Effects of Biobehaviorally-Assisted Relaxation Training on Blood Pressure, Plasma Renin, Cortisol, and Aldosterone Levels in Borderline Essential Hypertension

Angele McGrady, John W. Turner, Jr., Thomas H. Fine and James T. Higgins

Medical College of Ohio, Toledo, OH

This paper reports on the effect of two relaxation-based treatment modalities, biofeedback-assisted and restricted environmental stimulation therapy (REST), on blood pressure, cortisol and aldosterone levels, and plasma renin activity in 17 persons with essential hypertension. Sixty-seven percent of both groups achieved significant blood-pressure reductions across treatment. Decreases were also observed in the average levels of each hormone, but in some individuals the blood pressure changes were not associated with changes in hormone levels. These results are discussed in the context of adrenocortical activity and the volume regulation of blood pressure.

It has been demonstrated that patients with essential hypertension exhibit long-term decreases in blood pressure via behavioral treatments involving various forms of relaxation (Patel & North, 1975; Patel, 1975, 1977). Biofeedback(BF)-assisted relaxation adds the operant learning of a specific response, i.e., muscle tension, heart rate, and blood pressure, to generalized relaxation instructions (Basmajian, 1985). Flotation Restricted Environmental Stimulation Therapy(REST)-assisted relaxation is a technique involving brief restriction of environmental stimuli combined with relaxation instructions (Suedfeld, 1980). Although the mechanisms of blood-pressure reduction via behavioral treatments are unknown, measurements of physiological and biochemical parameters have previously been utilized to examine the mechanisms of blood pressure regulation (McGrady, Yonker, Tan, Fine & Woerner, 1981; Turner & Fine, 1983; Jevning, Wilson & Davidson, 1978; Stone & DeLeo, 1976).

McGrady et al. (1981) investigated the effects of forehead electromyograph (EMG) biofeedback-assisted relaxation on blood pressure and levels of aldosterone, cortisol, and renin in 38 essential hypertensives. Compared to a control group, the experimental group sustained significant decreases in systolic and diastolic blood pressure, forehead muscle tension, plasma aldosterone levels, and urinary cortisol levels. In a controlled study of normotensive subjects, Turner and Fine (1983) observed significant decreases

Write to Angele McGrady, Ph.D., M.Ed., Medical College of Ohio, Department of Physiology, C.S. 10008, Toledo, OH 43699.
This research was supported in part by BRS 94367 — Medical College of Ohio.
in BP and plasma cortisol across four relaxation sessions using flotation REST (hereafter termed REST). In addition, average plasma ACTH levels showed a decreasing trend across sessions in the REST group, but not in the control group. In controlled clinical studies of borderline essential hypertensives, Fine and Turner (1982, 1985) found significant decreases in systolic and diastolic pressures with 20 REST-assisted relaxation sessions.

The objective of the present study was to compare the effects of two combined treatments, BF-assisted relaxation and REST-assisted relaxation, on blood pressure and selected hormones in individuals with essential hypertension. Both treatments were combined with autogenic training, since it has been suggested that the addition of relaxation training enhances the effect of BF on blood pressure (Glasgow, Gaardner & Engel, 1982). Cortisol, aldosterone, and renin were chosen since these substances have been implicated in both the pathogenesis of hypertension and in the stress response. Our hypothesis was that both BF and REST treatments would be associated with equivalent and clinically significant decreases in blood pressure and with decreases in plasma and urinary levels of the measured hormones.

Method

Subjects

Twenty-one hypertensives (HT) were recruited through the Behavioral Medicine Clinic at the Medical College of Ohio. They were accepted into the study if their history and physical examination indicated that they had essential hypertension and no clinical evidence of secondary complications. Seven were on antihypertensive medications and were asked to withdraw medication with their physician's permission for the duration of the study. There were 7 white females, 9 white males and one black male. Their average age was 45 years (range 30 to 64).

Design and Treatment

At the first session all the participants were interviewed. A general data base comprised of demographic variables was obtained. Blood pressures were measured and the details of the study were explained. All participants signed an informed consent form. A staff physician (J. H.) conducted a cardiovascular examination on each participant and reviewed their medical history.

