.7±1.8 W M⁻² vs. 19.8±1.3 W M⁻²; p<0.05 and 33±7bpm vs. 44±5bpm, respectively; p=0.06). No significant association was found between heat strain response and the anthropometrical measurements or aerobic fitness in the various genotype groups. We suggest that the ACE I+ polymorphism may be considered as a possible candidate marker for increased heat tolerance.
Introduction

Physical exercise increases the rate of metabolic heat production and therefore, especially when performed in a hot environment, may cause hyperthermia and even fatal heat stroke (Epstein et al. 1999). In order to prevent hyperthermia, the balance between heat gain (metabolic and environmental) and heat dissipation must be maintained. Optimal balance in humans requires an efficient thermoregulatory system, which is mainly based on cardiovascular and sudomotor (sweating) functions (Gleeson 1998). However, it was found that in a normal thermoregulatory response to exercise heat stress, there is a wide range of variability (Frank et al. 2001; Havenith et al. 1998). Those individuals having a more severe heat-strain response to exercise in hot environments are defined as less tolerant to heat (Frank et al. 2001). The variability in heat tolerance in healthy humans has been shown to be related to gender (Sidman and Gallager 1995; Shapiro et al. 1980), physical aerobic fitness (Gisolfi and Robinson 1969; Havenith and van Middendrop 1990), and anthropometric measurements (Havenith et al. 1995). Nevertheless, it has been shown that even after adjustment of these phenotypic factors, individual differences in heat stress response still exist (Havenith 1997). Those individuals, especially among the young active population (athletes, soldiers, laborers), who are more susceptible to hyperthermia, are at risk to contract heat injuries.

When phenotypic characteristics fail to explain the variability in heat stress response, genotype characteristics become an attractive candidate. To the best of our knowledge, no study has yet directly characterized a possible genotype association with heat tolerance in human or animal models.

Over the last few years, some studies have suggested that the DNA sequence variation at the gene locus encoding angiotensin converting enzyme (ACE) is
associated with physical performance (Myerson et al. 1999; Gayagay et al. 1998) as well as with a number of pathological processes (Danser et al. 1995). Although still controversial, it was reported in a series of papers that the insertion (I) allele of the insertion/deletion (I/D) polymorphism in intron 16 of the ACE gene, is associated with better endurance performance whereas the DD genotype is associated with lower endurance performance (Montgomery et al. 1999; Gayagay et al. 1998; Myerson et al. 1999) and higher cardiovascular morbidity (Alvarez et al. 1998; Danser et al. 1995; Cambien et al. 1992). The DD genotype was also found to be associated with the highest plasma levels of ACE whereas the II polymorphism had the lowest levels of ACE (Tiret et al. 1992; Lindpaintner et al. 1995).

ACE is part of the Renin angiotensin system (RAS), which is found in both the circulation system (Finberg and Berlyne 1977) as well as various tissues (Danser et al. 1995; McKinley et al. 2003). The RAS is known to have an important role in thermoregulation via its influence on vascular mechanisms and fluid balance (Huang et al. 1985; Kosunen et al. 1976; Finberg et al. 1977). Although several studies pointed to the possible influence of the ACE on endurance performance and the important role of this enzyme in thermoregulation (McKinley et al. 2003; Kosunen et al. 1976), no study has directly analyzed the possible association between ACE genotypes to individual differences in heat stress response. We therefore hypothesized that it may be associated, directly or indirectly, with heat stress response. Therefore, in order to evaluate the potential contribution of the ACE genotype on heat stress response, we analyzed the association between the different ACE genotypes with the variability in exercise heat stress response in humans. Such an association may be an important marker, together with other phenotypic (and probably genotypic) factors, for predicting heat tolerance. Because of the reported advantage of the I allele with
cardiovascular function as well as metabolic efficiency (Myerson et al. 1999), we hypothesized that the existence of the I allele would be associated with better thermoregulatory function, and therefore with better heat stress response.

**Subjects and Methods**

58 healthy Caucasian male volunteers participated in the study. Their physical characteristics were (mean±SD), age 22±1 years, height 174±7 cm, weight 73±11 kg, BMI 24±3 kg/m², BSA 1.8±0.15 m², body fat 16.5±5%. All subjects gave informed consent before participation, and went through a medical examination. The study was approved by the health ministry committee of human genetic studies.

