ISSN 0362-1197, Human Physiology, 2013, Vol. 39, No. 6, pp. 642–654. © Pleiades Publishing, Inc., 2013.
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# Low-Frequency Rhythmic Electrocutaneous Hand Stimulation during Slow-Wave Night Sleep: Physiological and Therapeutic Effects

**P. A. Indursky[a], V. V. Markelov[a], V. M. Shakhnarovich[a], and V. B. Dorokhov[b]**

[a] *J. S. Co. NEUROCOM, Russia*

[b] *Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, 117485 Russia*

Received May 17, 2013

**Abstract**—Neocortical EEG slow wave activity (SWA) in the delta frequency band (0.5–4.0 Hz) is a hallmark of slow wave sleep (SWS) and its power is a function of prior wake duration and an indicator of a sleep need. SWS is considered the most important stage for realization of recovery functions of sleep. Possibility of impact on characteristics of a night sleep by rhythmic (0.8–1.2 Hz) subthreshold electocutaneous stimulation of a hand during SWS is shown: 1st night—adaptation, 2nd night—control, 3d and 4th nights—with stimulation during SWA stages of a SWS. Stimulation caused significant increase in average duration of SWS and EEG SWA power (in 11 of 16 subjects), and also well-being and mood improvement in subjects with lowered emotional tone. It is supposed that the received result is caused by functioning of a hypothetical mechanism directed on maintenance and deepening of SWS and counteracting activating, awakening influences of the afferent stimulation. The results can be of value both for understanding the physiological mechanisms of sleep homeostasis and for development of non-pharmacological therapy of sleep disorders.

*Keywords:* slow wave sleep, EEG delta waves, electrocutaneous stimulation, the subjective sleep estimation

**DOI:** 10.1134/S0362119713060054

Good night sleep is a necessary condition for effective activity during the day time. There are two main phases of sleep: the NREM (slow) and REM sleep (paradoxical) having different mechanisms and constituting the night cycle that lasts for 1.5 h. According to the international classification of Rechtschaffen and Kales [1], night sleep is divided into four stages: (1, 2) light sleep and (3, 4) deep sleep. Stages 3 and 4 are characterized by the high-amplitude slow-wave EEG activity (SWA) within the frequency range of 0.5–4.0 Hz; therefore, these stages are also called slow-wave sleep (SWS) stages or delta sleep due to the dominant delta rhythm.

According to the recent guidelines of the American Association of Sleep Medicine (AASM) of 2007, stages 3 and 4 were combined into a single stage 3 [2]. Deep delta sleep, which determines the sleep quality, is considered the most important stage for the body's recovery after sleep. Sleep control is known to obey the rules of homeostasis: the longer the wakefulness caused by sleep deprivation the longer the duration of the slow-wave sleep (SWS) after that [3, 4].

The sleep cycles differ in their structure. Deep delta sleep predominates during the first half of the night. In the first two cycles, the delta wave amplitude is the highest, but later it decreases gradually to reach the lowest values by the end of the night, because of the reduced sleep requirement. In the second half of the night, the light sleep is dominant (stage 2), and the phase of paradoxical sleep is lengthened [5].

Local control of delta sleep emphasizes the homeostatic role of this phase. During restorative night sleep after sleep deprivation, the amplitude of slow delta wave is still high in the frontal cortical areas that are involved in all psychical functions [6–9]. The highest delta wave amplitude is reported to be in the cortical regions that were the most active during wakefulness, which also confirms the local control of delta sleep. For example, strong stimulation of the right hand during wakefulness led to an increase in the night delta rhythm in the cortical projection of the somatosensory cortex of the left hemisphere [9]. Conversely, immobilization of the right hand reduced the delta rhythm power in the proper cortical projection [10].

Experiments with variation of circadian rhythms also confirm the homeostatic function of SWS. Many sleep parameters proved to be sensitive to changes in circadian rhythms, but the duration of the SWS depends only on the time of previous wakefulness regardless of the circadian phase [11].

Thus, the need for delta sleep depends on its homeostatic function, because numerous important physiological processes occur during this deep sleep stage and its disorders lead to various pathologies [12–16]. Participation of slow sleep in learning and consolidation of human declarative memory has been

reported in recent years [17, 18]. Much attention is attracted by Tononi's hypothesis [19], suggesting that the effect of sleep on memory consolidation is related to plastic rearrangements, when synaptic activation increases during wakefulness, while sleep is required to restore synaptic homeostasis. This hypothesis is useful for understanding the consequences of sleep deprivation and for the development of new diagnostic and therapeutic approaches to the treatment for sleep and neuropsychic disorders.

The range of sleep disorders is extremely wide. At the beginning, this is the lack of sleep and/or abnormal biorhythm. There are many reasons for these disorders and, when they are neglected, lead to somatic and psychosomatic diseases. Because of sleep deficiency or disorders of SWS one feels physically broken after waking, sleep does result in good spirits [20], and the memory is worsened [21].

However, there is evidence that SWS duration varies significantly in different individuals and depends on sex, age, and genetic factors. The question arises on the functional role of SWS and whether sleep quality and subsequent activity during wakefulness depend on individual differences in the slow sleep's duration [13, 22, 23].

Non-drug therapy is of special interest for sleep medicine. At present, a set of nonpharmacological methods of sleep treatment is available. The American Academy of Sleep Medicine proposes the following [24]: (1) training of sleep hygiene, (2) control of external stimuli, (3) recommendations on a sleep schedule and sleep restriction, (4) learning the principles of chronotherapy, (5) practical training for "paradoxical intensions" to eliminate insomnia, (6) multicomponent cognitive-behavioral therapy, (7) training the progressive muscle relaxation, (8) various types of sensory therapy, and (9) training of the biofeedback function control.

The first seven methods are aimed at developing the behavioral skill of a patient to eliminate sleep disorders; they are nonspecific and can influence sleep in general. The instrumental methods (methods 8 and 9) are different in that they use various technical approaches to induce and control normal sleep. Comparison of different nonpharmacologic methods of sleep improvement demonstrates that the instrumental methods are more effective than the behavioral ones [25].