The baseline period continued for six weeks after the initial interview. Blood pressures were measured in the clinic with a mercury sphygmomanometer. Three measurements, two minutes apart, were taken once a week from patients in the sitting position after a ten-minute rest. Subjects were provided with a calibrated Marshall 114 self-monitoring sphygmomanometer. All subjects were taught to measure their own blood pressure and were asked to record it three times a day for the duration of the study. The measurement technique of each subject was verified by one of the investigators. Logs were collected weekly. Mean arterial pressure (MAP) was calculated from the systolic (S) and diastolic (D) values from the equation MAP = 1/3 (S − D) + D. Three measurements of forehead muscle tension levels were made, similarly to previous BP studies (McGrady et al., 1981). Plasma and urinary cortisol levels, plasma aldosterone, and plasma renin activity were also measured 3 times during baseline for both groups. One of the plasma renin activity determinations during baseline was made under furosemide(Lasix)-stimulated conditions. This permitted classification of the low-renin hypertensives, who have been reported to be less likely to respond to biobehavioral interventions than normal- or high-renin hypertensives (McGrady, Turner, Woerner, Higgins & Custodio, 1986).

The 21 subjects were randomly assigned to two treatment groups, BP (n = 11) and REST (n = 10). Four subjects dropped out of the REST group during the early weeks of treatment
because of various personal problems unrelated to treatment. The groups then consisted of 11 subjects in BF and 6 subjects in REST.

All subjects underwent 20 sessions of 50–60 minutes duration over a 10-week period. Eleven of the subjects underwent 20 EMG BF-assisted relaxation sessions and 6 subjects experienced 20 REST-assisted relaxation sessions. Each BF session included: 10 minutes sitting quietly; 3 BP measurements 2 minutes apart; 5 minutes forehead EMG baseline; 25 minutes EMG feedback from forehead muscles; 5–10 minutes debriefing. Each REST session included: 10 minutes sitting quietly; 3 BP measurements 2 minutes apart; brief shower; 35 minutes in REST; shower; 5–10 minutes debriefing. All subjects were taught autogenic-type relaxation exercises (Green, Green & Norris, 1980). They listened to a tape of these exercises during their BF or REST sessions and were asked to practice the exercises twice daily for fifteen minutes. Compliance with these instructions was not formally monitored.

**Instruments and Measurement Techniques**

Muscle tension levels were measured from the forehead with gold surface electrodes by an Autogen 1700 electromyograph. This technique is identical to that used previously with subjects with essential hypertension (McGrady et al., 1981; McGrady, Turner, Woerner, Higgins & Custodio, 1986). Data were collected and printed as an integral average every 5 minutes by a Texas Instruments TI-59 data acquisition system. The REST chamber was purchased from Samadhi Tank Company (Los Angeles). The chamber is a rectangular box 8' long, 4' wide and 42" high, constructed of styrofoam backed with black plastic. The box is lined with 20 gauge vinyl and contains a saturated epsom salt solution of specific gravity, 1.3. Temperature control of the solution was maintained at 94.0 ± 0.5 °F through the use of a waterbed heater with a solid state thermoregulator. The chamber is completely enclosed, eliminating light and attenuating sound to less than 10 decibels. The subjects float in a supine position with their arms at their sides. Subjective reports from previous studies have described the experience as deeply relaxing (Suedfeld, Ballard & Murphy, 1983; Lilly, 1977).

The blood sampling protocol was structured for control of the diurnal variation in cortisol levels and for its episodic secretion (Weitzman, Fukushima, Nageire, Roffwarg, Gallagher & Hellman, 1971). The blood samples were drawn by an experienced phlebotomist between the hours of 12 noon and 2 PM; two samples were drawn twenty minutes apart. The samples were centrifuged immediately to separate cellular and plasma components, snap frozen in liquid nitrogen and stored at −60 °C until assay.

On one occasion during baseline, 80 mg of Lasix was administered to the subjects in a divided dose (one dose late evening and one dose early morning). One blood sample was drawn at 10 AM from the fasting subject for determination of lasix-stimulated renin. Twenty-four-hour urine collections were used as a source for urinary cortisol measurements. The cortisol value was divided by the creatinine concentration to control for individual variations in collection. Urinary, plasma levels of cortisol, and urinary creatinine were measured by the Department of Pathology, cortisol by competitive radioassay, and creatinine by fluorimetry. Plasma levels of aldosterone and renin activity were measured by radioimmunoassay; cortisol: RIA kit code KCORD, Diagnostic Products, Los Angeles; aldosterone: RIA kit code KALD2, Diagnostic Products, Los Angeles; PRA: RIA kit code NEAO26, New England Nuclear, Boston, Mass., now E. I. DuPont De Nemours.

