The $\alpha$-adducin Gly460Trp polymorphism and the antihypertensive effects of exercise among men with high blood pressure

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ABSTRACT

The $\alpha$-adducin Gly460Trp polymorphism alters renal sodium transport and is associated with hypertension. Despite the immediate sodium- and volume-depleting effects of aerobic exercise, the influence of the $\alpha$-adducin Gly460Trp polymorphism on PEH (postexercise hypotension) has not been studied. In the present study we examined the effects of the $\alpha$-adducin Gly460Trp polymorphism on PEH among 48 men (42.6 ± 1.6 years; mean ± S.E.M.) with high BP (blood pressure; 144.0 ± 1.7/84.7 ± 1.1 mmHg). Subjects completed three experiments: non-exercise control and two cycle exercise sessions at 40 % (light exercise) and 60 % (moderate exercise) of maximal oxygen consumption. Subjects left the laboratory wearing an ambulatory BP monitor. PCR and restriction enzyme digestion determined the genotypes. No subjects had the Trp460Trp genotype due to the low frequency of 5 % in the population. Repeated measure ANCOVA tested whether BP differed over time between experimental conditions and genotypes (Gly460Gly, $n=36$; Gly460Trp, $n=12$). Among Gly460Gly genotypes, SBP (systolic BP) was reduced by 5.2 ± 1.4 mmHg after moderate exercise compared with non-exercise controls over 9 h ($P<0.01$). Among Gly460Trp genotypes, SBP was lowered by 7.8 ± 2.3 mmHg; after light exercise compared with non-exercise controls over 9 h ($P<0.05$). The SBP reductions after light exercise (0.6 ± 1.3 compared with 7.8 ± 2.3 mmHg; $P<0.05$) but not moderate exercise (5.2 ± 1.4 compared with 3.8 ± 2.4 mmHg; $P>0.05$) differed between the Gly460Gly and Gly460Trp genotypes respectively. Men with Gly460Gly had a reduced SBP after moderate exercise, whereas men with Gly460Trp had a reduced SBP after light exercise. However, only the SBP reductions after light exercise differed between genotypes. Our findings indicate that the $\alpha$-adducin Gly460Trp genotype may be useful in identifying men who have a reduced BP after lower intensity aerobic exercise.

INTRODUCTION

Adducin is an essential protein for assembly of the spectrin–actin network and cell signal transduction in the kidney [1,2]. Single nucleotide polymorphisms in genes encoding adducin account for 50 % of the difference in BP (blood pressure) levels between Milan hypertensive and normotensive rats. These differences are mediated by alterations in renal sodium handling [2,3]. In humans the ‘risk’ $\alpha$-adducin Trp$^{460}$ allele of the $\alpha$-adducin Gly460Trp polymorphism is associated with higher activity of the sodium pump, increased proximal renal tubular sodium reabsorption, and volume-expanded, low-renin hypertension [1–4]. The $\alpha$-adducin Trp$^{460}$ allele also demonstrates greater BP reductions in response to diuretic therapy and sensitivity to changes in sodium balance than the $\alpha$-adducin Gly$^{460}$ allele [4–6].

Key words: $\alpha$-adducin, blood pressure, hypertension, kidney, physical activity, polymorphism, postexercise hypotension, sodium.

Abbreviations: BMI, body mass index; BP, blood pressure; DBP, diastolic BP; HR, heart rate; PEH, postexercise hypotension; SBP, systolic BP; $\dot{V}O_{2}$max, maximum oxygen consumption.

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Aerobic exercise decreases BP by 5–7 mmHg [7,8] and is recommended as a non-pharmacological therapy to prevent, treat and control hypertension [7]. Some, if not all, of the BP-lowering effects of aerobic exercise training programmes are attributed to the acute or immediate BP benefits that result from an isolated exercise session termed PEH (postexercise hypotension) [8]. However, PEH does not occur in 25–33 % of people with hypertension [9]. The inherited tendency toward hypertension predominately resides in the kidney [10]. The renin–angiotensin–aldosterone system is a major BP regulatory system, therefore genetic variants that alter renal function are logical candidates to explain some of the individual variability in the BP response to exercise. Indeed, we recently reported that men with multiple risk alleles of selected renin–angiotensin–aldosterone system polymorphisms exhibited greater BP reductions after a session of lower intensity aerobic exercise compared with men with fewer risk alleles [11].