An example of sensory therapy is exposure to the intermittent subthreshold electromagnetic field of 27.12 MHz, which reduces the latent period of sleep stage 2 and increases the duration of this stage [26]. Various relaxation methods, both strictly behavioral and those using the biological feedback from different physiological functions such as breathing, muscle tone, heart rate, and body temperature, also proved to be helpful [27]. The methods based on the parameters of the brain's electrical activity represent a special group and are used for instrumental sleep control and correction [28]. The methods that are popular abroad, such as Brain Wave Synchronization and Audio-Visual Entrainment, employ low-frequency sensory stimulation at a frequency coinciding with the EEG rhythms. In Russian studies, the methods of audiovisual stimulation are assumed to have the resonance effects dependent on interactions between the afferent stimulation frequency and that of the endogenous brain processes reflected in EEG rhythms [27]. An example of this effect is the "brain's music" obtained by transformation of EEG rhythms recorded during night sleep into music, which the same patient can hear before falling asleep. In some cases, this reduces the time before the onset of sleep and increases sleep duration [29, 30].

Recent studies have demonstrated the possibility of exposure to SWA night of sleep by central stimulation of the brain, using as a trigger to start the stimulation of high-amplitude delta waves when they appear in SWS. The following techniques have been used: transcranial magnetic stimulation [31], transcranial direct current [32, 33] or pulse current [34] stimulation, as well as intracranial electric stimulation in animal experiments [35]. The low-frequency acoustic stimulation during SWS proved to be also effective in SWA enhancement [36]. Note that stimulation before sleep, on the contrary, increased the latent period of sleep onset, which demonstrates the dependence of stimulation efficiency on the functional state of brain. In the next report [37], the authors described an approach using a closed-loop acoustic stimulation synchronized with the slow delta wave phase. Only synchronized stimulation enhances slow-wave activity and improves consolidation of the declarative memory, while stimulation that was not synchronized with the SWS was ineffective [37].

Thus, the above studies [31–37] suggest that both central and peripheral stimulation during the SWS stage increases SWA, which is accompanied by processes leading to the consolidation and reproduction of the declarative memory. On the contrary, selective SWS deprivation in the night before learning affected the learning capacity and preservation of memory traces [38]. These results contribute to the idea that SWS is involved in the consolidation and reproduction of memory [18, 19].

The premise of the present study was the fact that we found the close relationship dynamic states in clinical forms of depression and neurosis with a full sleep patterns. In particular, when the sleep structure is spontaneously restored, the patient's mood in the morning improved as compared to that before sleep [39, 40].

Here, we studied whether electrocutaneous low frequency stimulation (0.8–1.2 Hz) during the slow-wave stage of night sleep can improve the physiological parameters of the delta sleep quality. The subjective therapeutic effects of stimulation were also analyzed using WAM (well-being, activity, mood) questionnaire

for the patients with low emotional tone and sleep disorders. The preliminary results were published earlier [41].

## METHODS

Sixteen subjects (nine men and seven women) 30 to 60 years of age participated in our study. In order to obtain the pronounced therapeutic effects, we selected subjects with slight insomnia and some complaints, such as low emotional tone and night sleep disorders. All of the subjects knew about the research conditions and they gave their informed written consent in accordance with the Helsinki Declaration and the regulations of Russian and international law. This study has been approved by the Ethic Commission of the J. S. Co. NEUROCOM.

**Data recording** was conducted using a SAGURA polysomnograph (Germany). Electroencephalograms were recorded using eight electrodes placed according to the international 10–20 scheme ($Fp_1$, $Fp_2$, $C_3$, $C_4$, $T_7$, $T_8$, $O_1$, $O_2$); in order to obtain an electrooculogram (EOG) of the horizontal eye movements, electrodes were placed near the outer corners of the eye slits. In addition, electromyogram (EMG) from the submental muscles and breathing pneumograms were recorded using a piezo sensor with a belt. Combined mastoid electrodes (A1 and A2) served as reference electrodes. The gilt cup electrodes and adhesive electrode gel from Grass (United States) were used. The signal sampling rate was 200 Hz; the digit capacity of the analog-to-digit converter was 12 bit.

Similar electrodes were used for electrocutaneous stimulation and EEG recording. For electrostimulation, electrodes were placed on the right hand palm (the internal side) of the subject. The stimulation frequency ranged from 0.8 to 1.2 Hz and corresponded to the individual properties of a subject's delta rhythm. The current was 80% of the current perceived by the subject during wakefulness, but it was not higher than 100 μA. The pulse duration ranged from 100 to 300 ms. The effectiveness of stimulation parameters was tested by recording the evoked potentials in $Fp_1$ and $Fp_2$ derivations.

Stimulation was switched on automatically 30 min after the appearance of the EEG delta rhythm during sleep stages 3 and 4 and stimulation was over when delta rhythm declined significantly. An electronic software device has been designed for on and off exactly stimulation stages SWS. This device triggered stimulation when delta waves stabilized, and it turned off when the closed-loop completion of stimulation occurred (Fig. 1b). The program determined in real time the threshold value of the delta wave amplitude for the beginning and completion of stimulation.

Each subject slept in the laboratory four nights in succession. The data of a polysomnogram recorded during the first adaptive night were not considered in our analysis. In the second night, the complete polysomnographic study but without stimulation was conducted (the background analysis). During the third and fourth nights, polysomnogram recording and stimulation were performed simultaneously. Electrodes for the subthreshold hand stimulation were installed during all four nights. The details of the experiment were not discussed with the subjects, and they did not know which night stimulation was applied.

The nights when there were some technical problems with polysomnographic recording were not included in the analysis but rather only the nights without any artifact recordings. Thus, the recordings made during 39 nights have been selected for the analysis: 16 background recordings (the second night without stimulation) and 23 recordings with stimulation (the third and fourth nights), among which there were seven recordings made in the fourth night.

