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BEHAVIORALLY INDUCED SECRETION OF ARGinine VASOPressIN

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Plasma vasopressin levels were found to be elevated before, during, and after the practice of Transcendental Meditation compared to levels at other times of the day, and to levels in non-meditating controls who rested. This effect was not due to the usual mechanisms responsible for vasopressin release, and may be of importance in mediating the benefits of Transcendental Meditation for learning, memory, and behaviour.

The meditators were also found to have lower state and trait anxiety scores before and after Transcendental Meditation, compared to the controls. Furthermore, galvanic skin resistance increased more markedly during Transcendental Meditation than relaxation.—EDITORS
Determination of vasopressin concentrations in blood plasma of subjects before, during, and after the practice of Transcendental Meditation revealed markedly elevated levels compared to nonmeditating subjects. Skin resistance, EEG and anxiety indices rule out stress as a contributor. This effect is probably not the result of homeostatic processes or needs and may mediate changes in behavior reported in long-term Transcendental Meditation practitioners.

INTRODUCTION

Arginine vasopressin (AVP) is a nonapeptide which is synthesized within the central nervous system in medial hypothalamic nuclei. It is axonally transported to various brain regions including ependymal cells lining the third ventricle as well as to the posterior lobe of the pituitary gland from where it is secreted into the systemic circulation. Well established physiologic actions of AVP include regulation of total body fluids, blood volume and vasoconstrictor effects on the smooth muscle of the vascular system (1). Although the mechanisms are obscure, recent studies of the effects of peripheral and central administration of exogenous vasopressin and its neurally-active analogues in animals and humans suggest involvement in a variety of cognitive processes including learning and memory functions (2) and, more specifically, the acquisition and retention of adaptive behavior patterns (3). Additional reported effects of AVP in humans suggest psychotherapeutic and behavior-modifying properties (4) as well as improvement of attentional processes (5). Implicit in many of these reports is the notion that naturally occurring modification of existing, or acquisition of new behavior patterns may be facilitated by an increase of endogenous AVP activity centrally and/or peripherally. However, except for states of stress, potentiation of AVP secretion associated with behavior modification or adaptation has not been demonstrated.

We now report dramatically increased levels of plasma AVP in individuals who have regularly elicited rest/relaxation by the stylized mental technique of Transcendental Meditation (TM) on a long-term basis (5–10 years). TM is practiced twice daily for periods of 20–40 minutes by the regular practitioner in the morning and evening. TM practice in such subjects is accompanied by numerous physiological changes consistent with relaxation including decreased cortisol secretion, decline of oxygen consumption of both entire body and forearm, increased galvanic skin resistance (GSR) and increased central and frontal alpha activity in the electroencephalogram (6–8). Previous reports of endocrine effects of TM also include increased plasma prolactin secretion (9) and serotonin turnover (10). Additionally, changes in global and specific personality variables (11) have been reported to accompany long-term TM practice.

METHOD

SUBJECTS—Twelve subjects, six long-term TM practitioners and six non-meditating individuals ("ordinary rest" group), were studied. All subjects were healthy and did not use tobacco, alcohol or regular medication. Their ages ranged from 22 to 31 years (mean of 26). Each group consisted of 4 men and 2 women. The ordinary rest group was composed of individuals who did not practice any form of systematic relaxation nor any meditation technique.

PROCEDURE—Blood sampling procedures were conducted in a small, semi-soundproof enclosure and all samples were collected between 9 and 10:30 A.M., a time period which approximates the typical time in the morning at which these subjects regularly practice TM. Subjects were familiarized with the laboratory and its personnel on a day previous to the day of the experiment. Written informed consent was obtained from each subject on this occasion.

Arterial and venous catheters were inserted into the arms of recumbent subjects following local anesthesia with a 1% lidocaine solution. Electroencephalographic (EEG) and galvanic skin resistance (GSR) leads were also attached (12). After a 1.5 hour equilibration period to allow any changes associated with catheter placement to be attenuated, subjects were seated in a comfortable chair inside the enclosure. Intravenous extension lines were then attached, allowing blood to be drawn from outside the enclosure without disturbing the subject (13). To facilitate meditation/relaxation, room lights were dimmed and noise was minimized during the experiment.

Using a time series experimental design (14), blood samples were drawn at 15 minute intervals
over a 90 minute period, divided into a 15 minute (eyes-open) pre-meditation/pre-rest period, a 45 minute (eyes-closed) meditation/rest period and a 30 minute (eyes-open) post-meditation/post-rest period. For the purpose of assessing psychologic stress each subject completed a Spielberger State-Trait Anxiety Inventory or STAI (15) both before and following the experimental period. Forearm oxygen consumption, an indicator of skeletal muscle activity was also determined. An additional single blood sample was taken from each TM subject at a time different from the routine TM practice period time (12–1 PM) on a separate day.