The volunteers arrived to our institute on three consecutive days at 0800 a.m. On the first day they went through a medical examination and anthropometric measurements which included weight, height and body fat %. Body fat was measured using multiple skinfold-thickness measurements that were performed by one experienced researcher. The mean of two skinfold-thickness measurements made with calipers at each of two sites (triceps and subscapular) (McArdle et al. 1991) was calculated to assess percentage of body fat. Body mass index (BMI) was calculated as weight (kg) divided by height (m). Body surface area (A_D) was calculated as:

\[
A_D (m^2) = W^{0.425} \cdot h^{0.725} \cdot 0.007184; \text{ where } W \text{ is weight (kg) and } h \text{ is height (cm)} \text{ (Du Bois and Du Bois 1989).}
\]

9cc of blood were taken from each subject for genetic analysis. On the second day the volunteers performed a maximal oxygen consumption test (VO_{2\text{max}}) in order to evaluate their aerobic fitness. VO_{2\text{max}} was determined by using on-line computer-assisted open circuit spirometry (Sensor Medics, Yorba Linda, USA) during incremental exercise on a motorized treadmill. The volunteers ran on the treadmill (5.5-6 mph), with the grade being increased every
2min by 2.5%. A valid VO\textsubscript{2max} was accepted when at least three of the following criteria were met: 1) a plateau in oxygen consumption with increasing work rate, 2) a respiratory exchange ratio (RQ) at maximal exercise > 1.10, 3) achievement of age predicted maximal heart rate (220-age), and 4) subjective exhaustion. Anaerobic threshold (AT), which is an important factor in aerobic fitness, was determined according to the minute ventilation/VO\textsubscript{2} ratio (VE/VO\textsubscript{2}) dynamics and from the respiratory exchange ratio (RQ≥1).

On the third day the subjects performed a heat tolerance test (HTT) in order to evaluate their physiological response to exercise heat stress. All tests were performed in the winter in order to prevent the effects of natural heat acclimatization. The HTT included walking on a treadmill (3.5mph) under heavy heat load (40°C, 40%rh) for two hours in a climatic chamber. During heat exposure, rectal temperature (T\textsubscript{re}) was continuously measured using a rectal thermistor YSI-401 (Yellow Springs Instruments – USA) inserted 10cm beyond the anal sphincter. Skin temperature was continuously measured at three sites (arm, chest and leg) using skin thermistors (YSI-409). Mean skin temperature (T\textsubscript{sk}) was calculated according to Burton’s equation (Burton 1935); T\textsubscript{sk}=0.5T\textsubscript{chest}+0.34T\textsubscript{leg}+0.16T\textsubscript{arm}. All measurements were continuously recorded by a computerized system (Envidas, Envitech, Israel) and displayed online on a screen. Heart rate (HR) was continuously monitored using a heart watch with data logger (Polar, USA INC., Stamford, CT, USA).

Average heat storage (S) in W m\textsuperscript{-2} was calculated from the equation S = [(m\textsubscript{b}⋅c\textsubscript{b})/A\textsubscript{D}] ⋅ (∆T\textsubscript{b}/∆t), where m\textsubscript{b} is the mean body weight (kg); c\textsubscript{b} is the specific heat constant (0.965 Wh\textsuperscript{-1} ⋅ °C\textsuperscript{-1} ⋅ kg\textsuperscript{-1}); A\textsubscript{D} is the DuBois surface area (m\textsuperscript{2}); ∆T\textsubscript{b} is the change in mean body temperature (°C) where T\textsubscript{b} =0.2T\textsubscript{sk} + 0.8T\textsubscript{re}; and ∆t is the exposure time (h) (Gonzalez 1988). Physiological Strain Index (PSI), based on T\textsubscript{re} and
HR and calculated on a universal scale of 0-10 (Moran et al. 1998), was calculated at 10-min intervals in order to assess the relative level of heat strain as follows:

$$\text{PSI} = 5(T_{\text{ret}} - T_{\text{re0}})(39.5 - T_{\text{re0}})^{-1} + 5(HR_t - HR_0)(180-HR_0)^{-1},$$

where $T_{\text{ret}}$ and $HR_t$ are simultaneous measurements taken at any time during heat exposure, $T_{\text{re0}}$ and $HR_0$ are the initial resting values, and 39.5 and 180 represent maximal core temperature ($^\circ$C) and heart rate (bpm), respectively. Sweat rate ($m_{\text{sw}}$) in g/h was calculated according to the difference between pre-test and post-test nude body weight, with the post-test weight corrected for fluid input and urine output, divided by the time of exposure.

