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Modulation of Red Cell Metabolism by States of Decreased Activation: Comparison Between States

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JEVNING, R., A. F. WILSON, H. PIRKLE, S. GUICH AND R. N. WALSH. *Modulation of red cell metabolism by states of decreased activation: Comparison between states.* PHYSIOL BEHAV 35(5) 679-682, 1985.—Marked decline of red cell metabolism has been described during the acute state of decreased activation associated with the stylized mental technique of transcendental meditation (TM) in long-term meditators (5-10 years regular elicitation, TM instructors). It is not known whether unstylized rest is accompanied by a similar effect and it is not known what effector(s) may contribute to red cell metabolic changes in these states. In the present study ordinary, unstylized rest was found to be accompanied by small increase of red cell glycolytic rate. Apparently, either repeated elicitation of TM behavior or some special feature of this practice become associated with new mechanisms of metabolic control than those previously in operation. Although the data of this study do not permit isolation of the precise psychological determinants of this effect, the range of possible physiological effectors can be delimited. Blood pH, PCO₂, PO₂, and phosphate can be eliminated as significant for red cell metabolic control during both TM and rest, and based upon related studies, several known hormones such as insulin, T₃, T₄, arginine vasopressin, oxytocin, prolactin and growth hormone can also be eliminated as responsible effector(s).

Red cell metabolism Transcendental meditation Consciousness Behavior Lactate

METHOD

Subjects and Experimental Protocol

We studied two separate groups of subjects: (1) 22 normal, lean, college educated adults (6 women, 16 men, ages 25-36) who had no experience of a stylized rest/relaxation procedure and were studied prior to learning TM; (2) 30 individuals of similar background (7 women, 23 men, ages 21-34) who were long-term TM practitioners (that is, 6-10 years of regular elicitation for 30 to 40 minute periods twice daily). The long-term TM practitioner subjects were also TM instructors. We studied this precise group of TM subjects because several particularly marked physiologic changes have been recently identified during these individuals' elicitation of this state, including approximately a fivefold increase of arginine vasopressin (AVP; [18]), 40-60% declines of oxygen consumption [5], and prevalence of high amplitude theta bursts in the electroencephalogram (EEG) [8]. These two groups are referred to as "rest" and TM groups in this report.

Subjects of each of the 2 groups were studied on 2 occasions, approximately 2 weeks apart, each subject serving as his or her own control. Subjects fasted since midnight and were observed between 10:30 and 12:00 a.m. On one (practice) occasion TM subjects were asked to close their eyes and practice TM for 45 minutes followed by an eyes-open recovery period of 30 minutes; analogously, subjects of the rest group were asked to close their eyes and simply rest on the practice occasion for 45 minutes followed by an eyes-open 30 minute recovery period. On the other (control) oc-

ACUTE modulation of whole blood glycolytic metabolism, accounted for principally by decreased red cell glycolysis, has been identified during the physiological state of decreased activation induced by the "transcendental meditation technique" (TM) in the long-term practitioner [12]. Practiced while seated comfortably, TM is a stylized mental technique that allegedly requires no physical or mental control and, by report, is enjoyable and easily learned [17,32]. Since this technique is widely and uniformly taught, there exists a large and uniformly instructed group of individuals who have been regularly eliciting this state in a uniform manner for 30-40 minutes twice daily over the course of 5-10 years. Rapid metabolic and cardiovascular changes consistent with decreased activation have been extensively described during this behavior [10-12, 29]. While decreased erythrocyte metabolism during TM is a unique finding under normal physiologic circumstances, it is not known whether other ordinary, unstylized rest states may have the same effect. It is also not known what agent(s) participate in the mechanism of this response.

For study of these questions we measured whole blood glycolysis during ordinary unstylized rest behavior for comparison with red cell effects observed previously during TM. Since several relevant physiologic variables during these behavioral rest states are now well characterized, including circulatory, hormone, and blood gas changes [10-12, 29], and red cell metabolic control is comparatively well studied, the data on rest and TM may contribute to better understanding of normal red cell metabolic control in general and its significance in these states in particular.