Blood samples were placed in chilled tubes and serially centrifuged (5°C) at 6,000 g for 8 minutes and the separated plasma specimens stored at −70°C until assayed. Plasma arginine vasopressin (pAVP) was quantitated using a specific radioimmunoassay described by Skowsky (16).

RESULTS

Concentrations of pAVP (mean ± S.E.) for both groups are shown in figure 1. Mean values for the TM group ranged from 2.6 to 7.1 times the corresponding mean values for the rest group throughout the experiment. Of the 42 data points in each group, there was complete separation except at one of these points. The TM group exhibited a significant (p < .05) linear increase in pAVP concentration over the experiment period, with no significant trend observed in the rest group. Mean pAVP values for the rest group were within the normal range for measurements in this laboratory on healthy subjects (0.75±0.50 μU/ml; 16). Levels of pAVP in the single samples drawn on another day separate from the experiment from TM subjects were also within the normal range.

Plasma osmolality values for both groups were within the range of values for normal ambulatory subjects (289±5; 16). Plasma osmolality did not vary significantly over time for either group, nor was there any significant difference between groups.

Scores on the STAI were significantly lower (p < .01) for the TM group compared to the rest group both before and following the sampling period for both "A-state" and "A-trait" anxiety indices (table 1).

EEG recordings showed that subjects were awake for 90 percent of the time during meditation or ordinary relaxation. Approximately 10% of the time was spent in stage I sleep. Initial GSR values (taken at the start of the eyes-closed, meditation/relaxation period) showed no significant difference between subject groups. Both groups showed significant increase of GSR levels (figure 2) over the duration of

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>STATE</th>
<th>Trait</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-experimental (TM)</td>
<td>23.17 (2.84)</td>
<td>25.32 (2.29)</td>
</tr>
<tr>
<td>Post-experimental (TM)</td>
<td>22.05 (1.81)</td>
<td>24.19 (2.86)</td>
</tr>
<tr>
<td>Pre-experimental (rest)</td>
<td>34.61 (4.98)</td>
<td>36.24 (7.56)</td>
</tr>
<tr>
<td>Post-experimental (rest)</td>
<td>32.10 (4.69)</td>
<td>34.38 (7.31)</td>
</tr>
</tbody>
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FIG. 1. PLASMA CONCENTRATIONS (MEAN ± S.E.) FOR THE TM GROUP AND FOR THE ORDINARY REST GROUP BEFORE, DURING, AND AFTER AN EYES-CLOSED PERIOD OF EITHER MEDITATION OR REST. The additional point for the TM group was taken on another day.

FIG. 2. MEAN GSR VALUES DURING AND FOLLOWING THE EYES-CLOSED PERIOD FOR THE TM GROUP AND FOR THE ORDINARY REST GROUP.
the eyes-closed meditation/relaxation period with a significantly larger increase ($p < .01$) associated with TM.

**DISCUSSION**

The observed $pAVP$ values in the TM group are unusually high for healthy subjects. That the observed elevation of $pAVP$ in the TM group is a transient event is indicated by the normal levels of AVP in samples taken on the separate, non-experimental occasion in each TM subject. Further, if the increase in AVP levels had been sustained over a period of several hours prior to the experiment, plasma osmolality values would have been expected to be lower than those observed (due to antidiuresis). Moreover, none of the TM practitioners studied in our laboratory during the past 7 years have exhibited any obvious signs of abnormally high water retention, nor has this been reported by other investigators.

These elevated values may be explained by either decreased AVP clearance or increased AVP secretion from the posterior pituitary. The first alternative is unlikely, since AVP is primarily cleared by the liver and kidneys and previous study (17) of the distribution of blood flow during TM and rest found no difference of hepatic/renal blood flow between TM and rest prior to the eyes-closed meditation/rest period. Although a 40% decline of hepatic blood flow in the TM group occurred during the meditation period (with a 12% non-significant decline in the rest group), this decline would be expected to increase AVP values by a maximum of 70% during TM, assuming an 18 minute half-life for AVP in whole blood and a secretion rate averaging 2,000 µU/15 minutes (18). However, mean values of $pAVP$ in the TM group exceeded rest group values by 2.6 to 7.1 fold throughout the sampling period (figure 1). Therefore, decreased clearance of AVP by itself is insufficient to explain the consistently high levels of $pAVP$ observed, and suggests primary contribution by increased rate of AVP secretion.