Exclusion criteria: Any one of the following criteria was used for removal of a subject from heat exposure: $T_{\text{re}} > 39^\circ$C, $HR > 170$ bpm, nausea, weakness, dizziness, subject’s request, or the decision of the physician in charge.

The volunteers were instructed to rest for at least three days before the experiment, and to drink 0.5l of non-caffeine beverages on the night before and on each morning of the experiment in order to ensure body euhydration. Throughout the exercise period the subjects were allowed and encouraged to drink ad libitum.

DNA was extracted from peripheral leukocytes (obtained from 3 ml peripheral blood drawn into EDTA-containing tubes) using PUREGENE™ DNA purification kit (PUREGENE, Gentra systems, Minnesota, USA). DNA concentration was calculated from absorbance at 260nm measured by an Ultraspec 2000, UV/VIS spectrophotometer (Amersham Pharmacia Biotech, USA). Purity was estimated by the ratio of absorbance at 260/280nm.

Screening for the ACE I/D polymorphism was done by polymerase chain reaction (PCR). A set of primers designed to amplify the fragment encompassing the I/D polymorphism (the sense and antisense primers were 5’-TGGGACCACAGCGCCCGCCACTAC-3’ and 5’-CTGGAGACCACTCCCATCCTTCT-3’, respectively).
The PCR 190 bp fragment for the D allele and 490 bp fragment for the I allele were separated by electrophoresis using 2% agarose gel (Tamar, Israel) and visualized by ethidium bromide staining. As opposed to other studies (Dehnert et al. 2002), there was no difficulty in distinguishing between the DI and DD allele due to preferable amplification. Therefore, the three primer method was not used in this study. We focused in our analysis on the possible difference in the association between the heat strain response to the existence of the ACE I allele (I+) compared to the DD genotype.

**Statistical Analysis**

The significance of differences between continuous variables was assessed using the Student’s t test. The pooled form of statistics tested equality of variance; correction for unequal variances was performed when appropriate. All tests of significance were two tailed. Pearson correlation coefficients were used to analyze the interrelationship between anthropometric, physiologic and genetic variables. The relative contribution of the variability of the physiologic, anthropometric and genetic factors to heat tolerance was analyzed by multiple regression analysis. The independent variables used in the model were anthropometric, physiologic and genetic data recorded before the exercise heat exposure. A stepwise selection method was used to delineate a set of contributory variables to the variability of risk factors. Variables were added one by one to the model, and the F statistics for a variable to be added had to be significant at the 0.15 level. After a variable was added, the stepwise method looked at all the variables included in the model and deleted any variable that did not produce an F statistic significant at the 0.05 level. Only after this assessment was made and the necessary deletions accomplished could another variable be added to the model. The stepwise process ended either when none of the variables outside
the model had an F statistic significant at the 0.15 level, or every variable in the model was significant at the 0.05 level, or when the variable to be added to the model was the one just deleted from it. The relative contribution of an independent (predictor) variable to the relative change of a risk factor was measured by partial squared correlation. The significance of the genotype distribution was assessed by $\chi^2$ test. All data is presented as mean±SE. The data were analyzed using PROC REG of SAS 8.2 software.

**Results**

The anthropometrical and physiological results of the two genotype study groups (DD and I+) are presented in Table 1. No significant differences were found in the anthropometrical and physiological characteristics between the groups. It should also be emphasized that no differences in these characteristics were found between the three genotype groups (DD, DI and II) (data is not shown). Genotype frequencies of the genotype groups were in Hardy-Weinberg equilibrium, making selection bias less likely.

The associations between the two genotypes and the various physiological heat stress responses are presented in Table 2. No significant differences were found in the baseline physiological measurements ($T_{re0}$, $T_{sk0}$, $HR_0$) prior to exposure to exercise heat stress. However, after 120 min, all the physiological measurements that express heat strain level were higher in the DD genotype group compared to the I+ genotype group (although for the $T_{re}$ P value was only 0.08). When the differences ($\Delta$) between the physiological measurements at baseline to the end of the exercise period were calculated, it was clearly confirmed that heat strain was higher in the DD group compared to the I+ group. Calculated heat storage (S) during the exposure was also
significantly higher in the DD group compared to the I+ group. Worth noting, PSI was higher in the DD group compared to the I+ group, although not significantly.

