A Higher Cellular Sodium Turnover Rate in Cultured Skin Fibroblasts from Blacks

SATORU KURIYAMA, LASZLO HOPP, HIROKAZU TAMURA, NORMAN LASKER, AND ABRAHAM AVIV

SUMMARY Differences in cellular Na⁺ and K⁺ regulation may relate to the pathogenesis of essential hypertension and the predisposition of blacks to this disease. To explore these tenets, we examined several aspects of cellular Na⁺ homeostasis in serially passed, cultured skin fibroblasts from 30 subjects (15 hypertensive blacks and whites and normotensive subjects matched for sex, age, and race.) Fibroblasts from blacks demonstrated higher cellular Na⁺ turnover rates than did those from whites. This difference was expressed by accelerated Na⁺-K⁺ pump activity (ouabain-sensitive Na⁺ washout rate, 3.46 ± 0.216 for blacks vs 1.84 ± 0.283 mEq/L/min for whites; p = 0.0006) and a higher rate of cellular accumulation of Na⁺ in the presence of ouabain (0.964 ± 0.0743 vs 0.562 ± 0.0440 mEq/L/min for blacks and whites, respectively; p = 0.0045). Associated with these findings, fibroblasts from blacks had higher cellular Na⁺ concentration than did those from whites (9.78 ± 0.512 vs 7.50 ± 0.400 mEq/L; p = 0.0170, as measured by atomic absorption, and 7.84 ± 0.470 vs 5.03 ± 0.980 mEq/L; p = 0.0141, as derived from the equilibrium distribution ratio of ²²Na⁺). It is concluded that blacks differ from whites with respect to cellular Na⁺ turnover rate, which is evidenced by an increased Na⁺ influx and accelerated Na⁺-K⁺ pump activity in their fibroblasts. Our findings support the tenet that innate racial differences in cellular Na⁺ regulation may underlie the predisposition of blacks to hypertension. (Hypertension 11: 301-307, 1988)

KEY WORDS * Na⁺-K⁺ pump • cellular sodium • sodium uptake • sodium washout • essential hypertension

THE last decade has witnessed a burst of research using red blood cells (RBCs) as a model system to study cellular Na⁺-K⁺ homeostasis in essential hypertension (for review, see References 1-3). It has been speculated that abnormalities identified in RBCs from patients with essential hypertension or others predisposed to this disease represent a generalized phenomenon occurring in other cells, including vascular smooth muscle cells. Unfortunately, a major uncontrolled element in studying Na⁺-K⁺ regulation using RBCs is the influence of endogenous extracellular factors that can substantially modify the behavior of several Na⁺-K⁺ transport systems. Thus, it is difficult to differentiate innate differences in these cells from the influence of circulating factors that may contribute to the predisposition to essential hypertension. Research using cultured cells introduces a new dimension to studies addressing the pathophysiology of essential hypertension, as these cells are grown under well-defined conditions that obviate the potential effects of extracellular factors that may differ between hypertensive and normotensive persons. Provided that the in vitro conditions do not alter in vivo characteristics of cells that distinguish hypertensive from normotensive persons, studies using cultured cells are well suited to identify intrinsic cellular variations that may predispose to essential hypertension. This report describes findings relating to racial differences in Na⁺ regulation among serially passed skin fibroblasts derived from black and white normotensive and hypertensive subjects.