Despite the immediate sodium- and volume-depleting effects of aerobic exercise, the influence of the α-adducin Gly460Trp polymorphism on PEH has not been studied. Therefore, in the present study, we examined the effects of the α-adducin Gly460Trp polymorphism on the BP response to acute dynamic exercise. Owing to the greater BP responsiveness of the α-adducin Trp460 allele to therapeutic intervention [4–6], we hypothesized that men who were carriers of the α-adducin Trp460 allele would manifest PEH to a larger degree than men with the α-adducin Gly460Gly genotype.

### MATERIALS AND METHODS

#### Subjects

Volunteers were 48 men between 18 and 55 years of age with high normal to Stage 1 hypertension [SBP (systolic BP) ≥ 130–139 mmHg and/or DBP (diastolic BP) ≥ 85–99 mmHg]. Subjects were excluded if they had a SBP ≥ 160 mmHg and/or DBP ≥ 100 mmHg, symptomatic atherosclerotic cardiovascular disease, diabetes mellitus, asthma, thyroid dysfunction, pancreatitis, acute illness and/or were on antidepressant medication. Subjects were generally sedentary, had no physical limitations prohibiting exercise and did not smoke. Subjects signed an informed consent form, which was approved by the Institutional Review Boards of the University of Connecticut and Hartford Hospital.

Any medication potentially influencing the BP response to exercise, including antihypertensives, antilipemic agents, anticoagulants, non-steroidal anti-inflammatory agents, nutritional supplements (other than a 1-a-day vitamins), cold medication and herbal supplements were stopped at least 4 weeks prior to any testing. When medication for high BP was withdrawn, study investigators regularly monitored the BP of the participants during the washout period. Men in whom the cessation of antihypertensive medication resulted in a resting SBP ≥ 160 mmHg and/or DBP ≥ 100 mmHg were excluded from the study.

#### Procedures

The methods used in this investigation have been published previously [11–13]. In brief, subjects participated in an orientation session to familiarize them with the study and to ensure that their BP met the inclusion criteria. BP was measured three times, 5 min apart in each arm by auscultation and averaged. Body composition measurements were waist circumference, and height and weight on a standard balance beam scale (Model 339, Detecto), which was used to calculate the BMI (body mass index).

During the orientation session, participants were instructed to maintain their usual diet throughout the study with the exception of a standard pre-testing meal of 240 ml (1 cup) of low-fibre cereal or a choice of one of the following: two slices of white toast, an English muffin or a 8.9 cm (3.5 in) diameter plain bagel. This meal was accompanied by 120 ml (4 oz) of 2 %, 1 % or skimmed milk and 240 ml (8 oz) of orange juice. The entire meal was consumed 2 h prior to any testing session. Participants were also instructed to refrain from any caffeinated beverage on the morning of all testing sessions and to drink caffeinated (< 480 ml (2 cups)) and alcoholic (< 2 drinks/day) beverages in moderation throughout participation in the study. Weight maintenance, defined as ± 2.25 kg (5 lb) of orientation weight, was used as an indication that volunteers were adhering to their usual dietary patterns throughout the study. Men were weighed prior to the graded cardiopulmonary exercise test and each of the three experiments to ensure weight maintenance.

At the conclusion of the orientation session an ambulatory BP monitor (Accutracker II automatic noninvasive ambulatory BP monitor, Suntech Medical Instruments) was attached to each subject to familiarize them with the unit and ensure their BP met the study inclusion criteria. The same investigator attached the ambulatory BP monitor to all subjects, and then performed a calibration check with a mercury sphygmomanometer using a t-tubule according to the manufacture’s guidelines. The calibration check consisted of three test runs to ensure that three successive ambulatory BP measurements were within 5 mmHg of the auscultatory BP measurements. The intra-investigator coefficient of variation between the ambulatory and auscultatory BP measurements made during these test runs was 0.7 % for SBP and 1.8 % for DBP. The monitor was programmed to record BP and HR (heart rate) approximately every 20 min. BP and HR were taken three times an hour until 23.00 hours. All subjects left the laboratory with instructions to proceed with their usual activities, not to engage in formal exercise for the remainder of the day.
to leave their arm still while the monitor was recording and to return the monitor the following day. The computerized ambulatory BP recordings were considered acceptable if at least 80% of the potential BP readings were obtained. The Accutrack II ambulatory BP monitor has demonstrated less disparity and closer levels of agreement with intra-arterial BP than clinicians’ measurements at rest and during exercise [14,15] and greater reproducibility over office determinations [16].