**Analysis of individual data.** Only the EEG data recorded from the right frontal electrode $Fp_1$ were analyzed. In the comparative EEG analysis, the rapid Fourier transform was used (SAGURA software). Spectral analysis of the relative and absolute changes in the delta wave power was performed in each epoch (30 s) of the first half of the night before and after stimulation during delta sleep and separately for each of the 16 subjects. The most distinct and pronounced recordings of the SWS of the first half of the night (the first or second cycle) were selected before and after stimulation. For each subject, the parameters of the same cycles were taken into account. The relative EEG power was calculated as the ratio of power in delta band (05–2.0 Hz) to the total EEG power within the range of 0.5–30 Hz.

In comparative analysis, $t$ test and the STATISTICA 7 software were used. In order to verify normal distribution, the Shapiro–Wilk test was used.

**Analysis of summarized data.** The following parameters were used to analyze the night sleep structure: sleep effectiveness in percent; the relative sleep effectiveness (the ratio of the real sleep time to the time of staying in bed); LPSWS, latent period of the SWS; SWS%, the relative duration of the SWS; SWS, absolute duration of the SWS; SWS (1–4), SWS duration in four successive cycles of sleep; LPREM, the latent period of rapid sleep; REM%, the relative duration of rapid sleep; REM (1–4), rapid sleep duration in four successive stages; EM (1–4), intensity of rapid eye movements (the average number of rapid eye movements per minute) in four successive stages of sleep; awakening, %, the relative duration of awakenings in the night sleep; and awakening, total duration of awakenings during the night sleep.

The summarized data on the sleep parameters were processed statistically using the Mann–Whitney $U$ test and the software packet STATISTICA 7.

**Testing of sleep quality.** The subjects were asked to fill the questionnaire WAM (health (the way one feels), activity, mood) [41] before and after sleep to

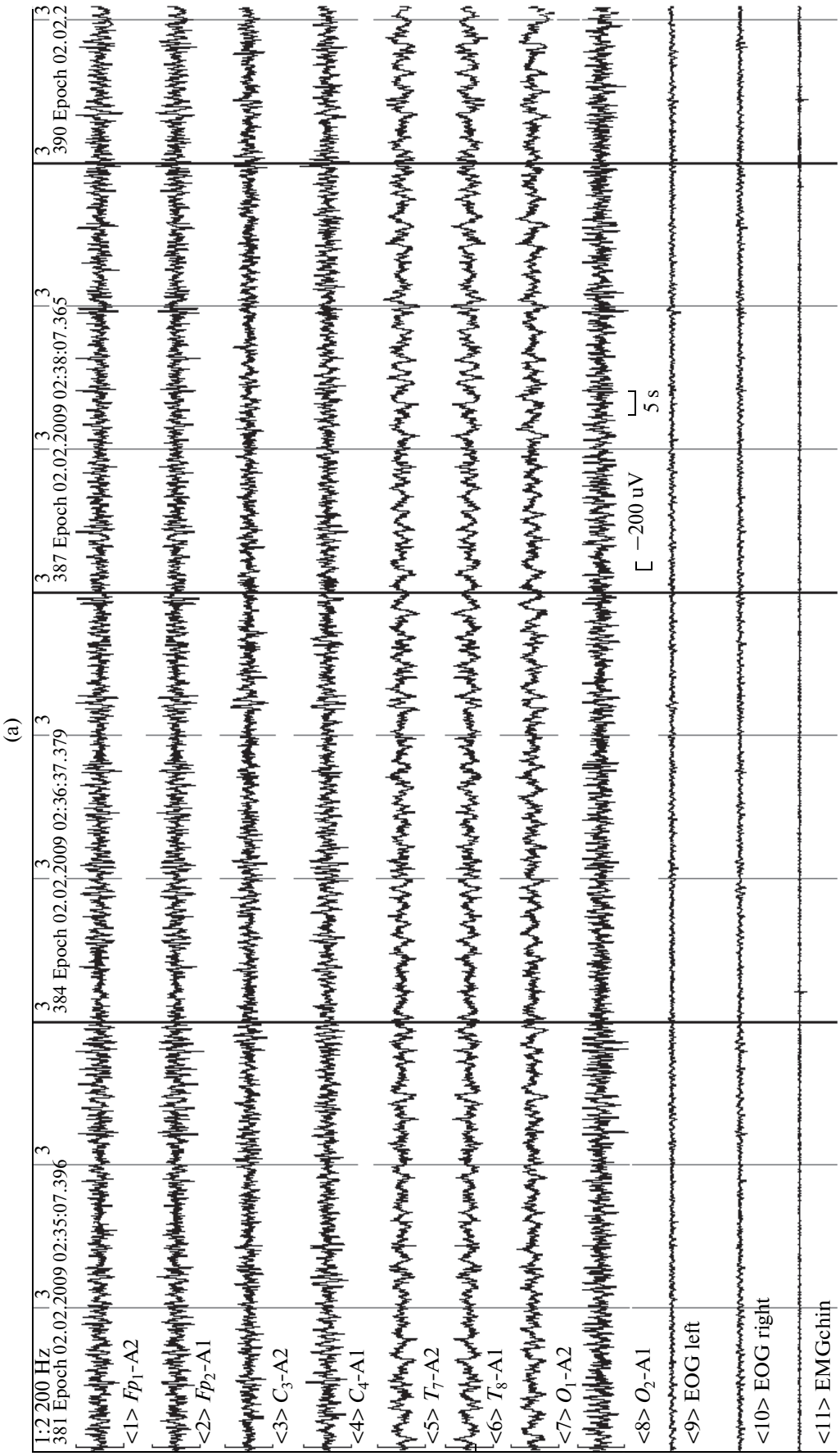


**Fig. 1.** Polysomnogramms of subject M.V. as obtained for two nights. (a) An epoch of delta sleep without stimulation; (b) an epoch of delta sleep with stimulation. Vertical lines mark electrical stimuli within the pulse bursts during sleep stages 3–4. It can be seen that the amplitude of EEG delta waves increases in response to stimulation especially in the frontal derivations ($Fp_1$ and $Fp_2$). $X$ axis (above), time and the 30-s epoch numbers; $Y$ axis top-down, polysomnogram channels: (1–8) EEG; (9, 10) EOG; (11) EMG; (12) breathing. Vertical bracket on EEG channels 1–8 (to the left), amplitude calibration 200 μV.