Materials and Methods

Skin fibroblasts from 15 subjects with established essential hypertension (8 black men, 3 black women, 3 white men, and 1 white woman) and 15 normotensive...
subjects matched for age (maximal paired difference of 5 years), race, and sex were examined. Eleven hypertensive subjects were receiving antihypertensive medications at the time of the skin biopsy; in some, blood pressure was poorly controlled. Antihypertensive medications and dietary therapy are unlikely to affect Na\(^+\) transport in serially passed, in vitro–grown fibroblasts from hypertensive subjects, as these cells manifest characteristics that reflect their genetic makeup and not the in vivo environment. All subjects signed informed consent approved by the Institutional Review Board of the University of Medicine and Dentistry of New Jersey. Various parameters of this population are presented in Table 1. A skin biopsy specimen (2 × 3 mm) was taken from each subject from the medial aspect of the left arm. Specimens were processed to obtain cultured skin fibroblasts as previously described.4 Cells from Passages 6 through 10 were examined. Three days before an experiment, 6 × 10\(^3\) cells were inoculated into each well of Nunc-6-well (35 mm in diameter) clusters (Hazleton, Lenexa, KS, USA). The growth medium in these wells consisted of Dulbecco’s modified Eagle’s medium (DMEM; Na\(^+\), 145 mEq/L; K\(^+\), 5 mEq/L), 10% fetal bovine serum (FBS), and 2 mM L-glutamine (95% air, 5% CO\(_2\)).

At the termination of each washout experiment, cells were rapidly washed three times with 5-ml aliquots of ice-cold DMEM plus 10% FBS and loaded with \(^{22}\)Na\(^+\) in fresh medium for 20 minutes (20 μCi/ml; Amersham, Arlington Heights, IL, USA) in the absence of ouabain and for 3 hours (8 μCi/ml) in the presence of 10\(^{-4}\) M ouabain. In preliminary studies we found that steady states with respect to Na\(^+\) transport in serially passed, in vitro–grown fibroblasts were attained at the indicated intervals. Thereafter, cells were rapidly washed three times with 5-ml aliquots of ice-cold DMEM plus 10% FBS. The washing step lasted for less than 15 seconds and was followed by a 15-second prewarming interval in the washout medium. The washout experiments were then initiated by the periodic additions and aspirations of washout medium. The washout experiments were then used as initial estimations for nonlinear regression analyses. The intercept of each curve with the ordinate was fixed according to the first measurement. This parameter was slightly less than unity as some radioactivity had left the cells during the prewarming step. To calculate the hypothetical time (t\(_0\)) of the initiation of the washout, each exponential function was solved for t when the fractional cellular activity (A\(_c\)) of \(^{22}\)Na\(^+\) is 1. The initial washout (exchange) rate constant (k\(_e\)) was obtained as described previously:

\[k_e = a_1 \cdot k_1 \cdot e^{-k_1 t} + a_2 \cdot k_2 \cdot e^{-k_2 t} + a_3 \cdot k_3 \cdot e^{-k_3 t}\]  

where a\(_{1-3}\) are the exponential coefficients and k\(_{1-3}\) are the exponential factors. Terms a\(_{1-3}\) and k\(_{1-3}\) represent the fractional intracellular \(^{22}\)Na\(^+\) pools and the respective washout rate constants associated with these pools. Approximations of these parameters were obtained by the sequential peeling method. These values were then used as initial estimations for nonlinear regression analyses. The intercept of each curve with the ordinate was fixed according to the first measurement. This parameter was slightly less than unity as some radioactivity had left the cells during the prewarming step.

The relative size of each cellular compartment (A\(_i\)) at the initiation of the washout was computed as:

\[A_i = a_x \cdot e^{-k_x t}\]  

where x = 1–3.

A similar approach was undertaken with respect to the washout of \(^{22}\)Na\(^+\) in the presence of ouabain, except that the data were fitted by a two exponential function.

### Table 1. Clinical Findings in the 30 Subjects Studied

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Quetelet index (kg/m(^2))</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black (n=22)</td>
<td>39.7 ± 2.11</td>
<td>23.8 ± 0.84</td>
<td>137.5 ± 7.10</td>
<td>90.6 ± 4.00</td>
</tr>
<tr>
<td>White (n=8)</td>
<td>44.8 ± 6.36</td>
<td>24.2 ± 0.54</td>
<td>137.8 ± 8.90</td>
<td>82.5 ± 5.82</td>
</tr>
<tr>
<td>Hypertensive (n=15)</td>
<td>42.3 ± 3.04</td>
<td>24.2 ± 0.70</td>
<td>160.7 ± 3.94</td>
<td>104.3 ± 2.62</td>
</tr>
<tr>
<td>Normotensive (n=15)</td>
<td>39.7 ± 3.45</td>
<td>23.6 ± 1.07</td>
<td>114.4 ± 2.15</td>
<td>72.6 ± 1.79</td>
</tr>
</tbody>
</table>