Participants then completed a maximum graded exercise stress test that was used to calculate the workload of the exercise sessions. The graded exercise stress test was performed on a cycle ergometer (Monark Ergomedic 818E) and consisted of continuous cycling at a constant cadence of 60 rev./min with the resistance increased by 0.5 kp (30 W) every 2 min until volitional exhaustion. \( V_{O_2}\max \) (maximal oxygen consumption) was determined with breath-by-breath analysis of expired gases (Sensormedics Vmax 29 Metabolic Chart; SensorMedics). HR was recorded continuously with a 12-lead ECG system. The same investigator measured BP by auscultation 30 s prior to the conclusion of each 2 min incremental stage. At the conclusion of the graded exercise stress test, subjects were again attached to the same ambulatory monitor to further acquaint them with the equipment.

Prior to the three experiments, a 20 gauge, 32 mm indwelling Teflon catheter was inserted into the antecubital vein of the right arm and kept patent with a 0.9% saline solution. Each experiment began with a 20 min baseline period of seated rest. During the baseline period, the HR and BP were recorded every 2 min. The HR was measured with a HR monitor (Model 1902750; Polar Electro), and BP was measured by auscultation. The same study investigator took all of the BP measurements during every experiment for all of the subjects. The BP measurements taken during the baseline period were averaged, and these values were designated as the baseline BP.

Following the 20 min baseline period, volunteers performed three 40 min experiments in a random order: a 40 min non-exercise control session of seated rest, followed by two 30 min exercise bouts on an upright cycle ergometer performed at light (40% \( V_{O_2}\max \), light exercise; equivalent in physical exertion to leisurely walking) and moderate (60% \( V_{O_2}\max \), moderate exercise; equivalent in physical exertion to jogging) intensity with a 5 min warm-up and cool down of free wheeling to total 40 min of exercise. The experiments were blinded to the subject until the conclusion of the baseline period and separated by at least 48 h. Subjects left the laboratory wearing an ambulatory monitor at 23.00 hours with an average hook up time of 12.5 h.

**Blood sampling and analysis**

Blood samples were drawn into anticoagulated EDTA tubes after the baseline period, at 30 min of each 40 min experiment, and at 15 and 45 min after the conclusion of the experimental sessions while still in the laboratory but prior to attachment to the ambulatory BP monitor. Samples were centrifuged at 2500 g at 23°C for 6 min. Plasma samples were transferred to storage tubes and frozen at −80°C until analysis. Direct renin concentrations were measured by RIA and performed with low-, normal- and high-quality control values in a commercial laboratory (Quest Diagnostics).

**Genotype analysis**

DNA was isolated from anticoagulated EDTA blood samples and genotyped for the \( \alpha \)-adducin Gly460Trp polymorphism [ADD1NM_014189.2:c.1566G>T(p.Gly460Trp)]. DNA was purified for PCR analysis using the Puregene DNA Isolation Kit (Gentra Systems). A primer set that has been described previously [17] was used to determine the \( \alpha \)-adducin Gly460Trp genotypes.

**Statistical analyses**

A mean replacement strategy was performed for the small number of missing BP values. Ambulatory BP values were then averaged at hourly intervals. No subject was found with the \( \alpha \)-adducin Trp460Trp genotype due to the low frequency of 5% in the general population [17]. Therefore descriptive statistics (means ± S.E.M.) and bivariate correlations were generated on all study variables for the total sample and for \( \alpha \)-adducin Gly460Trp genotype groups, i.e. Gly460Gly and Gly460Trp. Independent Student’s \( t \) tests determined whether there were differences in subject characteristics between the \( \alpha \)-adducin Gly460Trp genotype groups.

