Registration and analysis of bioelectric activity of sensory-motor cortex during the electrical stimulation of nucleus caudate in rats

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Abstract

Background and purpose: The caudate circuit takes part in cognitive control of motor activity. The purpose of the present work was registration and analysis of basic bioelectrical activity of ventral and dorsal sensory-motor cortex and nucleus caudate, study of the changes in EEG after nucleus caudate electrical stimulation and to identify of threshold level of electrical stimuli responsible for changes of electrical activity in registered brain area.
Materials and methods: We used 28 albino Wistar rat of both genders. After the animal fixation on stereotaxic apparatus to dry bone, the places for electrode fixation were marked. Two days after the electrodes had been implanted an EEG was registered so that the animals would adjust to the conditions and so they would repair the tissue reactions. EEG was registered with bipolar electrodes with ten-channeled apparatus. For first half an hour spontaneous activity of the brain was registered, and after that the head of nucleus caudate was stimulated with altered impulses of various voltages, frequency and duration.
Results and conclusions: Threshold values of electric stimulus intensity from 3 to 5 V, frequency from 3 to 5 Hz, duration from 3 to 5 ms, by stimulation the head of nucleus caudate of rat, lead to the change of basal bioelectric activity of cerebrum. The change of bioelectric activity is firstly recorded in equilateral cortex, and with the higher intensity of the stimulus the changes overtake the contra lateral cortex.

KEY WORDS: nucleusc caudate, basal bioelectric activity, sensory-motor cortex

Introduction

The basal ganglia and the cerebellum present key elements in two parallel re-entrant systems that receive input from and return their influences to the prefrontal, premotor, and motor cortex through ventrolateral thalamus (1, 2). Main role of basal ganglia is in performing complex motions, i.e. it regulates the intensity of a motion as well as time synchronization of movement. Caudate nucleus receives cortical projections primarily from multimodal association cortices and from motor areas in frontal lobe that control eye movements. Current concepts of the role of the basal ganglia consider that their function is to facilitate behaviour and movements that are required and appropriate in any particular context and to inhibit unwanted or inappropriate movements. When a movement is initiated from the cerebral cortex, impulses discharge not only through corticospinal and corticobulbar pathways but also through the corticostriatal glutamatergic excitatory projection to the striatum (1, 3). Basal ganglia disorders are characterised by the presence of abnormal movements, psychiatric signs and symptoms, and varying degrees of cognitive impairment. In recent years there has been increasing recognition of the non-motor consequences of disease of the basal ganglia. Evidence indicates a role for the basal ganglia in learning and memory and that basal ganglia and medial temporal lobe memory system are activated simultaneously. The caudat circuit takes part in cognitive control of motor activity, the mind processes in the brain which are established with use of sensory information that flows into the brain, and information which is already stored in memory (4). The aim of this study was:

- Registration and analysis of the basic bioelectrical activity of ventral and dorsal sensory-motor cortex and nucleus caudate
- Identification of the threshold level of electrical stimuli responsible for changes of electrical activity in registered brain area,
- Analysis of changes of the brain bioelectrical activity in term stimulation during various combinations of electrical stimuli.

Material and methods

We used 28 albino Wistar rats of both genders, weighing 250-300 grams. Animals were kept under the same microclimatic conditions and dietetic rating in the laboratory and in separate cages. Each animal was control to itself. Animals were anesthetized by intraperitoneal injection of 1 ml 10% urethane on 100 gr of body mass. After the animal fixation on stereotaxic apparatus to dry bone, the places for electrode fixation were marked (5). Two days after the electrodes were implanted an EEG was registered so that the animals would adjust to the conditions and so they would repair the tissue reactions. EEG was registered with bipolar electrodes with ten-channeled apparatus. During the registration of EEG the animals were awake and moving freely. EEG was taken between third and fifth day every day for three hours. For first half an hour spontaneous activity of the brain was registered and after that the head of nucleus caudate was stimulated with altered impulses of various voltages, frequency and duration. Head of nucleus caudate was stimulated with different combinations of electrical stimuli for 10 sec. during the Day 4 and 5. Time interval between stimulations was 20-25 sec. Every combination of electrical stimulus parameters was used only once:

- 3 V, 3 Hz, 3 ms
- 3.5 V, 3 Hz, 3 ms
- 4 V, 4 Hz, 4 ms
- 5 V, 5 Hz, 5 ms

At the end of the experiment, animals were sacrificed, and their brains analysed for the checkup of electrode positioning

Results

Spontaneous bioelectric activity of anterior and posterior sensory-motor cortex shows regular rhythm with good interhemispherical synchronization in adult rats. In the beginning of recording, the process of desynchronization which is characterised by low amplitude and high frequency was registered reflecting an expression of interest of animal for the environment. In the left sensory-motor cortex we registered the frequency 8-10 cps and amplitude 55 to 70 V. The synchronization process was registered in animals adapted to the environment which was characterised by slow wave with high amplitude activity that became increasingly expressed. We registered the frequency of 6, 5 to 8 cps and the amplitude of 70 to 100 V in the left sensory-motor cortex and frequency of 6 to 8 cps and amplitude of 70 to 90 V in the right sensory-motor cortex. Single spindle activity duration around 1 second, frequency of 5 to 7 cps and amplitude of 70-100 V was rarely registered. Spontaneous bioelectric activity of nucleus caudate is characterized by slow wave's delta type, frequency of 1. 5 μ to 2 cps, amplitude of 20 to 75 V and they continue as waves of low amplitude and high frequency of beta type.