Values are means ± SEM. Quetelet index is a criterion for the degree of obesity. SBP = systolic blood pressure; DBP = diastolic blood pressure.
Intracellular Na\(^+\) was determined after washing the cells five times with 5 ml of ice-cold 0.1 M MgCl\(_2\). The cells were lysed with 1 ml of distilled deionized water, frozen (for 30 minutes on dry ice), and thawed. Aliquots were measured in a Perkin-Elmer atomic absorption spectrometer (Norwalk, CT, USA). The intracellular water volume was obtained from the equilibrium distribution of \(^{14}\)C urea following a 15-minute incubation in DMEM with 10% FBS and rapid washing four times with ice-cold MgCl\(_2\). Within the incubation period, the radioactivity in the cells reached steady state. Na\(^+\) accumulation \(Y\) in response to the introduction of 10\(^-4\) M ouabain was fitted according to the equation

\[
y = \frac{f}{k_e} (1 - e^{k_e t}) + N
\]

where \(f\) is the influx rate and \(k_e\) (a negative number) is the efflux rate constant. \(N\) is the value of Na\(^+\) concentration at the initiation of the experiment. This value represents the basal cellular Na\(^+\) concentration.

Results obtained for black and white hypertensive and normotensive subjects as well as possible interactions were examined by a two-factor analysis of variance (ANOVA). Data analyses were performed using the Statistical Analysis System general linear models procedure for unbalanced two-way ANOVA, with further comparisons using the Newman-Keuls test with a two-tailed level of significance. Data are presented as means \(\pm\) SEM.

### Results

The \(^{22}\)Na\(^+\) washout data are summarized in Tables 2 and 3 as well as in Figure 1. The curves in the figure depict the fitness of the observed results to three and two exponential models of \(^{22}\)Na\(^+\) washout in the absence and presence of ouabain, respectively. The presence of the cardiac glycoside caused the apparent disappearance of the first exponent, defined by the three exponential function when the Na\(^+-\)K\(^+\) pump is active. No statistically significant differences were observed in the absence of ouabain for the \(^{22}\)Na\(^+\) exchange parameters between normotensive and hypertensive subjects. However, blacks (see Table 2) showed significantly higher \(k\) values compared with whites. These differences were primarily due to higher \(k\) and \(k_e\) values in normotensive blacks than in normotensive whites. In the presence of ouabain (see Table 3) there were no statistically significant differences in the exponential parameters among the groups.

Calculations of the intracellular Na\(^+\) concentrations from the distribution ratio of \(^{22}\)Na\(^+\) between the medium and cellular milieu and the intracellular water space indicate that in both the absence and presence of ouabain (see Tables 2 and 3) the intracellular Na\(^+\) is higher in blacks than in whites \((p = 0.0141\) in the absence of ouabain and \(p = 0.009\) in the presence of ouabain). The higher intracellular Na\(^+\) concentration in blacks does not appear to result from a racial difference in intracellular water space. Although the intracellular water volume in fibroblasts from blacks was lower than that in whites \((2.18 \pm 0.178\) vs \(2.45 \pm 0.154\) \(\mu l/10^6\) cells), this difference was not statistically significant. There were also no statistically significant differences in this parameter between hypertensive and normotensive subjects. Intracellular Na\(^+\) concentrations were not significantly different between normotensive and hypertensive subjects for cells incubated without ouabain. However, the overall analysis indicates significantly lower Na\(^+\) concentrations in whites.