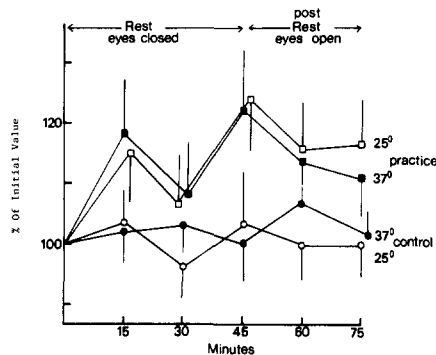


FIG. 1. Change of aerobic lactate generation rate by whole blood during and after unstylized eyes closed rest (practice) or control periods. Rest incubations at 37° (■); 25° (□). Control incubations at 37° (●); 25° (○). Values displayed for each 15 minute interval are means (\pm S.E.) of percentages of initial value.

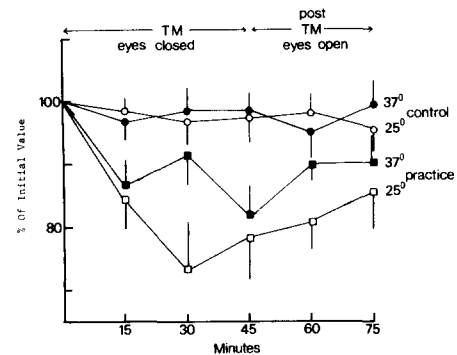


FIG. 2. Change of aerobic lactate generation rate by whole blood during and after TM practice or reading control periods. TM aerobic incubations were at 37° (■), and 25° (□); control aerobic, at 37° (●) and 25° (○). Means (\pm S.E.) of percentages of initial value.

casation, subjects of each group were asked to read a "relaxing" work of their own choice for 45 minutes followed by a 30 minute recovery period without reading. Details of sleep recording, measurement of galvanic skin resistance (GSR), and procedures of blood drawing have been described previously [12].

Preparation of Blood and Metabolic Measurements

Eighteen milliliter arterial blood samples were drawn every 15 minutes into heparinized syringes throughout practice (i.e., rest or else TM) and post-practice periods at 0, 15, 30, 45, 60, and 75 minutes. Two milliliters of blood were used for blood gas determination (Radiometer ABL Blood Gas Laboratory, Radiometer, Copenhagen), glucose and hematocrit.

The remaining 16 ml of blood were immediately used for determining blood lactate generation rate, and concentrations of whole blood lactate. Generation rate was determined during 90 minutes of aerobic incubation of blood (that is, open to air) at 25° and 37° from slopes of best fit lines through lactate concentrations measured after 0, 30, 60 and 90 minutes of incubation.

Measurements of lactate concentration were performed in duplicate utilizing a Technicon autoanalyzer (Technicon Instrument Corp., Tarrytown, NY) by use of an enzymatic method [19], except that the supernate for analysis was prepared by delivery of 0.45 ml of sample into 0.90 ml of 5 N ice-cold perchloric acid followed by neutralization with 5.63 N K_2CO_3 according to the method of Beutler [2] with modifications of McManus (personal communication). Mean difference (\pm SE) between known and determined standard lactate concentrations in the assays was $4.1 \pm 1.8\%$ with correlations $0.97 \leq r \leq 0.99$.

Metabolic data consisted of rates of aerobic lactate generation rate every 15 minutes at 37° and 25° by whole blood. Data were analyzed by analysis of variance with group and time as classification variables [26].

RESULTS

Figure 1 indicates that small increases of aerobic blood glycolytic rate at 25° and 37° occurred during eyes closed rest without change on the control occasion for these subjects. For comparison, we show in Fig. 2 previously reported [12]

TABLE 1

WHOLE BLOOD INITIAL LACTATE GENERATION RATE

Rest		TM*	
37°	25°	37°	25°
2.8 ± 0.6	1.2 ± 0.7	3.2 ± 0.3	1.5 ± 0.2

Values are means \pm S.E. in μ moles/ml cells per hour.

*From [12].

aerobic blood glycolytic rate variation during TM and the corresponding control occasion for this group. Trends of increased glycolytic rate at 25° and 37° during rest differed significantly from the sharp declines of glycolytic rate at 25° and 37° found during TM. Initial (time 0) glycolytic rates at 25° and 37° in rest subjects did not differ significantly from initial blood glycolytic rates in the TM subjects (Table 1).