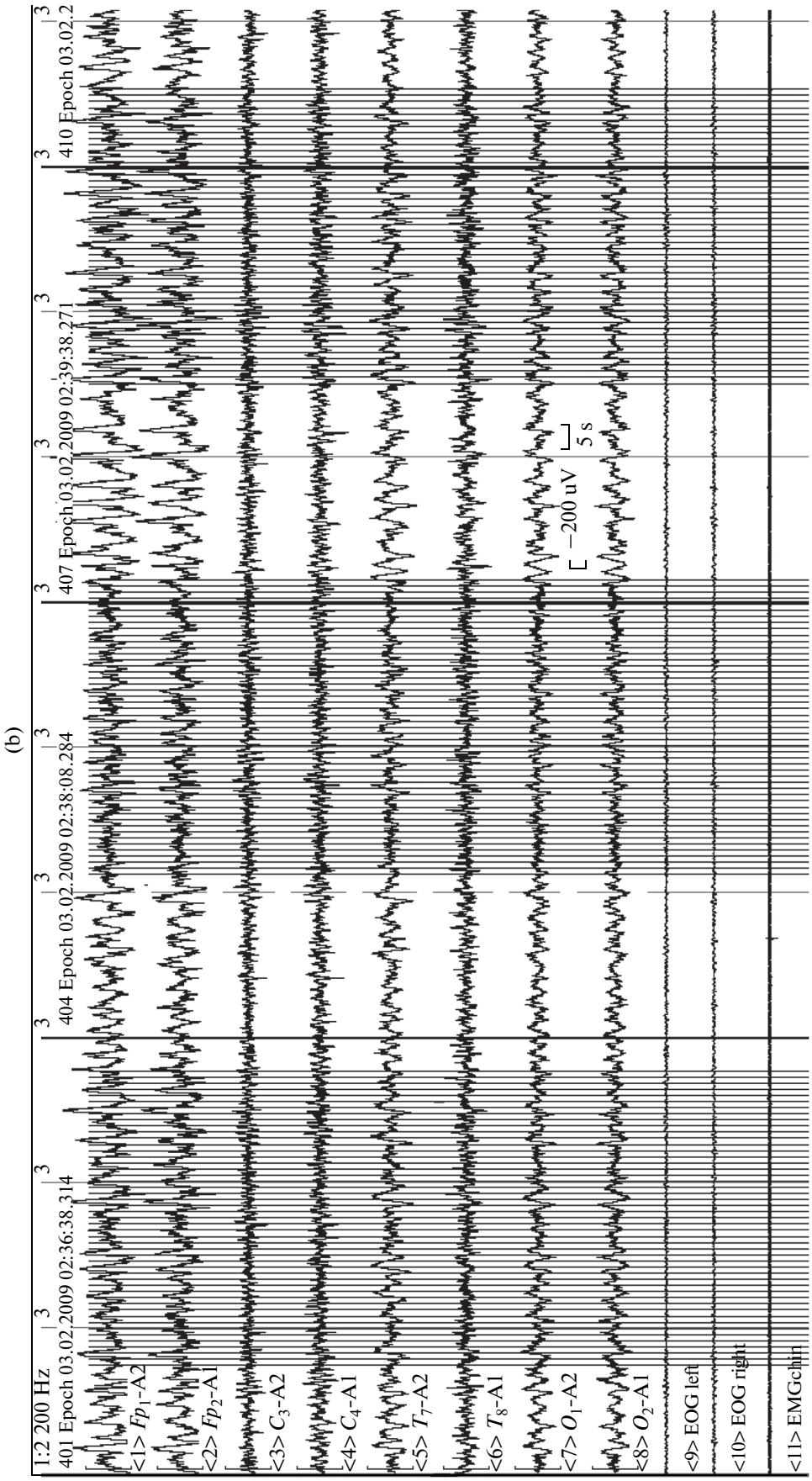
(b)
1:2 200 Hz
401 Epoch 03.02.2009 02:36:38.314
404 Epoch 03.02.2009 02:38:08.284
407 Epoch 03.02.2009 02:39:38.271
410 Epoch 03.02.2
<1> $Fp_1$-A2
<2> $Fp_2$-A1
<3> $C_3$-A2
<4> $C_4$-A1
<5> $T_7$-A2
<6> $T_8$-A1
<7> $O_1$-A2
<8> $O_2$-A1
<9> EOG left
<10> EOG right
<11> EMGchin
−200 uV
5 s

**Fig. 1.** (Contd.).

assess the quality of their night sleep with and without stimulation.

## RESULTS

Comparison of the effects observed in the nights with and without stimulation has demonstrated that stimulation improves sleep quality as determined from the objective polysomnogram data and according to the WAM questionnaire, the subjective sleep estimation also improved. The quantitative data can be seen in Tables 1–4.

Table 1 demonstrates that electrocutaneous hand stimulation during stages 3 and 4 led to an increase in the average sleep duration in these stages of the first and second cycles (SWS1, SWS2) as compared to sleep without stimulation. In the first cycles SWS1, sleep duration only tended to increase, while in the SWS2 cycle, the increase was significant. The reverse trend was observed in the third and fourth cycles of sleep (SWS3, SWS4); i.e., the SWS duration was shorter in the nights with stimulation. Thus, the average SWS duration remained almost the same before and after stimulation, but sleep duration in separate stages altered after stimulation: this parameter increased in the first half of the night, but it decreased in the second half of the night. Note that, in paradoxical sleep, the pattern was the reverse: the intensity of rapid eye movements (EM) increased significantly in the third and fourth cycles of sleep (EM3, EM4). Table 1 demonstrates also that stimulation caused a tendency of reducing the duration and frequent of awakening in sleep.