In the presence of ouabain (see Table 3), white normotensive and hypertensive subjects showed significantly lower intracellular Na\(^+\) concentrations than did their black counterparts \((p < 0.05\) for white vs black normo-
presence of ouabain does not affect or only minimally alters Na+-K+ pump independent transport pathways, which represents the ouabain-sensitive washout rate constant. This parameter (see $R^0$ in Table 2) was markedly higher in black than in white hypertensive subjects ($p < 0.05$) and in black than in white normotensive subjects ($p < 0.01$).

In further experiments, we used atomic absorption spectrometry to measure the intracellular Na+ accumulation in response to ouabain. The results of these experiments are presented in Figure 2 and Table 4. There were no apparent differences for the influx rate and $k_2$ values for Na+ between normotensive and hypertensive subjects. However, the influx rate, but not

**Table 2.** $^{22}$Na+ Washout Parameters in the Presence of $10^{-4}$ M Ouabain

<table>
<thead>
<tr>
<th>Subjects</th>
<th>$k_1$ (min$^{-1}$)</th>
<th>$A_1$</th>
<th>$k_2$ (min$^{-1}$)</th>
<th>$A_2$</th>
<th>$k'_1$ (min$^{-1}$)</th>
<th>$A'_1$</th>
<th>$Na^+$ (mEq/L)</th>
<th>$R$ (mEq/L/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black (n = 22)</td>
<td>0.094 ± 0.0045</td>
<td>0.978 ± 0.0155</td>
<td>0.019 ± 0.0027</td>
<td>0.022 ± 0.0043</td>
<td>0.094 ± 0.0046</td>
<td>81.1 ± 4.12</td>
<td>7.54 ± 0.619</td>
<td></td>
</tr>
<tr>
<td>White (n = 8)</td>
<td>0.098 ± 0.0102</td>
<td>0.978 ± 0.0150</td>
<td>0.017 ± 0.0051</td>
<td>0.023 ± 0.0014</td>
<td>0.095 ± 0.0092</td>
<td>53.7 ± 2.32</td>
<td>5.07 ± 0.503</td>
<td></td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.099 ± 0.0057</td>
<td>0.987 ± 0.0062</td>
<td>0.017 ± 0.0034</td>
<td>0.020 ± 0.0057</td>
<td>0.097 ± 0.0055</td>
<td>76.1 ± 6.14</td>
<td>7.47 ± 0.804</td>
<td></td>
</tr>
<tr>
<td>Normotensive</td>
<td>0.091 ± 0.0062</td>
<td>0.977 ± 0.0090</td>
<td>0.020 ± 0.0033</td>
<td>0.024 ± 0.0076</td>
<td>0.087 ± 0.0066</td>
<td>71.4 ± 4.66</td>
<td>6.29 ± 0.622</td>
<td></td>
</tr>
<tr>
<td>Black hypertensive (n = 11)</td>
<td>0.099 ± 0.0064</td>
<td>0.985 ± 0.0091</td>
<td>0.018 ± 0.0041</td>
<td>0.023 ± 0.0074</td>
<td>0.097 ± 0.0066</td>
<td>84.6 ± 6.62</td>
<td>8.28 ± 0.954</td>
<td></td>
</tr>
<tr>
<td>Black normoten- tive (n = 11)</td>
<td>0.089 ± 0.0063</td>
<td>0.982 ± 0.0059</td>
<td>0.021 ± 0.0034</td>
<td>0.020 ± 0.0044</td>
<td>0.087 ± 0.0063</td>
<td>77.5 ± 5.01</td>
<td>6.80 ± 0.769</td>
<td></td>
</tr>
<tr>
<td>White hypertensive (n = 4)</td>
<td>0.101 ± 0.0132</td>
<td>0.991 ± 0.0065</td>
<td>0.016 ± 0.0058</td>
<td>0.013 ± 0.0053</td>
<td>0.098 ± 0.0115</td>
<td>52.7 ± 3.21</td>
<td>5.24 ± 0.828</td>
<td></td>
</tr>
<tr>
<td>White normoten- tive (n = 4)</td>
<td>0.096 ± 0.0175</td>
<td>0.965 ± 0.0278</td>
<td>0.020 ± 0.0084</td>
<td>0.009 ± 0.0028</td>
<td>0.092 ± 0.0159</td>
<td>54.6 ± 3.88</td>
<td>4.19 ± 0.418</td>
<td></td>
</tr>
<tr>
<td>$p$ for BP</td>
<td>0.4522</td>
<td>0.1890</td>
<td>0.4738</td>
<td>0.6219</td>
<td>0.4187</td>
<td>0.6388</td>
<td>0.7353</td>
<td></td>
</tr>
<tr>
<td>$p$ for race</td>
<td>0.6480</td>
<td>0.6120</td>
<td>0.8120</td>
<td>0.1487</td>
<td>0.7931</td>
<td>0.0009</td>
<td>0.0010</td>
<td></td>
</tr>
<tr>
<td>$p$ for interaction (race × BP)</td>
<td>0.8216</td>
<td>0.3350</td>
<td>0.8704</td>
<td>0.9306</td>
<td>0.8393</td>
<td>0.4692</td>
<td>0.8821</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SEM.