Repeated measure ANCOVA (analysis of covariance) determined whether BP differed over time within and between experimental conditions (non-exercise control, light exercise and moderate exercise) and the \( \alpha \)-adducin Gly460Trp genotype groups. The covariates separately examined in these analyses were waist circumference, BMI, age and \( V_{O_2}\max \). All were found not to alter the main BP effects so that only unadjusted BP data are reported over the course of 9 h, the observed duration of PEH when all men were awake and out-of-bed [12]. A \( \chi^2 \) test, was used to examine whether there were differences between the number of men who had a lowered BP after light exercise or moderate exercise among the \( \alpha \)-adducin Gly460Trp genotype groups. Repeated measure ANCOVA was also used to test whether renin differed over time within and between the experimental conditions and the \( \alpha \)-adducin Gly460Trp genotype groups.

Sample size power calculations were conducted assuming a multivariate approach to analysing repeated measure BP data [18]. A series of power assessments were fitted to estimated BP means ± S.D. for the \( \alpha \)-adducin Gly460Trp genotype groups based on our previous work [11–13]. This previous research indicated that a moderate
effect size could be expected between the α-adducin Gly460Trp genotype groups with conservative estimates of 0.50 for BP correlations across time. On the basis of these assumptions, sample sizes of 15 men in each α-adducin Gly460Trp genotype group would be sufficient to provide adequate power for detecting a SBP within-method effect (non-exercise control, light exercise and moderate exercise) with a power of 0.815 and a SBP method by α-adducin Gly460Trp genotype interaction effect between α-adducin Gly460Trp genotype groups with a power of 0.740.

All statistical analyses were performed with Statistical Package for the Social Sciences for Windows version 14.0, with \( P < 0.05 \) established as the level of significance. BP and renin results are reported first for the within-method effect (non-exercise control, light exercise and moderate exercise) for the preliminary assessment of change over time. Results are then presented for the primary research question involving the method by genotype interaction effect between α-adducin Gly460Trp genotype groups.

### RESULTS

#### Subjects

Subjects (\( n = 48 \)) were overweight Caucasian men with high normal to Stage 1 hypertension (Table 1). Men were middle-aged with below average physical fitness [19]. Mean baseline renin that was taken prior to the start of the experiments was within normal limits. Three quarters of the sample were α-adducin Gly460Gly homozygotes and one quarter were Gly460Trp heterozygotes. Physical characteristics were not different among the α-adducin Gly460Trp polymorphism genotype groups (\( P > 0.05 \) (Table 1).

#### Total sample BP response

The total sample BP findings have been reported previously and are summarized for purposes of reference [12]. Among the total sample, SBP increased and DBP decreased from baseline following all experimental conditions over the course of 9 h (\( P < 0.001 \)) (Table 2). However, SBP was lowered by 4.7 mmHg after moderate exercise (\( P < 0.01 \)) and by 4.2 mmHg after light exercise (\( P < 0.05 \)) compared with the non-exercise control condition. The DBP response was not different between exercise and non-exercise controls over 9 h (\( P > 0.05 \)).

#### α-Adducin Gly460Trp polymorphism

##### BP effects

**Within-method (exercise intensity) effect**

Among men with the α-adducin Gly460Gly genotype, SBP was reduced from baseline SBP by a mean of