Analysis of the relative and absolute changes in delta wave power demonstrates that, in most subjects, electrostimulation caused a significant increase in the EEG power of the delta band in sleep stages 3 and 4. Note that the relative EEG power proved to be more sensitive to stimulation than the absolute power of the delta band. Stimulation caused a significant increase in the relative average delta wave power in 11 out of 16 subjects (68.75%, Table 2). The absolute average delta wave power increased significantly only in nine subjects (56.25%) in stages 3 and 4 of night sleep (Table 3). In Tables 2 and 3, the data are in a decreasing order of significance of the compared parameters. Table 2 demonstrates the ratios of delta wave power to the general EEG power in the same phase of SWS; Table 3 contains the absolute average values of the delta wave power.

The subjective estimate of night sleep with and without stimulation was obtained using the WAM questionnaire, which the subjects filled in before and after sleep. The results can be seen in Table 4.

Note that the subjective sleep estimation in the morning after the nights with stimulation was not always positive as compared to the nights without stimulation, and this depended on the initial state of the subject. In some of the subjects, there were actual sleep disorders, such as high anxiety, difficulties in falling asleep, recurrent awaking and other signs of insomnia, as well as age-related changes.

Along with general analysis of the subjective self estimates according to the WAM questionnaire, the relative parameters of the subjective estimates were compared after the nights with and without stimulation. Only the parameters that were increased by at least 0.5 were taken into account. After the night without stimulation, the subject condition in the morning was improved by 30% according to all of the subjective estimates. After the nights with stimulation, the number of subjects with the positive results increased: self rated well-being (W) and the mood (M) improved in 56% and 74% of the subjects, respectively. As for the subjects' activity (A), it remained unchanged (30%).

The results are presented graphically in Figs 1–3. Figure 1 are the recordings of epoch fragments in the SWS during two successive nights with and without stimulation (night A and night B, respectively), which were made in subject M.V. who had a high level of anxiety. The straight vertical lines mark the bursts of stimuli with 60–90 s duration and 30–60 s pauses. Stimulation switched on automatically with the appearance of the delta rhythm in the third stage of sleep and stimulation was over with the decline of the amplitude of the delta wave to a certain threshold. As soon as during the first night, stimulation led to pronounced delta wave activity (*B*).

Figure 2 demonstrates the hypnograms and spectral EEG characteristics obtained in three different subjects in the nights with and without stimulation. It can be seen that stimulation in the SWS stage of sleep promoted an increase in the amplitudes of the EEG delta band in the first and second sleep cycles primarily and the sleep structure became more cyclic.

Figure 3 represent the histograms that complement Table 1. The frequency of emerging different values of SWS duration in successive four sleep cycles with and without stimulation can be observed during all the nights.

## DISCUSSION

Studying the effect of the low-frequency electrocutaneous hand stimulation during the SWS stage of the night sleep on the objective (physiological) and subjective estimation of sleep has demonstrated that stimulation during the SWS of sleep substantially improves the sleep quality in most subjects (11 out of 16). Stimulation of this kind led to an increase in duration of SWS mostly in the first two cycles. In the first cycle (SWS1), only a tendency towards an increase of the average duration of the SWS was observed, while in the second cycle of sleep, there was a significant increase in the average duration of the SWS in the nights with stimulation. A different pattern was observed in the third cycle, where the average SWS duration in the nights with stimulation decreased significantly; a sim-

**Table 1.** Averaged values of sleep parameters in the successive four cycles of sleep in the nights with and without stimulation during the SWS stage (SWS) (23 and 16 nights, respectively)

| Parameter | Without stimulation 16 nights | With stimulation 23 nights | Mann–Whitney *U* test |
|---|---|---|---|
| $S_{eff}$, % | 94.8 (6.2) | 97.1 (4.5) | Tendency $0.05 < p < 0.1$ |
| Time of recording, min | 448.1 (80.0) | 439.0 (71.4) | |
| Time of sleep, min | 424.5 (77.7) | 425.4 (74.9) | |
| Time of falling asleep, min | 26.0 (18.1) | 24.0 (22.1) | |
| Stage 2, % | 45.0 (8.9) | 42.9 (8.3) | |
| Stage 2, min | 188.2 (40.4) | 183.3 (51.7) | |
| LPSWS, min | 13.3 (8.8) | 14.5 (16.8) | |
| SWS, % | 24.8 (13.1) | 27.1 (10.3) | Tendency $0.05 < p < 0.1$ |
| SWS, min | 107.0 (53.8) | 114.4 (47.1) | |
| SWS1, min | 55.1 (30.8) | 56.5 (20.5) | |
| SWS2, min | 26.0 (16.8) | 42.8 (26.1) | $p = 0.01$ |
| SWS3, min | 25.2 (12.8) | 15.6 (10.1) | Tendency $0.05 < p < 0.1$ |
| SWS4, min | 21.3 (16.4) | 12.8 (13.8) | |
| LPREM, min | 125.5 (39.7) | 97.1 (49.0) | |
| REM% | 13.0 (6.6) | 16.0 (5.6) | Tendency $0.05 < p < 0.1$ |
| REM, min | 58.5 (36.4) | 68.5 (27.3) | Tendency $0.05 < p < 0.1$ |
| REM1, min | 12.2 (7.0) | 11.0 (7.4) | |
| REM2, min | 12.7 (9.5) | 18.0 (10.1) | Tendency $0.05 < p < 0.1$ |
| REM3, min | 23.5 (6.4) | 19.9 (13.7) | |
| REM4, min | 24.2 (17.2) | 25.3 (11.2) | |
| EM1 | 4.8 (6.0) | 3.5 (4.2) | |
| EM2 | 3.8 (3.0) | 4.2 (3.0) | Tendency $0.05 < p < 0.1$ |
| EM3 | 4.7 (4.5) | 6.1 (3.2) | $p = 0.01$ |
| EM4 | 2.9 (2.5) | 8.8 (8.7) | $p = 0.05$ |
| Awakening, % | 5.3 (6.3) | 2.9 (4.5) | |
| Awakening, min | 23.6 (28.8) | 12.3 (17.9) | |