$A_1$ and $A_2$ are presented as fractions (see equation in Table 2).

$Na^+$ concentration was calculated from the distribution ratio of $^{22}$Na+ between medium and intracellular milieu.

See Table 2 for key to abbreviations.

* $p < 0.025$, compared with hypertensive blacks (by Newman-Keuls test).

† $p < 0.05$, compared with normotensive blacks (by Newman-Keuls test).
RACIAL DIFFERENCES IN FIBROBLAST Na+ TRANSPORT

k\textsubscript{1} value was significantly higher in blacks than in whites (p = 0.0045) and in black than in white hypertensive subjects (p < 0.05).

Discussion

The prevailing views pertaining to cellular abnormalities of Na\textsuperscript{+} regulation in essential hypertension are based on inconsistent experimental data, further complicated by racial differences. This is particularly obvious with respect to studies that examined RBC Na\textsuperscript{+} transport pathways (for reviews, see References 1–3). Discrepancies in data derived from various studies may represent different causes of essential hypertension as well as genetic, environmental, and clinical differences in the hypertensive population. They also are likely to reflect differences in techniques of measuring various RBC Na\textsuperscript{+} transport systems.

An important, yet uncontrolled, element of studying abnormalities in RBC Na\textsuperscript{+} transport is the lasting effect of in vivo circulating factors. The lack of precise information concerning the influence of such variables in each subject whose RBCs are examined increases the chance for incongruity and interindividual variations in heterogeneous cohorts of hypertensive and normotensive subjects. Thus, innate abnormalities of cellular Na\textsuperscript{+} transport in patients with essential hypertension or persons predisposed to this disease may be difficult to identify. For instance, the putative Na\textsuperscript{+} transport inhibitory factor\textsuperscript{8,9} may alter RBC Na\textsuperscript{+},K\textsuperscript{+}-adenosine triphosphatase (ATPase) activity. RBC Na\textsuperscript{+},K\textsuperscript{+}-cotransport\textsuperscript{10,11} and Na\textsuperscript{+} concentration\textsuperscript{12} positively correlate with plasma renin, while RBC Na\textsuperscript{+},K\textsuperscript{+}-ATPase activity correlates negatively with age in female but not male subjects.\textsuperscript{13,14} These findings support the concept that RBC Na\textsuperscript{+} regulation is governed by a multitude of in vivo circulating factors that can easily mask intrinsic differences in RBC Na\textsuperscript{+} transport.