When comparing the dynamics of T_r (Fig 1) and HR (Fig 2) during the 120 minute exercise heat exposure, we can see that the differences in the physiological strain between the two genotype groups is salient after the first 20 minutes and throughout the reminder of the exposure period.

Analysis of possible association differences between the three genotype groups (DD, DI, II) pointed to the same trend of results (Table 3). However, the small sampling did not allow for a significant statistical analysis.

No association was found between any of the baseline anthropometrical and physiological parameters (Table 1) to the various genotypes.

None of the subjects was excluded from the study.

Discussion

In the present study we have shown for the first time that the existence of the I allele (I+) of the human ACE gene is associated with increased heat tolerance during exposure to exercise heat stress. It was also found that the homozygosity of the II allele had the best heat tolerance results. This group was very small, however (n=7), so statistical analysis could not significantly support this result, although there was definitely a dose effect of the existence of the I allele.

Although various studies have pointed to the association of the ACE I allele with better endurance training effects and performance (Montgomery et al. 1999), similar to other studies (Taylor et al. 1999), no significant association between aerobic fitness and the ACE genotype was found in the present study.
Aerobic fitness and body morphometry are known as important factors in determining exercise heat tolerance (Wyndham et al. 1970; Havenith et al. 1995). Since no differences were found in these factors between the study groups, and since no association was found between any of these factors to the heat strain response, it may be suggested that the effects of the ACE genotype on exercise heat stress response do not result indirectly from higher aerobic fitness and/or differences in body composition. Although we can point to some possible mechanisms, it should be emphasized that, at this point, any attempts to clearly explain an association of the ACE I/D polymorphism with heat tolerance must remain speculative. ACE is an important part of the RAS system. This system, which is found in both the circulation (Finberg and Berlyne 1977) as well as various tissues (Danser et al. 1995; McKinley et al. 2003), has been shown to play an important role in thermoregulatory responses to exercise heat stress (Huang et al. 1985; Kosunen et al. 1976; Finberg and Berlyne 1977). Tissue RAS is part of the mechanisms that are responsible for precise matching of tissue blood flow, tissue oxygenation, tissue work, and tissue growth, while the circulating RAS, consisting of secretion of kidney-derived renin into the systemic circulation, mainly provides control of blood pressure (Myerson et al. 1999). The effect of ACE genotype on heat tolerance might be mediated through several different mechanisms. In the systemic endocrine level the mechanism may be associated with the different plasma levels of ACE, and therefore of Angiotensin II (Ang II) in the different genotype groups. It has been reported that DD polymorphism is associated with higher serum ACE and therefore with higher Ang II levels that may be connected to increased susceptibility to high blood pressure and cardiovascular morbidity (Danser et al. 1995; Cambien et al. 1992). Since the vasomotor function has an important role in the thermoregulatory mechanism (Moran et al. 1996), the
vulnerability to cardiovascular morbidity, and therefore to decreased function, might be a possible explanation for the mechanism by which different ACE genotypes influence the thermoregulatory response to exercise heat stress. It is interesting to note in this context, that although significant differences were found in most parameters of heat stress response, no differences were found in sweat rates between the groups. This fact may strengthen our hypothesis regarding the advantage of the cardiovascular function in the I+ group. Since no changes in the evaporation rate are expected between the groups, the main candidate mechanism that influences the thermoregulatory function is the cardiovascular system. It is also interesting to note, in this context, that administration of Ang II blockade to 6 men and 3 women in another study was not found to impair the thermoregulatory responses during exercise in the heat (Mittleman KD 1996). These results may weaken our present suggested mechanism, although, scientifically, using acute administration of the drug can not necessarily be compared to our methodology, results and mechanisms. It should also be mentioned that a different hypothesis was previously published (Moskowitz DW 1996). This hypothesis claimed that the ACE DD polymorphism which may be associated with the predisposition to hypertension in the Sub-Saharan Africans is also responsible to their better survival in extreme heat conditions. This hypothesis, however, dealt with a specific ethnic group with no suggested mechanisms.

In the central system the RAS have been found to have a local influence on the brain thermoregulatory center (Huang et al. 1985; McKinley et al. 2003). Although not yet extensively studied, ACE polymorphism might therefore play a role in this regulatory level as well.

In muscle tissue it has been suggested that local RAS have an important metabolic effect, were lower ACE activity, such as in the existence of the I allele
(Danser AH et al. 1995) improves muscle metabolic efficiency (Myerson et al. 1999). We suggest, therefore, that this mechanism may also be associated with reducing exercise heat stress response.