Notes: Sleep effectiveness, %, the relative sleep effectiveness (the ratio of the real sleep time to the time of staying in bed); Stage 2,%, relative time of light sleep, Stage 2, absolute time of light sleep, LPSWS, latent period of the SWS; SWS%, the relative duration of the SWS; SWS, absolute duration of the SWS; SWS (1–4), SWS duration in four successive cycles of sleep; LPRS, the latent period of rapid sleep; REM%, the relative duration of rapid sleep; REM (1–4), rapid sleep duration in four successive stages; EM (1–4), intensity of rapid eye movements (the average number of rapid eye movements per minute) in four successive stages of sleep; Awakening%, the relative duration of awakening in the night sleep; Awakening, total duration of awakenings in the night sleep. The summarized data on the sleep parameters were processed statistically using Mann–Whitney *U* test and the software packet

**Table 2.** Individual values of the relative average power of EEG delta waves in stages 3–4 of the night sleep with and without stimulation for 16 subjects

| The subject, age, years | The relative average power of delta waves | | | | | *t* test for the independent samples |
|---|---|---|---|---|---|---|
| | without stimulation | cycle | the number of epochs | with stimulation | the number of epochs | |
| M.I., 30 | 42.6% ± 5.2% | 2 | 72 | 49.2% ± 7.7% | 103 | $p < 0.00001$ |
| Sh.D., 30 | 56.8% ± 0.5% | 2 | 130 | 59.2% ± 4.2% | 120 | $p < 0.00002$ |
| E.T., 31 | 53.0% ± 6.9% | 2 | 114 | 56.0% ± 5.7% | 106 | $p < 0.00004$ |
| L.E., 42 | 52.0% ± 4.3% | 2 | 52 | 57.3% ± 8.4% | 46 | $p < 0.0001$ |
| Sh.L., 39 | 42.4% ± 5.1% | 1 | 43 | 48.1% ± 4.4% | 45 | $p < 0.0001$ |
| M.V.,33 | 49.7% ± 7.0% | 2 | 101 | 53.3% ± 7.0% | 103 | $p < 0.0003$ |
| M.P., 36 | 48.3% ± 6.2% | 2 | 99 | 53.3% ± 4.9% | 82 | $p < 0.001$ |
| D.P., 34 | 52.0% ± 4.1% | 1 | 57 | 54.1% ± 3.4% | 82 | $p < 0.001$ |
| K.V., 58 | 41.5% ± 4.5% | 1 | 68 | 48.6% ± 8.1% | 105 | $p < 0.001$ |
| K.A., 31 | 49.6% ± 4.8% | 2 | 43 | 52.3% ± 6.4% | 54 | $p < 0.02$ |
| G.V., 36 | 48.4% ± 6.8% | 1 | 62 | 53.0% ± 6.6% | 78 | $p < 0.04$ |
| C.L., 50 | 39.4% ± 4.2% | 1 | 49 | 40.6% ± 3.4% | 78 | Tendency, $p < 0.06$ |
| U.B., 46* | 51.3% ± 7.0% | 2 | 72 | 52.0% ± 4.2% | 102 | *ns* |
| S.E., 46* | 52.5% ± 4.2% | 2 | 59 | 52.0% ± 6.0% | 56 | *ns* |
| A.I., 60* | 54.5% ± 5.8% | 1 | 68 | 53.8% ± 7.9% | 80 | *ns* |
| D.L., 60* | 42.2% ± 8.1% | 1 | 60 | 41.0% ± 5.9% | 70 | *ns* |

* Insignificant differences (*ns*).

ilar tendency occurred in the fourth cycle of sleep. It can be suggested that such a difference in the SWS duration depends on the especial importance of this stage of sleep for the first half of the night and/or the resources of SWS are exhausted to a greater extent in the night with stimulation rather than in the nights without stimulation.

According to the search activity concept [21, 42–44], rapid sleep (REM sleep) plays a crucial role in the formation of the psychical context of a man in the night and during wakefulness after sleep, which is reflected in the intensity of rapid eye movements, which grows up from cycle to cycle in rapid sleep [39, 43]. In patients with depression, intensity of eye movements is positively correlated to the SWS duration [45].

However, the data reported in [46] are different from the results of this study. As described in [46], in patients with depression, the duration of SWS increases in the next cycle after the increase of eye movements (EM) in REM sleep. In our study, the number of EM and their intensity increased in healthy subjects during rapid sleep cycles after the deepening of the delta sleep in response to stimulation.

**Table 3.** Individual values of the absolute average power of EEG delta waves in stages 3–4 of night sleep with and without stimulation for 16 subjects

| The subject, age, years | The absolute average power of delta waves | | | | *t* test for independent samples |
|---|---|---|---|---|---|
| | without stimulation ± st. dev, μV | the number of epochs | with stimulation ± st. dev. | the number of epochs | |
| M.I. | 130.8 ± 35.1 | 72 | 147.9 ± 29.3 | 103 | $p < 0.006$ |
| Sh.D.* | 175.9 ± 31.2 | 130 | 179.2 ± 35.8 | 120 | *ns* |
| E.T. | 119.1 ± 33.9 | 114 | 141.2 ±37.5 | 106 | $p < 0.00006$ |
| L.E. | 144.1 ± 30.5 | 52 | 155.9 ± 42.8 | 46 | Tendency, $p < 0.1$ |
| Sh.L. | 79.6 ± 18.1 | 43 | 113.6 ± 48.1 | 45 | $p < 0.0004$ |
| M.V. | 77.7 ± 15.9 | 101 | 83.9 ± 25.3 | 99 | $p < 0.04$ |
| M.P. | 84.4 ± 34.3 | 99 | 103.9 ± 53.2 | 62 | $p < 0.005$ |
| D.P. | 104.0 ± 20.5 | 57 | 111.7 ± 23.0 | 82 | $p < 0.005$ |
| K.V.* | 109.3 ± 18.0 | 68 | 112.4 ± 19.4 | 105 | *ns* |
| K.A. | 111.3 ± 27.4 | 43 | 124.6 ± 20.2 | 54 | $p < 0.007$ |
| G.V. | 106.5 ± 21.4 | 62 | 112.8 ± 14.9 | 78 | $p < 0.04$ |
| S.L. | 63.7 ± 20.0 | 49 | 97.3 ± 14.1 | 78 | $p < 0.000001$ |
| U.B.* | 135.7 ± 48.6 | 72 | 133.5 ± 34.8 | 102 | *ns* |
| S.E.* | 84.9 ± 17.3 | 59 | 76.5 ± 27.8 | 56 | *ns* |
| A.I.** | 193.4 ± 60.6 | 68 | 171.9 ± 37.6 | 76 | $p < 0.01$ |
| D.L.** | 71.2 ± 46.3 | 60 | 55.5 ± 32.5 | 70 | $p < 0.03$ |

* Nonsignificant differences (*ns*), ** significant decrease in delta wave power.

