# RHYTHMS OF SLOW SLEEP AND WAKEFULNESS IN OSCILLATIONS OF THE CEREBRAL CORTICAL REDOX POTENTIAL

**T. B. Shvets-Ténéta-Gurii, V. N. Mats, and O. B. Kovchegova** UDC 612.825.015.06:612.821.7].088.7/.8

**Key Words:** cerebral cortex; redox potential; sleep; wakefulness.

Rhythmic oscillations of parameters of the oxidative metabolism of the brain were first found in experiments with polarographic recording of the free oxygen partial pressure ($pO_2$) in the brain tissue of animals and man [4, 10-12]. It has been suggested that rhythmic oscillations of $pO_2$ arise not only because of the rhythmic character of the $O_2$ supply to brain tissue (fluctuations of cerebral blood flow and of the pulse and respiration rates), but also because of certain other factors [2]. One such factor may be rhythmic changes in oxidative metabolism of brain tissue, demonstrated experimentally first during recording of the redox potential state (RPS) of the brain [6, 14], and later in fluctuations of the NADPH concentration, measured spectrophotometrically [13]. It has been shown in recent years [3] that the periods of a certain part of the spectrum of rhythmic oscillations of cat brain $pO_2$ are closely connected with the animals' functional state: on the transition from active wakefulness to slow-wave sleep the periods of the oscillations of $pO_2$ increase. One of us [8] showed previously that rhythmic oscillations of the cerebral cortical RPS of rabbits in the period of defensive-orienting behavior (the state of active wakefulness) are characterized by oscillations with the same period (measuring a few seconds) and of quasisinusoidal form.

In the investigation described below, in which chromic experiments were carried out on waking animals, rhythmic oscillations of RPS arising in two clearly distinct states, namely sleep, during which slow waves of high amplitude developed on the electrocorticogram (ECoG), and active wakefulness, judged by reduction of the amplitude of the ECoG, were investigated.

## EXPERIMENTAL METHOD

Potentiometric recording of the RPS of a biological object has been used for quite a long time [7]. However, its classical form (the use of an active platinum electrode, a standard nonpolarized comparison electrode, and a dc amplifier with high input resistance — from $10^{12}$ to $10^{14}$ Ω) is unsuitable for recording the RPS of the brain in chronic experiments under behavioral conditions for two reasons. First, it is virtually impossible to construct a nonpolarized electrode for chronic experiments which would have a standard potential when implanted. Second, under classical experimental conditions, electrical activity of the brain is superposed on the trace of RPS over a wide range of frequencies. The modification of the classical method of potentiometry of RPS, suggested previously [7], enabled slow changes of RPS (with a duration of 1-2 sec or more) to be separated from changes of the steady potential of the brain and enabled slow oscillations of RPS to be recorded in chronic experiments for a period of several months. The modification was that a platinum electrode, implanted into the cranial bone, was used as the comparison electrode, for according to our data, this does not detect oscillations of RPS commensurate with those of RPS of brain tissue [7], and also that a dc amplifier with low input resistance (1 MΩ) was used. The time constant of the system, namely the pair of platinum electrodes and input of the amplifier, in these experiments was 0.2-0.3 sec (Fig. 1a). Thus under the experimental conditions used, changes in steady potential were reliably removed from the recorded RPS, and the trace consisted of slow changes of RPS (duration 2-3 sec or more), on which the oscillations of the ECoG and of RPS with a frequency of more than 1 Hz were superposed in integral form.

Some of the experimental results were subjected to correlation analysis of the slow changes of RPS on a "Nord-100" computer.

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Laboratory of General Physiology of Temporary Connections, Laboratory of Morphology of the Central Nervous System, and Laboratory of Neurocybernetics. Institute of Higher Nervous Activity and Neurophysiology, Academy of Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. S. Rusinov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 108, No. 9, pp. 259-261, September, 1989. Original article submitted January 20, 1989.

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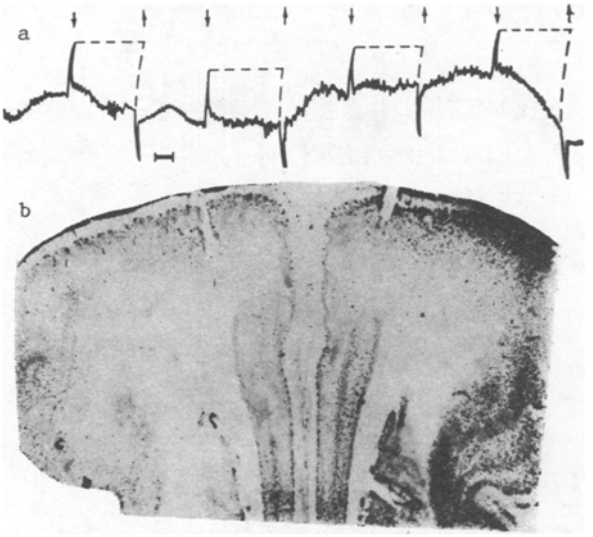


Fig. 1. Electrical characteristics of platinum electrodes: a) Recording of slow changes in RPS and square calibration pulses applied through two platinum electrodes (active electrode in cerebral cortex, comparison electrode in cranial bones); b) track of active electrode in cortex (right). Calibration: 1 mV, 1 sec.