**Statistical Analysis**

Values used for statistical analysis were averages of data obtained during weeks one through six (baseline) and averages of data obtained during a five-week posttreatment interval (posttreatment). Home BPs, though not used in the statistical analysis, were used to reinforce the results of relaxation practice. At the end of the posttreatment interval, subjects were classified as success-
er if they had sustained a decrease in systolic or diastolic BP of at least 10 mm Hg. Statistical analysis included 2-way ANOVA with repeated measures, 1-way ANOVA with repeated measures, and Pearson correlation.
Results

Table 1 shows the pretreatment and posttreatment values of the dependent variables. There were no significant differences between measurements made in the first three weeks of baseline and those made in the second three weeks of baseline, nor were there any significant differences between measurements made at two intervals of posttreatment. Comparisons were also made between the REST and BF groups on pretreatment values of the dependent variables. There were no significant differences between the two groups in any of the variables pretreatment.

Blood Pressure

Figure 1 shows the effect of REST- and BF-assisted relaxation on clinic BP (systolic, diastolic and MAP). Sixty-seven percent of both groups were classified as succeeders as defined above. The decreases in systolic, diastolic, and MAP that occurred in both groups were statistically significant.

Table 1
Baseline and posttreatment values of the dependent variables in the population.
Values are mean ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Early baseline 1–3 weeks</th>
<th>Late baseline 4–6 weeks</th>
<th>Early posttreatment 0–2 weeks</th>
<th>Late posttreatment 3–5 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP mm Hg</td>
<td>142.2 ± 2.2</td>
<td>144.0 ± 2.2</td>
<td>134.0 ± 2.0</td>
<td>130.1 ± 2.1</td>
</tr>
<tr>
<td>Diastolic BP mm Hg</td>
<td>91.4 ± 1.1</td>
<td>89.5 ± 1.6</td>
<td>85.9 ± 1.3</td>
<td>81.9 ± 1.4</td>
</tr>
<tr>
<td>Mean arterial pressure mm Hg</td>
<td>108.6 ± 1.6</td>
<td>107.1 ± 1.5</td>
<td>99.9 ± 1.5</td>
<td>98.6 ± 1.3</td>
</tr>
<tr>
<td>Urinary cortisol µg/g creatinine</td>
<td>67.1 ± 4.2</td>
<td>64.1 ± 4.6</td>
<td>49.6 ± 3.0</td>
<td>48.2 ± 3.2</td>
</tr>
<tr>
<td>Plasma cortisol µg %</td>
<td>12.7 ± 2.2</td>
<td>14.0 ± 1.9</td>
<td>10.6 ± 0.8</td>
<td>10.7 ± 0.9</td>
</tr>
<tr>
<td>Plasma aldosterone ng %</td>
<td>11.2 ± 1.86</td>
<td>10.4 ± 1.01</td>
<td>8.5 ± 0.6</td>
<td>7.1 ± 0.8</td>
</tr>
<tr>
<td>Plasma renin activity ng/mg/h</td>
<td>2.4 ± 0.5</td>
<td>2.2 ± 0.4</td>
<td>1.3 ± 0.33</td>
<td>1.6 ± 0.4</td>
</tr>
</tbody>
</table>

There were no significant differences between early baseline and late baseline or between early posttreatment and late posttreatment in any of the dependent variables. There were no differences in any of the dependent variables in the biofeedback and REST groups taken separately.
Figure 1
Systolic BP, diastolic BP, and MAP in baseline and posttreatment for HT in the REST and BP groups. Values are means ± S.E.M. of 15 determinations averaged over 5 sessions in baseline and 3–5 sessions posttreatment. Differences between baseline and posttreatment were significant: SBP: F = 9.5, df = 1.16, p < 0.01; DBP: F = 39.5, df = 1.16, p < .01; MAP: F = 10.7, df = 1.16, p < .01. Two-way analysis of variance with repeated measures.

Figure 2
Plasma aldosterone levels in baseline and posttreatment. Values are means ± S.E.M. of 6 determinations averaged over 3 sessions in baseline and 3 sessions posttreatment. Differences between baseline and posttreatment were significant for the REST group only F = 6.88, df = 1.9, p < .05. One-way analysis of variance with repeated measures.