### Table 1 Physical characteristics of the complete study sample and of the α-adducin Gly460Trp polymorphism genotype groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n = 48)</th>
<th>Gly460Gly (n = 36)</th>
<th>Gly460Trp (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.7 ± 1.6</td>
<td>42.6 ± 1.6</td>
<td>47.0 ± 2.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.6 ± 0.7</td>
<td>29.4 ± 0.8</td>
<td>30.2 ± 1.3</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>102.3 ± 2.0</td>
<td>101.9 ± 2.4</td>
<td>103.6 ± 3.9</td>
</tr>
<tr>
<td>24-h Ambulatory SBP (mmHg)</td>
<td>141.4 ± 1.5</td>
<td>140.3 ± 1.8</td>
<td>144.6 ± 2.8</td>
</tr>
<tr>
<td>24-h Ambulatory DBP (mmHg)</td>
<td>83.0 ± 1.0</td>
<td>82.2 ± 1.1</td>
<td>85.3 ± 2.5</td>
</tr>
<tr>
<td>Ambulatory awake SBP (mmHg)</td>
<td>145.1 ± 1.5</td>
<td>144.0 ± 1.7</td>
<td>148.0 ± 2.8</td>
</tr>
<tr>
<td>Ambulatory awake DBP (mmHg)</td>
<td>85.5 ± 1.1</td>
<td>84.7 ± 1.1</td>
<td>88.1 ± 2.6</td>
</tr>
<tr>
<td>Relative ( \dot{V}O_2 ) max (ml · kg⁻¹ · body weight · min⁻¹)</td>
<td>31.1 ± 0.9</td>
<td>31.7 ± 1.1</td>
<td>29.2 ± 1.7</td>
</tr>
<tr>
<td>Renin (μ-unit/ml)</td>
<td>20.7 ± 0.9</td>
<td>21.4 ± 2.2</td>
<td>18.4 ± 4.1</td>
</tr>
</tbody>
</table>

Table 2 BP change from baseline after exercise and in non-exercise controls over 9 h among the total sample and in the α-adducin Gly460Trp polymorphism genotype groups

Baseline is the BP (mean ± S.E.M.) of the pre-experiment 20 min period of seated rest. Post—pre-experiment change is the mean ± S.E.M. of the hourly BP averages over the course of 9 h after the experiments minus the average baseline BP. *\( P < 0.05 \) and †\( P < 0.01 \) compared with non-exercise control; ‡\( P < 0.05 \), compared with Gly460Gly during light exercise.

<table>
<thead>
<tr>
<th></th>
<th>SBP response (mmHg)</th>
<th>DBP response (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-exercise</td>
<td>Moderate exercise</td>
</tr>
<tr>
<td>Total sample (n = 48) Baseline</td>
<td>125.2 ± 1.6</td>
<td>12.0 ± 1.3</td>
</tr>
<tr>
<td>Post—pre-experiment change</td>
<td>7.2 ± 1.5†</td>
<td>10.5 ± 1.4</td>
</tr>
<tr>
<td>Gly460Gly (n = 36) Baseline</td>
<td>124.5 ± 1.8</td>
<td>12.7 ± 3.8</td>
</tr>
<tr>
<td>Post—pre-experiment change</td>
<td>7.4 ± 1.5†</td>
<td>10.5 ± 1.4</td>
</tr>
<tr>
<td>Gly460Trp (n = 12) Baseline</td>
<td>127.2 ± 3.8</td>
<td>13.4 ± 2.0</td>
</tr>
<tr>
<td>Post—pre-experiment change</td>
<td>13.4 ± 2.0</td>
<td>9.6 ± 2.5</td>
</tr>
</tbody>
</table>

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5.2 mmHg after moderate exercise compared with non-exercise controls over 9 h (\(P < 0.01\); Table 2 and Figure 1a). These changes resulted in a lower average SBP after moderate exercise (130.7 ± 1.7 mmHg) compared with non-exercise controls (133.9 ± 1.9 mmHg) over this time period (\(P < 0.001\)). In contrast, neither the SBP change from baseline (Table 2 and Figure 2a) nor the average SBP was different after light exercise (132.6 ± 1.8 mmHg) compared with non-exercise controls among men with the \(\alpha\)-adducin Gly460Gly genotype over 9 h (\(P > 0.05\)). Under these conditions, the DBP response was not different in the \(\alpha\)-adducin Gly460Gly homozygotes over 9 h (\(P > 0.05\)) (Table 2).

Among men with the \(\alpha\)-adducin Gly460Trp genotype, the SBP was lowered by 7.8 mmHg after light exercise compared with non-exercise controls over 9 h (\(P < 0.05\)) (Table 2 and Figure 2b) and the average SBP tended to be lower after light exercise (134.1 ± 3.1 mmHg) compared with non-exercise controls (136.8 ± 2.8 mmHg; \(P = 0.059\)). In contrast, neither the SBP change from baseline (Table 2 and Figure 1b) nor the average SBP was different after moderate exercise (136.7 ± 3.8 mmHg) compared with non-exercise controls among \(\alpha\)-adducin Gly460Trp heterozygotes over 9 h (\(P > 0.05\)). Under these conditions, the DBP response was not different among men with the \(\alpha\)-adducin Gly460Trp genotype over 9 h (\(P > 0.05\); Table 2).