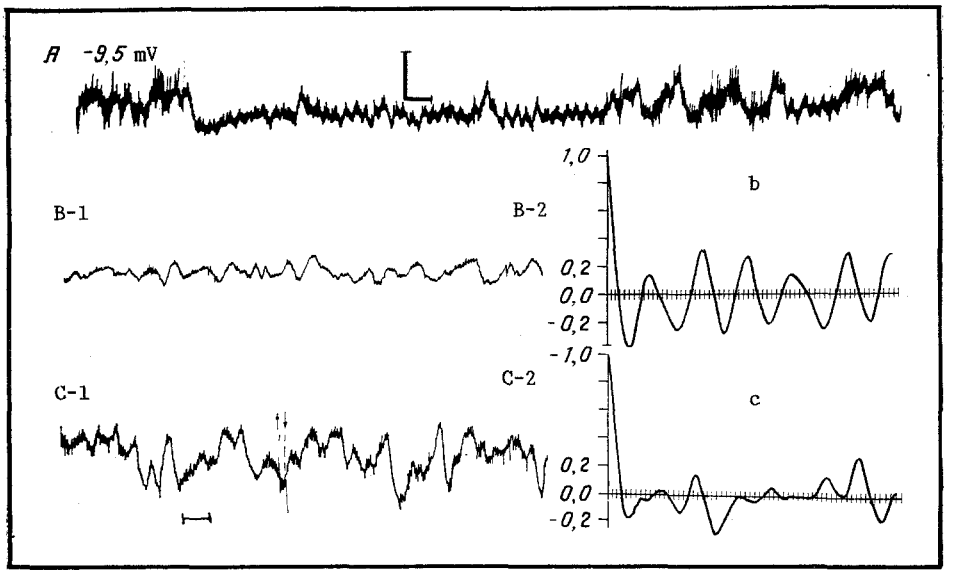


Fig. 2. Oscillations of RPS during sleep and wakefulness (A), wakefulness (B), and sleep (C) and corresponding correlation functions (b, c). Abscissa (b and c), time intervals 1 sec in duration; ordinate, coefficient of correlation. Calibration: 1 mV, 10 sec.

Altogether 205 experiments were carried out on nine rabbits and 118 electrodes were used (46 electrodes were implanted down to the dura, 72 into the cortex).

## EXPERIMENTAL RESULTS

In 120 experiments (523 traces, including 224 from the dura and 299 from the cortex; all fragments recorded from one electrode in the course of one experiment were taken to be the trace) distinct and frequent changes were observed in cycles of slow-wave sleep and active wakefulness, reflected in the character of the ECoG. In 16 ± 5% of traces (95% confidence interval calculated as in [1]), obtained from the dura without causing damage to it (a morphological investigation revealed no

traces of these electrodes on the brain surface), and in 63 ± 6% of traces obtained from electrodes implanted into the substance of the cortex (Fig. 1b), cycles of active wakefulness were accompanied by the formation of quasisinusoidal oscillations of RPS (period 3-10 sec), and cycles of slow-wave sleep were accompanied by the appearance of oscillations of a complex form, of longer duration (period 15-40 sec), and a higher amplitude (Fig. 2A). The results of visual analysis were confirmed by correlation analysis of 17 traces (nine in a state of sleep, eight in a state of wakefulness). Graphs of autocorrelation functions of changes in RPS in a state of sleep took the form of curves with a more complex rhythm, the peaks of which pointed to the presence of oscillations with periods of 20-30 sec (Fig. 2C). It can thus be concluded from correlation analysis that quasiperiodicity with a period of a few seconds occurred in the changes in RPS during active wakefulness, whereas oscillations with periods of several tens of seconds were found in the changes of RPS during slow sleep.

The formation of rhythmic oscillations in oxidative metabolism is regarded in the literature as the result of the appearance of metabolic strain [8]. Rhythmic oscillations of RPS of the brain observed in chronic experiments with implanted electrodes are largely determined by an increase in the strain on oxidative metabolism of the cortex, due to the fact that the momentary integrative work of the brain is complicated by the need to compensate the traumatic action of the electrodes, i.e., it takes place under conditions of an additional load on the oxidative metabolism of the brain [8].

These facts suggest that during transitions from wakefulness to slow-wave sleep and vice versa there is a shift of the maxima of oxidative metabolism between biochemical systems, which are characterized by differences in their rhythm of self-regulation. During sleep rhythmic oscillations develop in the whole range of redox systems (ROS), including systems with periods with a duration of several tens of seconds. During the transition to wakefulness, either synchronization of the work of all ROS takes place in one single, faster rhythm, or rhythmic oscillations are preserved only in one ROS and they are sharply depressed in the others. ROS forming oscillations of RPS may be found either in different functional cells (neurons of glial cells, for example), or in the same cells, in which they may perform different functions. In all situations, the formation of rhythmic oscillations of integral RPS is based on the ability of individual ROS to synchronize their own intrinsic oscillations (biochemical synergism) [15] and to interact through biological membranes [5]. In our view, certain rhythms of brain electrical activity are formed by synchronous changes in cell membrane potentials arising as a result of biochemical synergism of ROS maintaining the electrochemical gradient on their membranes, such as the theta-rhythm in regions acquiring a pacemaker role [9].

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