Figure 3
Plasma renin activity in baseline and posttreatment. Values are means ± S.E.M. of 6 determinations averaged over 3 sessions in baseline and 3 sessions posttreatment. Differences between baseline and posttreatment were significant F = 8.17, df = 1.13, p < .05. Two-way analysis of variance with repeated measures.
Hormones

Figures 2, 3 and 4 illustrate the effects of BF and REST on plasma aldosterone (Figure 2), plasma renin activity (Figure 3), plasma and urinary cortisol (Figure 4). Significant decreases were found in the REST group for each hormone tested. Posttreatment renin levels were below the range of normal in some individuals in the REST group. In the BF group, significant decreases were observed in plasma and urinary cortisol levels, and in plasma renin activity; there was no significant decrease in plasma aldosterone levels.

Interrelationship of Blood Pressure and Hormones

A Pearson Correlation was calculated between the percent change in MAP and the percent change in each of the hormones for both the REST and BF groups. For the combined REST and BF groups, significant correlations were found between percent change in mean blood pressure and percent change in plasma and urinary cortisol. Change in urinary cortisol was correlated with change in plasma aldosterone and plasma renin activity. Change in plasma aldosterone was correlated with changes in urinary and plasma cortisol. Change in plasma renin was correlated with change in plasma aldosterone. However, all subjects who lowered BP (succeeders) did not show decreased hormone levels and vice versa, i.e., the changes in hormone levels were not dependent on whether the subjects lowered their BP (Table 2, succeed/nonsucceed). A difference between treatment groups was observed in the change in urinary cortisol and plasma aldosterone with the REST group showing a larger response that the BF groups (one-way ANOVA $p < 0.05$ ($F = 5.91$, df = 16, and $F = 5.39$, df = 16, respectively)).
Table 2
Pearson correlations among percent change in blood pressure and hormones in combined REST and BF.

<table>
<thead>
<tr>
<th></th>
<th>MAP</th>
<th>PC</th>
<th>UC</th>
<th>PRA</th>
<th>ALDO</th>
<th>S/NS</th>
<th>BF/REST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Arterial Pressure (MAP)</td>
<td>0.51*</td>
<td>0.44*</td>
<td>0.21</td>
<td>0.23</td>
<td>0.80*</td>
<td></td>
<td>-0.2</td>
</tr>
<tr>
<td>Plasma Cortisol (PC)</td>
<td>0.22</td>
<td>0.17</td>
<td>0.38</td>
<td>0.32</td>
<td>0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Cortisol (UC)</td>
<td>0.71*</td>
<td>0.56*</td>
<td>0.37</td>
<td></td>
<td>0.53*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma Renin Activity (PRA)</td>
<td>0.66*</td>
<td>0.16</td>
<td></td>
<td>0.37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma Aldosterone (Aldo)</td>
<td></td>
<td></td>
<td>0.31</td>
<td>0.51*</td>
<td></td>
<td></td>
<td>-0.09</td>
</tr>
<tr>
<td>Succeeders/Non-succeeders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Correlation coefficient significant (P > 0.05 for values ≥ 0.46, DF = 16) for BF and REST groups combined.

Discussion

Our objective was to compare the effects of REST-assisted relaxation training and BF-assisted relaxation training on BP and several hormones in essential hypertensives. The present study did not address the issue of which component of the treatments was effective. The length of the baseline (six weeks) and the stability of the baseline values (Table 1) allowed each subject to serve as their own control. In terms of BP the results support the initial hypothesis and confirm previous reports that REST-assisted (Suedfeld, 1980) and BF-assisted relaxation (McGrady et al., 1981; Glasgow et al., 1982) were associated with clinically and statistical significant decreases in BP across treatment. A previously unreported finding was the demonstration of equivalent effectiveness of the two treatment modalities in lowering BP. In contrast the equivalence hypothesis for REST and BF effects on hormone patterns was not confirmed. In fact, subjects in the REST group exhibited hormonal changes more consistently, showing decreases in all measured hormones in 83% of subjects compared to 33% of biofeedback subjects showing this response. Other studies of adrenal hormone changes associated with relaxation methodologies such as transcendental meditation (Engel, Gaardner & Glasgow, 1981; Jevning, Wilson, Van Der Laan & Levine, 1975), deep muscle relaxation (Michaels, Huber & McCann, 1976; Davidson, Winchester, Taylor, Alderman & Ingels, 1979) and BF-assisted relaxation (McGrady et al., 1981) have also revealed inconsistent hormonal responses, i.e., similar to the BF treatment group in the present study. Jevning et al. (1975) reported a 26% decrease in plasma cortisol in 30 minutes of transcendental meditation in regularly practicing meditators with 3–5 years of experience, while Michaels et al. (1976) found no decrease in plasma cortisol after 20–30 minutes of TM in meditators with 2 years of experience. In across-session studies of EMG biofeedback-assisted relaxation and cortisol in hypertensives, McGrady et al.
(1981) found no statistically significant effect of 16–30-min biofeedback sessions on plasma cortisol, but they observed significant decreases in urinary cortisol levels.