It is interesting to note, however, that the increased metabolic efficiency was not expressed in aerobic fitness of the different genotype groups in the present study. We therefore suggest that since aerobic fitness only partly influences heat tolerance, this genotype may be at an advantage, especially during situations of high heat stress.

Although various possible mechanisms have been suggested, it should be noted that the thermoregulatory process involves complex mechanisms and probably results from multifactorial polygenic characteristics with the ACE genotype only a part of them. These assumptions should be further studied.

Our data should also be interpreted with caution, since not all of the results were significant (although the trend was definitely consistent), the sample was relatively small, and only Caucasian males were studied.

In conclusion, it is proposed that a genetic factor associated with the ACE I allele in young Caucasian males might provide an advantage during exercise heat stress. More studies are required in order to decide whether the existence of the ACE I allele may be a candidate prediction marker for better tolerance to exercise heat stress.
References


Burton AC (1935) Human calorimetry II. The average temperature of the tissues of the body 9:261-280


Wyndham CH, Strydom NB, Rensburg AJV, Benade AJS, Heyns AJ (1970) Relation between VO$_{2\text{max}}$ and body temperature in hot humid air condition. J Appl Physiol 29:45-50
Table 1 Anthropometric and physiological characteristics (mean ±SE) of the DD and I+ genotype groups of the ACE gene; BMI- body mass index, BSA – body surface area, VO\textsubscript{max} - maximal oxygen consumption, AT- anaerobic threshold.

Table 2 The association between the two ACE genotype groups (DD and I+) with the baseline physiological levels and the physiological heat strain responses after exposure to a 120 min exercise heat stress (mean±SE). \(T_{re0}\) – baseline rectal temperature; \(T_{sk0}\) – baseline mean skin temperature; \(HR_{0}\) baseline HR; \(T_{re120}, T_{sk120}\) and \(HR_{120}\) – rectal temperature, mean skin temperature and HR after 120 min, respectively; \(\Delta T_{re}, \Delta T_{sk}, \Delta HR\) – the difference between baseline and 120 min rectal temperature, mean skin temperature and HR, respectively; PSI – physiological strain index; S – heat storage; \(m_{sw}\) – sweat rate. *When P was lower than 0.1 the precise result was also recorded.

Table 3 The association between the three ACE genotype groups (DD, DI and I+) with the baseline physiological levels and the physiological heat strain responses after exposure to a 120 min exercise heat stress (mean±SE). \(T_{re0}\) – baseline rectal temperature; \(T_{sk0}\) – baseline mean skin temperature; \(HR_{0}\) baseline HR; \(T_{re120}, T_{sk120}\) and \(HR_{120}\) – rectal temperature, mean skin temperature and HR after 120 min, respectively; \(\Delta T_{re}, \Delta T_{sk}, \Delta HR\) – the difference between baseline and 120 min rectal temperature, mean skin temperature and HR, respectively; PSI – physiological strain index; S – heat storage; \(m_{sw}\) – sweat rate. Because of the low sampling no statistical analysis was done (see text).

Fig. 1 The dynamics of \(T_{re}\) during the 120 min exposure to exercise heat stress in the two genotype groups (DD and I+).

Fig. 2 The dynamics of HR during the 120 min exposure to exercise heat stress in the two genotype groups (DD and I+).
Table 1