We have found that threshold values of electric stimulus with intensity of 3 to 5 V, frequency of 3 to 5 Hz and duration of 3 to 5 ms lead to the change of basal bioelectric activity of cerebrum during the stimulation of the head of nucleus caudate in rats. A small number of animals reacted to this low intensity stimulation, but by increasing the parameters of electrical stimulation, changes in activity was present in more animals. The lowest electrical stimulation intensity of 3V generated the changes in bioelectrical activity in 20-30% of animals. The change of bioelectric activity was initially recorded in equilateral cortex but with the higher intensity of the stimulus the changes overtook the contralateral cortex.

I day of experiment

1.Use of electrical stimulus - 3 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 30% of animals. The changes were presented as slow waves in stimulation rhythm as a well organized response added to basic activity. The response followed rhytm of nc. Caudatus electrical stimulation frequency. Activity with frequency of 3 cps and the amplitude of 70 to 100 μV was registered in the left sensory-motor cortex cortex and of 50 to 80 μV in the right. At the other animals we found slow wave activity with frequency of 6 to 7 cps and amplitude of 70 to 80 μV in the left and frequency of 6 to 7 cps and amplitude of 60 to 70 μV in the right sensory-motor cortex, but also high frequency activity with frequency of 8 to 10 cps and amplitude of 50 to 70 μV in the left and frequency of 7 to 8 cps and amplitude of 40 to 60 μV in the right sensory-motor cortex. A slight decrease in frequency was found during stimulation when compared to the period before stimulation. Single spindle activity lasting around 1 second, with frequency of 6 cps and amplitude from 70-80mV was rarely registered.
2. Use of electrical stimulus – 3. 5 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 30% of animals. This was registered activity with frequency of 3.5 cps. A synchronized activity lasting 1 to 3 sec and spindle activity lasting 1 sec were found in the other animals. An activity with frequency of 6 to 8 cps and amplitude of 50 to 120 mV and 40 to 100 μV was registered in the left and right sensory-motor cortex respectively.
3. Use of electrical stimulus - 4 V, 4 Hz, 4 ms. It led to changes in basic bioelectrical activity in 40% of animals. This was registered activity with frequency of 4 cps and amplitude of 60 to 120 μV in the left sensory-motor cortex cortex and of 50 to 90 in the right. We found frequency of 6 to 9 cps and amplitude of 60 to 100 μV in the left and frequency of 6 to 8 cps and amplitude of 50 to 90 μV in right sensory-motor cortex in other animals. Single spindle activity was present in all animals.
4. Use of electrical stimulus - 5 V, 5 Hz, 5 ms. It led to changes in basic bioelectrical activity in 50% of animals. This was registered activity with frequency of 5 cps and amplitude of 90 to 150 μV in the left sensory-motor cortex cortex, and of 60 to 150 in the right. Spindle activity from 1 to 3 sec in duration, with frequency from 6 to 8 cps and amplitude from 100 to 110 μV was emphasised. Activity with frequency of 7 to 10 cps and amplitude of 60 to 110 μV was registered in both hemisphere in the remaining animals.

II day of experiment

1.Use of electrical stimulus - 3 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 10% of animals. An organized response was found in stimulation rhytm added to basic activity with frequency of 3 cps and amplitude of 100 μV in the left and 50 μV in the right sensory-motor cortex. There was no significant regularity in EEG changes in the remaining animals. Registered slow wave and high amplitude activity had the same frequency as the one during the first day, with slightly higher frequency of up to 120 μV in the left and 100 μV in the right sensory-motor cortex. High frequency and low amplitude activity was expressed in both hemispheres with similar frequency and amplitude as the one during the first day with slight increase in amplitude. Also, spindle activity from 1 to 2 sec in duration was emphasised.
2. Use of electrical stimulus - 3, 5 V, 3 Hz, 3 ms. There was change in basic bioelectrical activity in 10% of animals. This was registered activity with frequency of 3.5 cps and the same amplitude as the one in the combinations of electrical stimulus parameters with 3 V. In the remaining animals we found periods of synchronization and desynchronization with similar frequency as the one at lower electrical stimulus parameters, with amplitude of 150 μV in the both hemispheres.
3. Use of electrical stimulus - 4 V, 4 Hz, 4 ms. It led to changes in basic bioelectrical activity in 20% of animals, those one with registered changes at 3 V during the first day of experiment. This was registered activity with frequency of 4 cps and higher amplitude (up to 150 μV in the left and 100 μV in the right sensory-motor cortex) than during the first day even with lower electrical stimulus parameters. Registered periods of high frequency and low amplitude activity had the same characteristics of frequency and amplitude as those at the lower electrical stimulus parameters. It was registered single spindle activity from 1 to 2 sec in duration.
4. Use of electrical stimulus - 5 V, 5 Hz, 5 ms. It led to