Assuming that the decrease in plasma levels of the measured hormones are part of the relaxation response, one possible explanation for the difference in the present study is that REST may be more potent than biofeedback as a mediator of the relaxation response, producing deeper relaxation. In a previous study reported from this laboratory (Turner & Fine, 1983) subjects with no prior REST experience showed an average 20% decrease in plasma cortisol during 35-minute REST sessions. If decreased plasma cortisol is a part of the relaxation response, then naive REST subjects appear to have experienced relaxation equal to or greater than that of meditators with 2–5 years TM experience. Another possibility is that the differences in hormonal responses reflect a difference in the process of REST-assisted and BF-assisted relaxation. Certainly the procedures of REST and BF are different. Biofeedback is an active learning process that utilizes outside stimuli (Basmajian, 1985). Although REST may include active learning, the REST process is mediated only through internal stimuli (Suedfeld, 1980). Since both treatments include autogenic relaxation, the hormonal results cannot be attributable to autogenic relaxation alone. A complicating factor in the present study was the dropout of several subjects in the REST group, which may suggest that the final REST group was more self-selected than random. The suggestion that REST-assisted relaxation produces a deeper relaxation than BF-assisted relaxation needs to be retested with a larger group of subjects and expanded hormone profiling.

In designing this study we chose cortisol as an adrenocortical index of the relaxation response, and designated renin and aldosterone as indices of the volume regulation of BP. Although these designations were admittedly somewhat arbitrary, it is interesting that in both treatment groups there was a significant correlation between BP changes and plasma and urinary cortisol changes, while there was no correlation between the changes in BP and renin or between the changes in BP and aldosterone. This was true for renin whether low-renin subjects were included or excluded in data analysis, a result which was not surprising since only 2 of the 17 subjects were classified as low-renin. In addition, the reason for the below-normal range levels of renin in some subjects is unknown. The variable and inconsistent relationship among changes in BP, renin and aldosterone suggest that over the long term, relaxation affects BP via complex, interactive pathways. It is, therefore, unlikely that this relationship can be accurately assessed or monitored simply through these neuroendocrine measurements.

One reasonable conclusion that can be made from the present data is that the BP response and hormonal response to relaxation training can be independent, with responsiveness varying from subject to subject. Cugini, Piernatale, Tomassini, Centanni, Salandi and Scavo (1982) have suggested that the diurnal rhythm of cortisol, aldosterone, and renin is altered in hypertensives, particularly in low-renin hypertensives. Although we attempted to control for normal diurnal variation in hormone release patterns by drawing all blood samples between noon and 1400 hours, it was not known whether our sample contained persons with normal, aberrant, or a mixture of rhythms. Furthermore, different types of stressors such as psychological versus physiological or mental task versus stressful imagery produce varying patterns of hemodynamic responses (Stephenson, 1984). Stress has been shown to increase sympathetic activity, blood pressure, heart rate, vasoconstriction, renin activity, cortisol, aldosterone, and growth hormone — but not all in a single subject or single group of subjects. Recent studies (Cowley, Skelton & Velasques, 1985) have demonstrated sex differences in the
endocrine pattern of essential hypertensives, with lower plasma renin activity being correlated with hypertension in women, but not in men. Finally, Fredrikson, Danielssons, Engel, Frisk-Holmberg, Strom and Sundin (1985) have shown that hypertensive patients exhibit greater individual response specificity in BP reactivity than do normotensives, i.e., the BP responses to various stimuli are more consistent in hypertensives than in normotensives. Thus, there appears to be a wide range of potential moderating factors and notable differences in responses among hypertensive individuals and between hypertensives and normotensives. In this regard, it may be that a single-subject, repeated-measures experimental design offers the best opportunity to probe possible relationships between BP and hormones, and to elucidate the mechanism(s) by which relaxation-based treatments lower BP in hypertensives.

In the present study of hypertensives, the average starting levels of all hormones were within the clinically defined range of normal. However, the fact that beginning hormone levels and the changes following treatment were within the range of "normal" does not mean the BP effects are not hormonally mediated. It is possible that even a small change in the setpoint of a hormonal feedback loop may produce significant long-term physiological realignment, with one consequence being lowered BP. The stability of both baseline and posttreatment values lend support to this concept.

REFERENCES