**Interaction method (exercise intensity) by genotype effect**

Only the SBP reductions after light exercise [0.6 ± 1.3 mmHg (Figure 2a)] compared with 7.8 ± 2.3 mmHg (Figure 2b); \(P < 0.05\)] but not moderate exercise [5.2 ± 1.4 mmHg (Figure 1a)] compared with 3.8 ± 2.4 mmHg (Figure 1b); \(P > 0.05\)] compared with non-exercise controls differed between the \(\alpha\)-adducin Gly460Gly
and Gly460Trp genotype groups respectively (Table 2). In addition, the α-adducin Gly460Trp polymorphism differentiated among men with lowered SBP after exercise compared with non-exercise controls; 83% of the men with the α-adducin Gly460Trp genotype had a reduced SBP after light exercise compared with 56% of those with the α-adducin Gly460Gly genotype (P = 0.081). Approx. 60% of the men had a lowered SBP after moderate exercise compared with non-exercise controls, regardless of the α-adducin Gly460Gly or Gly460Trp genotype (P = 0.424).

α-Adducin Gly460Trp polymorphism renin effects

Figure 3 shows the change in renin from baseline during and after exercise and in non-exercise controls by α-adducin Gly460Trp genotypes. Among men with the α-adducin Gly460Gly genotype, renin increased during and after exercise, and the increase was greater with moderate exercise than light exercise (P < 0.001). These changes resulted in a higher average renin concentration with moderate exercise (31.4 ± 3.95 µ-units/ml) than in non-exercise controls (24.2 ± 2.9 µ-units/ml); however, there was no difference in the average renin concentration between light exercise (25.7 ± 2.9 µ-units/ml) and moderate exercise or non-exercise controls (P ≥ 0.05) among α-adducin Gly460Gly homozygotes. Among men with the α-adducin Gly460Trp genotype, renin increased during and after exercise compared with non-exercise controls (P < 0.05). Nonetheless, average renin was no different after moderate exercise (20.3 ± 4.1 µ-units/ml) and light exercise (22.3 ± 5.7 µ-units/ml) compared with non-exercise controls (21.2 ± 6.3 µ-units/ml) (P ≥ 0.05). Only the increase in renin after moderate exercise (7.3 ± 1.3 compared with 2.7 ± 2.2 µ-units/ml; P < 0.05), but not light exercise (3.1 ± 0.8 compared with 2.0 ± 1.4 µ-units/ml; P ≥ 0.05), compared with non-exercise controls differed between the α-adducin Gly460Gly and Gly460Trp genotype groups respectively.

DISCUSSION

In the present study we examined the effects of the α-adducin Gly460Trp polymorphism on the BP response immediately following aerobic exercise performed at light intensity and moderate intensity among 48 men with high normal to Stage 1 hypertension. The major findings of the study were that the α-adducin Gly460Trp polymorphism interacted with exercise intensity to alter the SBP response to acute dynamic exercise. In α-adducin Gly460Gly homozygotes, SBP decreased by 5 mmHg after moderate exercise; whereas among α-adducin Gly460Trp heterozygotes SBP decreased by 8 mmHg after light exercise, compared with non-exercise controls. However, only the SBP reductions after light exercise differed between the α-adducin Gly460Trp (8 mmHg) and Gly460Gly (1 mmHg) genotypes. The α-adducin Gly460Trp genotype appeared to differentiate between men who responded to light exercise as antihypertensive therapy; with 83% of the men with this genotype having a lowered SBP after light exercise compared with only 56% of those with the α-adducin Gly460Gly genotype. Approx. 60% of the men responded to the SBP-lowering effects of moderate exercise, regardless of α-adducin Gly460Gly or Gly460Trp genotype.
Our present results suggest that the α-adducin Gly460Trp polymorphism may be useful in identifying men who have a reduced SBP after aerobic exercise. In particular, the α-adducin Gly460Trp genotype appeared to identify men who responded to lower intensity (light exercise) aerobic exercise as antihypertensive therapy. These observations are novel and have clinical and public health significance because lower intensity, aerobic exercise, equivalent in physical exertion to leisurely walking, is enjoyable, well-tolerated and safe for people with high BP [8,12]. Our findings are hypothesis-generating and need to be validated in a larger sample containing sufficient numbers of all three α-adducin Gly460Trp polymorphism genotypes. Nonetheless, they support the notion that genetic information may be used by clinicians to individualize the prescription of exercise to maximize its effectiveness as an antihypertensive therapy.