Our examination of Na\textsuperscript{+} transport in cultured skin fibroblasts has used two independent approaches: washout experiments of the tracer Na\textsuperscript{+} and direct cellular Na\textsuperscript{+} measurements. The initial exchange (washout) rate constant (k\textsubscript{1}) derived from the washout experiments in the presence of ouabain is not equivalent to the efflux rate constant (k\textsubscript{2}) obtained from time-dependent atomic absorption measurements of cellular Na\textsuperscript{+} in the presence of the cardiac glycoside. Whereas the k\textsubscript{1} represents the unidirectional transport of \textsuperscript{22}Na\textsuperscript{+} from the intracellular to the extracellular compartments, the k\textsubscript{2} reflects the net efflux of the Na\textsuperscript{+} ion, which is the sum of multiple transport systems of which major portions are bidirectional (e.g., the Na\textsuperscript{+}-Na\textsuperscript{+} exchange and the Na\textsuperscript{+}-K\textsuperscript{+} cotransport). Thus, the k\textsubscript{1} values are but mere fractions of the k\textsubscript{2} values. In addition, higher intracellular Na\textsuperscript{+} concentrations (in the presence of ouabain) are likely to saturate transport systems of the ion to a greater extent and thus reduce the respective Na\textsuperscript{+} transport rate constants. Whereas the k\textsubscript{2} values are derived from a model that is dependent on values of intracellular Na\textsuperscript{+} concentration, the k\textsubscript{1} is independent of this parameter.
In previous investigations we found that the first and fastest exponent of $^{22}\text{Na}^+$ washout from cultured rat fibroblasts and vascular smooth muscle cells also as well as human skin fibroblasts primarily represented the Na$^+$/K$^+$ pump and its respective cellular compartment, inasmuch as subjecting these cells to ouabain or K$^+$-deficient medium resulted in essentially complete disappearance of the fastest component. Moreover, based on the equilibrium distribution ratio of $^{22}\text{Na}^+$ between the medium and the cellular milieu at the initiation of the washout experiments, the calculated cellular Na$^+$ concentrations agreed quite well with direct measurements of the ion using atomic absorption spectrometry. Such findings suggest that all exponents of the $^{22}\text{Na}^+$ washout originate from the cellular milieu, and they are supported by the results of the present investigation.

It has been shown that in cultured human fibroblasts even micromolar concentrations of ouabain alter passive K$^+$ and Na$^+$ transports. Therefore, the ouabain-sensitive Na$^+$ and K$^+$ (Rb$^+$) transport may not be sensitive to ouabain-sensitivity of the Na$^+$-K$^+$ pump units are lower in blacks than in whites. Among other factors, this predisposition may be partially related to racial differences in cellular Na$^+$ and K$^+$ regulation. Several studies have shown that RBC Na$^+$,K$^+$-ATPase activity and the number of Na$^+$,K$^+$-ATPase units are lower in blacks than in whites and that, associated with the lower RBC Na$^+$,K$^+$ pump density, blacks exhibit higher cellular Na$^+$ concentrations.

A lower density of the Na$^+$-K$^+$ pump cannot be a sole explanation for a rise in fibroblast Na$^+$, as such a process will not be associated with increased Na$^+$ turnover rate. The present investigation suggests an additional and intriguing possibility: namely, increased passive Na$^+$ entry and, consequently, higher Na$^+$ extrusion through the Na$^+$-K$^+$ pump in blacks. This has been shown to be the case in certain models of hypertension and in essential hypertension in humans. Under steady state the rate of Na$^+$ extrusion from the cell reflects the rate of its influx. A higher Na$^+$ efflux can be accomplished by a rise in cellular Na$^+$ without a change in density of the Na$^+$-K$^+$ pump, because such a rise stimulates the pump to operate at a higher fraction of its maximal capacity.