The question arises as to whether there is a reciprocal dependence between REM sleep and SWS: since satisfaction of the need of delta sleep is the first priority, the REM rapid sleep functionality is improved (at least due to the elimination of competition between the needs for SWS and REM sleep). Because of this, delta sleep is normally better expressed in the first two cycles and the REM sleep, in the last ones.

**Table 4.** Subjective estimation of sleep in the nights with and without stimulation (in percents). The averaged results according to the WAM questionnaire and total number of the positive subjective estimations in the morning (after the night sleep) as compared to estimation before sleep in the evening

| WAM questionnaire | Self-rated well-being | | Activity | | Mood | |
|---|---|---|---|---|---|---|
| Time of questioning | evening | morning | evening | morning | evening | morning |
| Without stimulation | 5.1 (1.0) | 5.1 (0.8) | 4.7 (0.8) | 4.4 (1.1) | 5.3 (0.8) | 5.2 (0.8) |
| With stimulation | 4.8 (0.9) | 5.5 (0.8) | 4.5 (0.9) | 4.9 (0.9) | 5.0 (0.9) | 5.9 (0.8) |
| Significance according to the *t* test for the dependent samples | $p < 0.002$ | | $p < 0.1$ (tendency) | | $p < 0.001$ | |

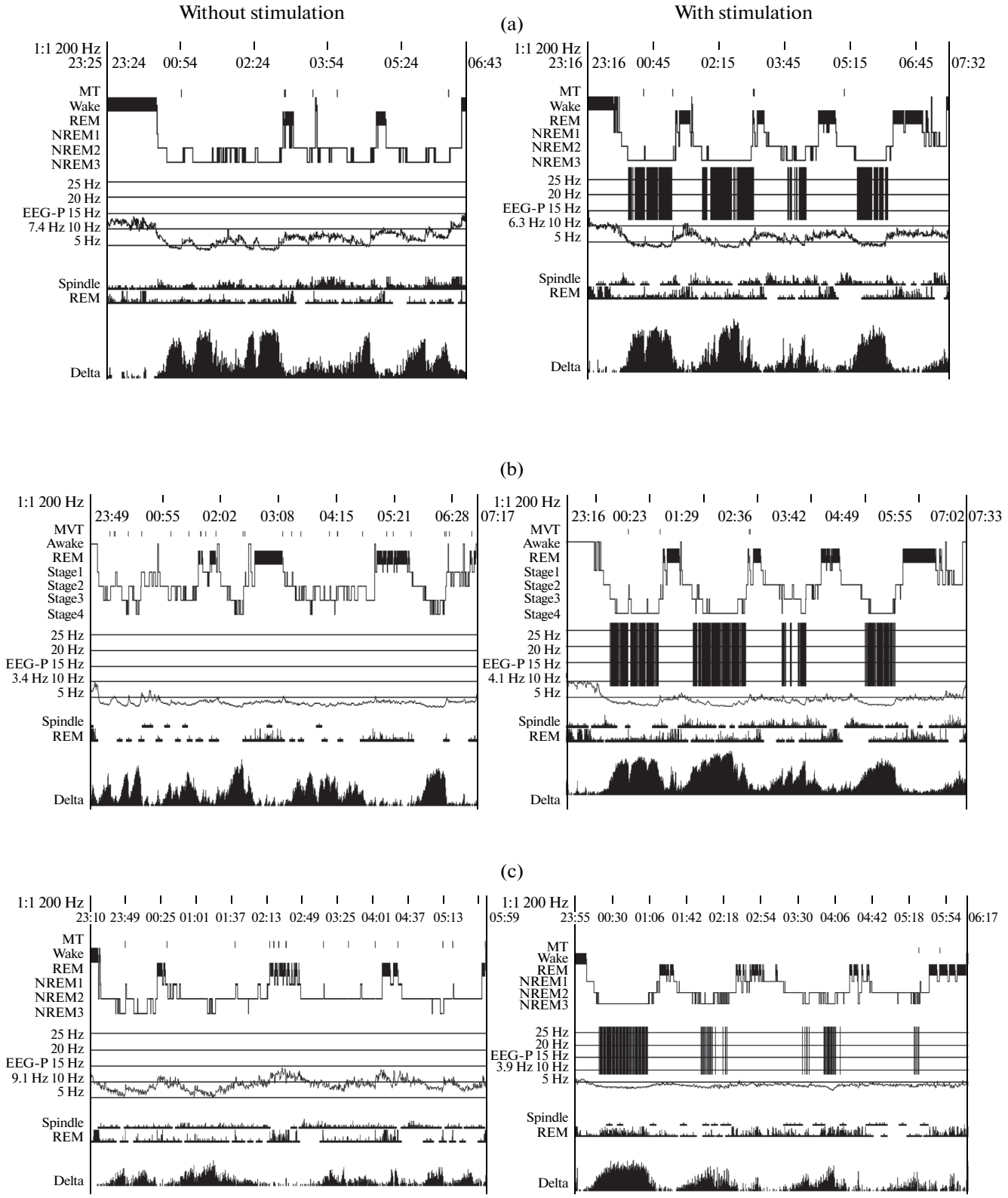


**Fig. 2.** Hypnograms and EEG spectral characteristics obtained in three different subjects ((a) M.I.; (b) Sh.D.; (c) M.V.) during the nights with and without stimulation in sleep stages 3–4. The vertical lines on the hypnograms (to the right) mark the electrical impulses. *Y* axis top-down, time scale, sleep stages, averaged power for all EEG channels and all frequency bands; sleep spindle hypnograms, eye movement histograms, power spectrum of EEG delta band. *X* axis (above), time.