Carriers of the Trp460 allele of the α-adducin Gly460Trp polymorphism have an increased risk of hypertension [2,3,17], notably volume-expanded low-renin hypertension [4]. People with the Trp460 allele have a lowered BP to greater levels in response to diuretic therapy [5], and are more responsive to sodium challenges [4] compared with α-adducin Gly460Gly homozygotes. These observations are attributed to associations of the Trp460 allele with increased Na+/K+-ATPase activity and renal tubular sodium reabsorption as well as elevated levels of plasma ouabain, a natriuretic hormone that has vasoconstrictive properties [1–3,20–22]. These alterations in renal sodium handling occur in a graded fashion based upon the number of copies of the α-adducin Gly460Trp allele. These reports suggest that men with the α-adducin Gly460Trp genotype may have even been more responsive to light exercise as an antihypertensive therapy than among men with the α-adducin Gly460Gly genotype. Nonetheless, how the BP of men with the α-adducin Gly460Trp genotype would have responded to light or moderate exercise remains unknown. The results from the present study are intriguing and biologically plausible; however, they need to be validated in a larger, more ethnically diverse sample of men and women containing sufficient numbers of subjects with all three α-adducin Gly460Trp polymorphism genotypes.

In summary, the major finding of the present study was that the α-adducin Gly460Trp polymorphism interacted with exercise intensity to alter the SBP response to acute dynamic exercise. Explanations for our findings appear to reside in the balance achieved between salt–volume and vasodilator–vasoconstrictor status after stressing the genotype with two different doses of exercise, i.e. moderate and light, and other genetic and environmental factors not known at the present time [11,13].

More researchers [24–26] than not [27] have found that adults with hypertension and low plasma renin levels have greater reductions in BP following endurance exercise training than those with higher renin levels. We did not find any statistically significant associations between baseline renin (Table 1), exercise-induced changes in renin, and the BP response to acute endurance exercise between the α-adducin Gly460Gly and Gly460Trp genotypes. Thus, the renin data obtained in the present study did not provide any insight into the reasons for our findings.

The present study is subject to several limitations. Our sample did not contain any men with the α-adducin Trp460Trp genotype due to its low frequency of approx. 5% in the general population. Alterations in renal sodium handling [1–3] and the BP response to diuretic therapy [5,6] occur in a graded fashion based upon the number of copies of the α-adducin Trp460 allele. These reports suggest that men with the α-adducin Gly460Trp genotype may have even been more responsive to light exercise as an antihypertensive therapy than among men with the α-adducin Gly460Gly genotype. Nonetheless, how the BP of men with the α-adducin Gly460Trp genotype would have responded to light or moderate exercise remains unknown. The results from the present study are intriguing and biologically plausible; however, they need to be validated in a larger, more ethnically diverse sample of men and women containing sufficient numbers of subjects with all three α-adducin Gly460Trp polymorphism genotypes.

In summary, the major finding of the present study was that the α-adducin Gly460Trp polymorphism interacted with exercise intensity to alter the SBP response to acute dynamic exercise. Explanations for our findings appear to reside in the balance achieved between salt–volume and vasodilator–vasoconstrictor status after stressing the genotype with two different doses of exercise, i.e. light and moderate. A long-term goal of research in the area of genetics and hypertension is to use genetic information to individualize antihypertensive treatment in order to maximize its effectiveness. Our results indicate that the α-adducin Gly460Trp polymorphism may be useful in identifying subsets of patients likely to benefit from the antihypertensive effects of aerobic exercise.

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