One of the most potent known stimuli of AVP release is blood hypertonicity. However, plasma osmolality values were normal for both groups at all points in the sampling series and there was no difference between the osmolality of the sample taken from TM subjects on a day separate from the experiment compared to those from the time series experimental set. Those data tend to exclude osmolality variation as a contributor to the effect. Additional, nonosmotic factors known to strongly potentiate AVP release in man include acute decline of arterial blood pressure, decrease in total blood volume, change in body posture and psychologic stress (18). Acute drop in arterial blood pressure can be excluded as a contributor because TM practice is not associated with acute variations in blood pressure (19). Experimental procedures eliminated significant alteration of total blood volume or body posture as possible contributors, since the small volumes of blood drawn during sampling were simultaneously replaced with identical volumes of isotonic saline; and subjects sat in an erect position throughout the period of sampling. Several measures obtained in this study also rule out contribution of psychologic stress: GSR data indicated progressive decrease of sympathetic nervous system activity during the eyes-closed period for both groups; the EEG activity recorded was consistent with a relaxed, wakeful state; and the marked decline of forearm muscle respiration in the TM group indicated muscular relaxation (20). Before and after the experiment, STAI scores for the TM group were not only significantly lower than those of the rest group but were well below average values for normal college age subjects (15) for both state anxiety (suggesting a decreased level of tension and apprehension) and trait anxiety (suggesting a decreased "anxiety proneness" or lessened tendency to respond to situations perceived as threatening with elevations in state anxiety intensity).

The high levels of $pAVP$ associated with TM practice, therefore, indicate the involvement of a releasing mechanism other than those strictly related to homeostatic functions. Repeated elicitation on a regular diurnal basis and/or subjective expectancy may be significant in the TM group, since acute variation of $pAVP$ did not accompany TM practice and the smaller degree of relaxation during eyes closed rest (indicated by GSR and muscle respiratory changes) was not accompanied by detectable $pAVP$ change. A role of subject selection is also possible, although it is unlikely, since $pAVP$ levels of the magnitudes observed in this study have not been observed in healthy individuals, such as these, in numerous other measurements in this laboratory. Based upon evidence of the ability of systemically-administered AVP and its analogs to modify human and animal behavior, it is tempting to specu-
late that increased AVP activity may mediate the reported effects of TM on learning and memory (21) and on psychotherapeutic processes (22). This finding is also, to our knowledge, the first report of a nonstressful behavior which evokes AVP secretion and may serve to further distinguish the physiologic state induced by TM practice from that of ordinary rest/relaxation.

BIBLIOGRAPHY


12. A monopolar EEG was recorded from C-left mastoid with F ground, using Grass silver cup electrodes. EEG records from a Grass model 7 polygraph with low and high half-amplitude filters set at .15 and 35 Hz, respectively were scored in 30-second epochs according to the criteria of Rechtschaffen and Kales: A. Rechtschaffen and A. Kales. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep States of Human Subjects. Los Angeles: Brain Information Science/Brain Research Institute, California Natural Institutes of Health, Publication no. 204. GSR measures were derived from 9 mm Ag/AgCl electrodes attached to thenar and hypothenar eminences of the right palm. A Grass DC amplifier was used. GSR data was analyzed by calculating relative fractional differences of resistance values during the eyes-closed period, compared to the value at the start of the eyes-closed period.

13. Blood samples were drawn through 3-way stopcocks, connected to 36-inch extension lines, kept patent with a heparinized saline solution.


16. W. R. Skowsky, A. A. Rosenbloom and D. A. Fischer. J. Clin. Endocrinol. Metab. 38, 278 (1974). Assay characteristics include a sensitivity of 0.2 μU/ml (0.6 pg/ml) and a C.V. of 4.8% within assay and 9.6% between assay. The antiserum used (R-71) showed negligible crossreactivity with arginine vasotocin (AVT); the ratio of AVT: AVP at 50% binding is 350:3, and oxytocin showed no significant cross reaction with labelled antigen.


20. Marked decline of forearm oxygen consumption, which is due primarily to decreased muscle metabolism, has been shown to accompany TM in a related study (R. Jevning, A. F. Wilson and J. P. O'Halloran. Physiology and Behavior. 29, 343 (1982)).


23. The authors wish to acknowledge gratefully the financial support of The National Institute of Health, Grant No. NHLBI27894 and the Macarthur Foundation in this research.