<table>
<thead>
<tr>
<th>Measure/Genotype</th>
<th>DD (n=25)</th>
<th>I+ (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>71.7±2.3</td>
<td>72.9±4.4</td>
<td>NS</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>17.1±1.2</td>
<td>16±0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>176±1</td>
<td>175±1</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.2±0.6</td>
<td>23.9±0.6</td>
<td>NS</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.87±0.03</td>
<td>1.88±0.02</td>
<td>NS</td>
</tr>
<tr>
<td>BSA/Weight (m²/kg)</td>
<td>0.026±0.001</td>
<td>0.025±0.000</td>
<td>NS</td>
</tr>
<tr>
<td>VO₂max (ml/kg/min)</td>
<td>47.3±2.1</td>
<td>49.9±1.5</td>
<td>NS</td>
</tr>
<tr>
<td>AT (ml/kg/min)</td>
<td>33.5±1.2</td>
<td>35.5±1.3</td>
<td>NS</td>
</tr>
<tr>
<td>AT/VO₂max (%)</td>
<td>70.8±2</td>
<td>71.1±3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Measure/Genotype</th>
<th>DD (n=25)</th>
<th>I+ (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T₀&lt;sub&gt;re&lt;/sub&gt; (°C)</td>
<td>37±0.1</td>
<td>37±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>T₀&lt;sub&gt;sk&lt;/sub&gt; (°C)</td>
<td>35.5±0.3</td>
<td>35.6±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>HR₀ (bpm)</td>
<td>78±3</td>
<td>75±2</td>
<td>NS</td>
</tr>
<tr>
<td>T₁₂₀&lt;sub&gt;re&lt;/sub&gt; (°C)</td>
<td>38±0.1</td>
<td>37.8±0.1</td>
<td>P=0.08*</td>
</tr>
<tr>
<td>T₁₂₀&lt;sub&gt;sk&lt;/sub&gt; (°C)</td>
<td>37.4±0.1</td>
<td>37.0±0.1</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>HR₁₂₀ (bpm)</td>
<td>127±5</td>
<td>115±3</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>ΔT&lt;sub&gt;re&lt;/sub&gt; (°C)</td>
<td>1±0.1</td>
<td>0.8±0.2</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>ΔT&lt;sub&gt;sk&lt;/sub&gt; (°C)</td>
<td>1.9±0.2</td>
<td>1.6±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>ΔHR bpm</td>
<td>33±7</td>
<td>44±5</td>
<td>P=0.06*</td>
</tr>
<tr>
<td>PSI (units)</td>
<td>4.4±0.39</td>
<td>3.62±0.22</td>
<td>P= 0.08*</td>
</tr>
<tr>
<td>S (W·m⁻²)</td>
<td>19.8±1.3</td>
<td>17.7±1.8</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>m&lt;sub&gt;sw&lt;/sub&gt; (g/h)</td>
<td>660±28</td>
<td>648±31</td>
<td>P=NS</td>
</tr>
</tbody>
</table>
Table 3

<table>
<thead>
<tr>
<th>Measure / Genotype</th>
<th>DD (n=25)</th>
<th>DI (n=26)</th>
<th>II (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&lt;sub&gt;re0&lt;/sub&gt; (°C)</td>
<td>37±0.1</td>
<td>37.1±0.1</td>
<td>36.8±0.1</td>
</tr>
<tr>
<td>T&lt;sub&gt;sk0&lt;/sub&gt; (°C)</td>
<td>35.5±0.3</td>
<td>35.6±0.3</td>
<td>35.5±0.4</td>
</tr>
<tr>
<td>HR&lt;sub&gt;0&lt;/sub&gt; (bpm)</td>
<td>78±3</td>
<td>75±3</td>
<td>74±3</td>
</tr>
<tr>
<td>T&lt;sub&gt;re120&lt;/sub&gt; (°C)</td>
<td>38±0.1</td>
<td>37.9±0.1</td>
<td>37.6±0.1</td>
</tr>
<tr>
<td>T&lt;sub&gt;sk120&lt;/sub&gt; (°C)</td>
<td>37.4±0.1</td>
<td>37±0.1</td>
<td>36.9±0.3</td>
</tr>
<tr>
<td>HR&lt;sub&gt;120&lt;/sub&gt; (bpm)</td>
<td>127±5</td>
<td>117±3</td>
<td>108±7</td>
</tr>
<tr>
<td>ΔT&lt;sub&gt;re&lt;/sub&gt; (°C)</td>
<td>1±0.1</td>
<td>0.8±0.1</td>
<td>0.8±0.1</td>
</tr>
<tr>
<td>ΔT&lt;sub&gt;sk&lt;/sub&gt; (°C)</td>
<td>1.9±0.3</td>
<td>1.5±0.3</td>
<td>1.3±0.4</td>
</tr>
<tr>
<td>ΔHR (bpm)</td>
<td>55±7</td>
<td>45±4</td>
<td>34±6</td>
</tr>
<tr>
<td>PSI (units)</td>
<td>4.4±0.4</td>
<td>3.69±0.24</td>
<td>3.33±0.6</td>
</tr>
<tr>
<td>S (W·m&lt;sup&gt;-2&lt;/sup&gt;)</td>
<td>19.8±1.3</td>
<td>18.1±1</td>
<td>17.3±1.2</td>
</tr>
<tr>
<td>ms&lt;sub&gt;sv&lt;/sub&gt; (g/h)</td>
<td>660±28</td>
<td>644±33</td>
<td>670±99</td>
</tr>
</tbody>
</table>