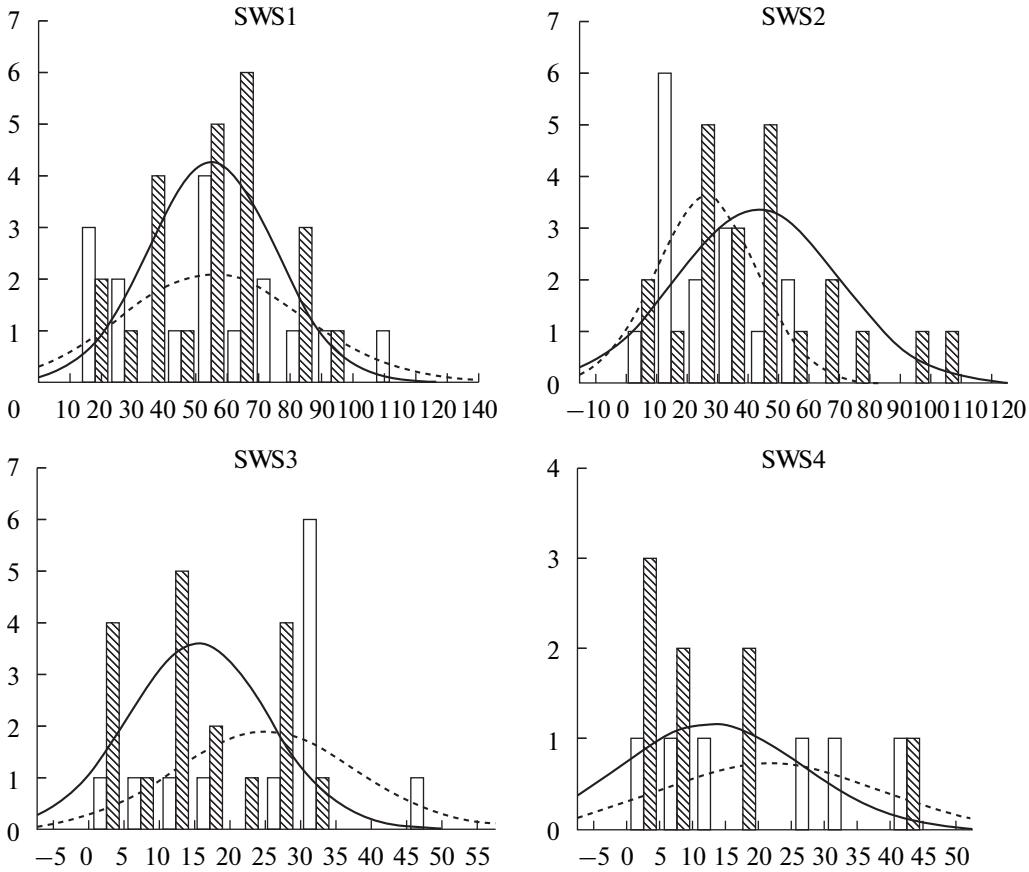


**Fig. 3.** Changes in duration of the SWS stages (SWS) in successive sleep cycles during the nights without and with stimulation (continuous and dotted lines, respectively). Histogram: the averaged SWS duration in successive four cycles of sleep (SWS1, SWS2, SWS3, and SWS4). *X* axis, SWS duration in minutes; *Y* axis, the number of nights with different SWS duration. Light columns, without stimulation; hatched columns, with stimulation.

As judged from the experiments with sleep deprivation, the body needs first of all the delta sleep compensation (if there is no heavy distress as in the case with depression). Some delta sleep deficiency probably affects the general sleep function and primarily the state of rapid sleep because of competition. The normalization of SWS, which is expressed in the longer duration of the delta sleep phase, creates a subjective sense of deep sleep. In turn, this seems to promote the normalization of rapid sleep.

We have found that those subjects who do not complain of sleep disturbance often experience additional sleep improvement after one or two nights with stimulation; they felt generally better and were in a better mood and had a desire for activity. In contrast, in the subjects dissatisfied with sleep, this was reflected in their polysomnograms in the nights without stimulation; the way they felt after sleep was rarely positive, and sometimes they were not pleased with the quality of their sleep. Nevertheless, the sleep structure becomes somewhat more positive: the duration of SWS increases, etc. Perhaps, in order to obtain a positive therapeutic effect in these subjects, stimulation for a longer time (i.e., recurrent stimulation) is required.

We have developed a compact device for electrocutaneous stimulation at home. Indeed, our pilot results demonstrated the effectiveness of recurrent stimulation during several nights (for several nights successively or with pauses). In the future, electrostimulation during delta sleep can be used in addition to other methods of treatment for insomnia and depressions. For the subjective estimation of sleep, more specific questionnaires have to be used, such as the sleep questionnaire, the Pittsburgh index of sleep quality, etc.

Deepening the SWS stage in response to the peripheral electrocutaneous stimulation suggests that a certain hypothetical defensive property of the SWS counteracts the activating and awakening effects of external stimuli. We believe that this proposed mechanism is nonspecific and, therefore, the stimuli of other physiological modality can be used.

## CONCLUSIONS

(1) Electrocutaneous low-frequency subthreshold stimulation of the internal side of a palm during the SWS has a positive effect on the sleep structure in 11 out of 16 subjects. The duration of the SWS stage increased in the first half of night sleep; this was accompanied by a significant increase in the EEG power of the delta band.

(2) In addition, stimulation promoted normalization of the rapid sleep stage, which was manifested in the higher intensity of eye movements during the successive cycles of sleep and in the improvement of the general sleep structure.

(3) Subjective sleep estimation after the nights with stimulation was more positive than after the nights without stimulation.

## ACKNOWLEDGMENTS

This study was partly supported by the Russian State Foundation for the Humanities, project no. 11-36-00242a1.

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*Translated by A. Nikolaeva*