Gourley and Matschner [7] reported marked increase of blood pH upon exposure to air, due probably to loss of CO_2 . In this study, whole blood pH during the 90 minute aerobic incubations increased to approximately 8.0 at 37° and to approximately 7.8 at 25°. Initial blood pH values of rest and control incubation series at times 0, 15, 30, 45, 60, and 75 were very similar (Table 2); they were also constant during the experiment and similar to those of the TM group [12].

Concentration of arterial lactate did not change during rest or control occasions, and there was no significant variation of arterial O_2 and CO_2 tensions (PO_2 and PCO_2 , respectively), base excess, hematocrit, or glucose (Table 2). The data in the TM group were similar except for lactate [12].

On the average, 84% of the unstylized rest period was spent in wakefulness and 16% in stage 1 sleep, almost identical with findings for the TM group (90% and 10%, respectively) [12]. Galvanic skin resistance (GSR) increased during both TM and rest with significantly greater increase during TM (Fig. 3).

DISCUSSION

Since 90–95% of whole blood glycolysis is accounted for by red cells [1], these data indicate probable small increase

TABLE 2
MEAN ARTERIAL BLOOD GAS AND LACTATE CONCENTRATION VALUES, FOR REST GROUP STUDIED ON PRACTICE AND CONTROL OCCASIONS

	0 Min	15 Min	30 Min	45 Min	60 Min	75 Min
Practice (Unstylized Rest)						
pH	7.39 ± 0.01	7.38 ± 0.01	7.38 ± 0.01	7.37 ± 0.01	7.39 ± 0.01	7.39 ± 0.01
PCO ₂ , mmHg	39.3 ± 0.6	39.8 ± 0.6	40.3 ± 0.5	40.2 ± 0.5	39.2 ± 0.6	39.9 ± 0.6
PO ₂ , mmHg	100.3 ± 1.8	100.1 ± 2.1	99.1 ± 1.6	100.2 ± 2.0	102.6 ± 2.3	99.4 ± 1.6
Base Excess, mEq/l	-0.94 ± 0.4	-1.10 ± 0.4	-1.28 ± 0.5	-0.97 ± 0.4	-1.09 ± 0.4	-0.82 ± 0.4
Lactate, μmol/ml	0.75 ± 0.05	0.72 ± 0.09	0.80 ± 0.10	0.78 ± 0.21	0.76 ± 0.40	0.78 ± 0.31
Glucose, mg/100 ml	68.0 ± 7.1	69.1 ± 4.8	67.1 ± 5.1	64.9 ± 8.7	67.8 ± 9.1	68.2 ± 7.1
Hematocrit, %	47.1 ± 8.1	46.8 ± 7.9	46.9 ± 8.0	47.2 ± 7.8	47.2 ± 7.8	46.9 ± 5.6
Control						
pH	7.38 ± 0.02	7.37 ± 0.04	7.39 ± 0.01	7.39 ± 0.01	7.37 ± 0.02	7.36 ± 0.03
PCO ₂ , mmHg	40.2 ± 0.7	40.7 ± 0.6	39.1 ± 0.5	39.9 ± 0.6	40.6 ± 0.4	41.1 ± 0.7
PO ₂ , mmHg	101.4 ± 2.1	99.8 ± 1.8	100.0 ± 2.0	99.1 ± 1.7	103.1 ± 2.6	99.1 ± 2.8
Base excess, mEq/l	-1.11 ± 0.6	-1.0 ± 0.7	-1.2 ± 0.7	-0.98 ± 0.4	-1.2 ± 0.3	-1.1 ± 0.6
Lactate, μmol/ml	0.69 ± 0.07	0.74 ± 0.12	0.72 ± 0.10	0.68 ± 0.21	0.70 ± 0.11	0.78 ± 0.4
Glucose, mg/100 ml	73.1 ± 10.1	70.8 ± 6.1	71.0 ± 6.7	72.4 ± 5.8	69.7 ± 4.9	70.8 ± 9.1
Hematocrit, %	48.4 ± 7.6	47.9 ± 45.7	47.1 ± 6.1	49.0 ± 5.2	48.7 ± 8.7	48.6 ± 7.2

Values are means ± S.E.

of red cell glycolysis during unstylized rest, as compared with marked TM-induced decline. This result is consistent with relative constancy of arterial lactate during rest (Table 2) as compared with decline during TM [12], since the red cell is a primary contributor to the lactate content of blood [16]. Since total sleep and sleep stage percent were almost identical in the 2 groups, sleep cannot account for the results.