What, then, is the cause for increased Na$^+$ turnover rate in fibroblasts of blacks? Our recent studies show that the activity of the Na$^+$/H$^+$ antiport is higher in cultured fibroblasts of blacks (unpublished data, 1988). This effect was demonstrated in quiescent, serum-deprived cells in which the Na$^+$/H$^+$ antiport was activated by either acidification of the cytosol or by the addition of serum to the medium. The cause of the hyperactivity of this transport system in fibroblasts from blacks is still uncertain, but it could relate to a higher cytosolic Ca$^{2+}$, as a rise in the concentration of this ion directly stimulates the Na$^+$/H$^+$ antiport. The cytosolic free Ca$^{2+}$ is elevated in platelets of patients with essential hypertension, and recently, the Na$^+$/H$^+$ antiport has been shown to be hyperactive.

TABLE 4. Cellular Na$^+$ Accumulation in the Presence of $10^{-4}$ M Ouabain

<table>
<thead>
<tr>
<th>Subjects</th>
<th>$k_e$ (min$^{-1}$)</th>
<th>I (mEq/L/min)</th>
<th>$R^0$ (mEq/L/min)</th>
<th>Na$^+$ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black (n=22)</td>
<td>0.012 ± 0.0007</td>
<td>0.964 ± 0.0743</td>
<td>1.03 ± 0.0897</td>
<td>9.78 ± 0.512</td>
</tr>
<tr>
<td>White (n=8)</td>
<td>0.010 ± 0.0010</td>
<td>0.562 ± 0.0440</td>
<td>0.583 ± 0.0593</td>
<td>7.50 ± 0.400</td>
</tr>
<tr>
<td>Hypertensive (n=15)</td>
<td>0.012 ± 0.0011</td>
<td>0.902 ± 0.1110</td>
<td>0.983 ± 0.1390</td>
<td>9.69 ± 0.635</td>
</tr>
<tr>
<td>Normotensive (n=15)</td>
<td>0.011 ± 0.0054</td>
<td>0.812 ± 0.0673</td>
<td>0.846 ± 0.0668</td>
<td>8.65 ± 0.568</td>
</tr>
<tr>
<td>Black hypertensive (n=11)</td>
<td>0.013 ± 0.0013</td>
<td>1.040 ± 0.1280</td>
<td>1.151 ± 0.1601</td>
<td>10.4 ± 0.753</td>
</tr>
<tr>
<td>Black normotensive (n=11)</td>
<td>0.012 ± 0.0006</td>
<td>0.892 ± 0.0771</td>
<td>0.936 ± 0.0716</td>
<td>9.19 ± 0.681</td>
</tr>
<tr>
<td>White hypertensive (n=4)</td>
<td>0.010 ± 0.0015</td>
<td>0.533 ± 0.0738*</td>
<td>0.536 ± 0.0997*</td>
<td>7.81 ± 0.505</td>
</tr>
<tr>
<td>White normotensive (n=4)</td>
<td>0.011 ± 0.0014</td>
<td>0.593 ± 0.0330</td>
<td>0.631 ± 0.0703</td>
<td>7.20 ± 0.655</td>
</tr>
</tbody>
</table>

Values are means ± SEM. The $R^0$ values were computed from the intracellular Na$^+$ concentrations at the plateau phases of the uptake and the $k_e$ values.

$p < 0.05$, compared with hypertensive blacks (by Neuman-Keuls test).
RACIAL DIFFERENCES IN FIBROBLAST Na⁺ TRANSPORT/Kuriyama et al.

in these cells. These findings therefore may indicate a cause and effect relationship. A similar phenomenon can occur in fibroblasts from blacks, thereby explaining their increased Na⁺ turnover rate.

Whether or not this speculation turns out to be correct, our results indicate that cultured fibroblasts from blacks manifest intrinsic differences in Na⁺ transport compared with their counterparts from whites. We propose that by themselves these underlying racial differences are not the cause of hypertension. However, in the presence of additional defects in cellular ion regulation, blacks are more likely to exhibit higher blood pressure levels than whites because of further disturbances of normal cellular ionic homeostasis. These additional abnormalities may be primary (i.e., innate to the structure of cells), or they may result from the effects of circulating factors. Finally, as our experiments were performed in a limited number of subjects, further investigations must be undertaken to confirm our findings.

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