Whereas the data of this study do not allow specification of mechanism of this effect, the agency of several effector(s) can be reduced in likelihood. For example, the data lend added support to the hypothesis [12] of lack of significant role of the powerful effector, pH (in plasma) in these metabolic effects of rest states, since, despite large difference of blood metabolic changes, pH differed little between the behaviors (Table 2 and [12]). This does not completely rule out the possibility of altered cell pH in the metabolism, but such alteration is unlikely because hydrogen ions are believed to be passively distributed across the red cell membrane in most circumstances according to Gibbs-Donnan equilibrium. The agency of weaker effectors, such as PO₂ and PCO₂ and variation of red cell numbers, can also be eliminated, since blood gases and hematocrit did not change. Finally, since facilitated glucose transport in the mammalian red cell is 2- to 250-times greater than rate of glucose phosphorylation [20,25], and glucose levels were unaltered, a role for blood glucose is unlikely.

These results support the specificity of TM in its metabolic control of the erythrocyte. However, the reasons for the difference between TM and unstylized rest remain

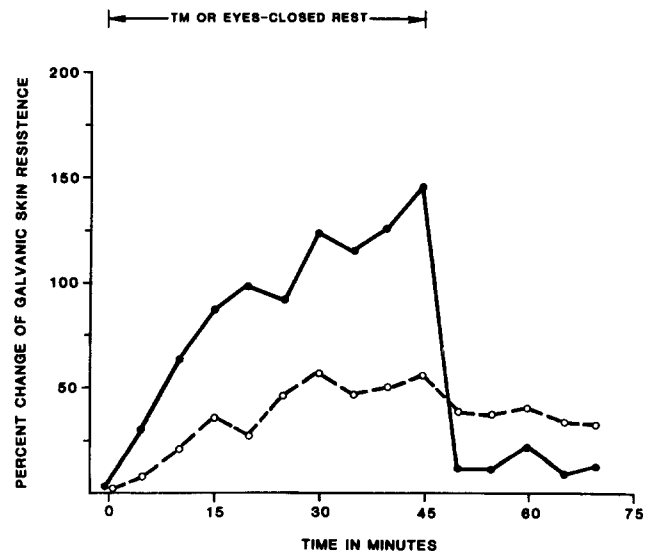


FIG. 3. Galvanic skin resistance (GSR) during and after TM (●) and during and after eyes closed rest (○) (practice occasions only).

unknown. The TM subjects of these investigations are long-term practitioners. Whereas the results of early research studying only whole body respiratory change were consistent with physiologic similarity of TM and rest, more recent measurements—specifically on TM subjects who have now

been eliciting this behavior for 5–10 years—indicate development of other fundamentally different hormonal, circulatory, and electrophysiologic changes [7, 11–14, 18] in this group.

Since participation of a humoral agent(s) in the TM-induced decline of red cell glycolysis is likely [12], it is possible that repeated elicitation or some special feature of this behavior is necessary for elaboration of the responsible effector. While some known hormones have been reported to affect red cell 2,3-diphosphoglycerate levels, deformability, osmotic fragility, membrane structure, and size [21], their significance for physiological control of human red cell metabolism is not established, except possibly for T_3 and T_4 (27). However, in a recent study [11], we found that T_3 and T_4 concentrations did not vary during either TM or rest.

Although insulin receptors have recently been identified in the red cell [22], their significance for red cell carbohydrate metabolism is unlikely [5], and we also found little variation of insulin concentration during these behaviors [11]. Finally, the temporal patterns of plasma arginine vasopressin (AVP), oxytocin, growth hormone, and prolactin [11, 14, 18] during TM diminish the likelihood of their participation in this response.

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