changes in basic bioelectrical activity in 70% of animals. This was registered activity with frequency of 5 cps and the same amplitude as those at stimulation with 4 V. Activity with frequency of 7 cps and amplitude of 80 μV was registered in both, left and right sensory-motor cortex in the remaining animals. Single spindle activity was found in all animals.

III day of experiment

1. Use of electrical stimulus - 3 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 20% of animals. The changes were presented as slow wave activity in stimulation rhythm as a well organized response added on basic activity. The response followed frequency rhitm of electrical stimulation of nc. Caudatus. It was registered activity with frequency of 3 cps in the both hemispheres and the same amplitude as those during the first day of experiment at the same stimulus parameters. Single spindle activity, periods of synchronous and non-synchronous activity with the same characteristics as those during the first day were emphasised.
2. Use of electrical stimulus - 3, 5 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 30% of animals, with slightly higher amplitude than those registered at lower electrical stimulus parameters. Amplitude was up to 139 μV in the left and 100 μV in the right, with frequency of 3.5 cps. We found the same activity as the one registered with stimulation at lower electrical stimulus parameters in the remaining animals.
3. Use of electrical stimulus - 4 V, 4 Hz, 4 ms. It led to changes in basic bioelectrical activity in 30% of animals. This was registered activity with frequency of 4cps and amplitude the same as those registered at the same electrical stimulus parameters during the second day of experiment. We found activity with the same frequency as those registered at the lower electrical stimulus parameters, with slightly higher amplitude up to 150 μV in the left and up to 100 μV in the right sensory-motor cortex in the remaining animals. We found spindle activity with frequency of 6 cps and amplitude up to 80 mV and also hipersynchronous activity with frequency of 11 cps and amplitude of 120 mV.
4. Use of electrical stimulus - 5 V, 5 Hz, 5 ms. It led to changes in basic bioelectrical activity in 90% of animals in the ipsilateral sensory-motor cortex and in 60% of animals in the contralateral sensory-motor cortex. This was registered activity with frequency of 5 cps and amplitude from 70 to 160 μV in the left sensory-motor cortex cortex and from 40 to 140 μV in the right. An emphasised spindle activity covering slow waves was found in stimulation rhytm with frequency from 7 to 10 cps and amplitude of 80 mV. Registered activity with frequency from 7 to 8 μV was found in both hemispheres in the remaining animals.

IV day of experiment

1. Use of electrical stimulus - 3 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 20% of animals. The recorded changes were presented as slow waves in the stimulation rhythm as a well organized response added on basic activity. The response followed rhythm of nc. Caudatus electrical stimulation frequency. This was registered activity with frequency of 3 cps and amplitude of 80 μV in the left sensory-motor cortex cortex and 60 μV in the right. Slow wave and high amplitude activity with the same characteristics as those in the previous was found in the remaining animals. Spindle activity and slow wave and low amplitude activity with frequency of 6 cps and amplitude from 30 to 50 μV were expressed.
2. Use of electrical stimulus - 3, 5 V, 3 Hz, 3 ms. It led to changes in basic bioelectrical activity in 30% of animals with frequency of 3.5 cps and rare wave of 70 μV amplitude. This registered amplitude was the same as those registered during the previous day. We found periods of synchronization and desynchronization in the remaining animals, with the same characteristics as those registered at lower electrical stimulus parameters. The single spindle activity was registered.
3. Use of electrical stimulus - 4 V, 4 Hz, 4 ms. It led to changes in basic bioelectrical activity in 50% of animals in the ipsilateral sensory-motor cortex and in 30% of animals in the contralateral sensory-motor cortex. This was registered activity with frequency of 4 cps and amplitude of 80 to 150 μV in the left sensory-motor cortex and of 80 to 120 μV in the right. We found waves, added to basic activity, with frequency of 7 to 9 cps and amplitude of 80 mV. Spindle activity was emphasized. There was registered dominant synchronised activity in the remaining animals with similar frequency and amplitude as those during the first day of experiment at the same electrical stimulus parameters.
4. Use of electrical stimulus - 5 V, 5 Hz, 5 ms. It led to changes in basic bioelectrical activity in 80% of animals in the ipsilateral sensory-motor cortex, and in 60% of animals in the contralateral sensory-motor cortex with frequency of 5 cps and similar amplitude as those during the first day of experiment at the same electrical stimulus parameters. Waves, covering over basic activity, with frequency of 7 to 9 cps and amplitude from 70 to 80 μV were also emphasized. We found the same activity in the remaining animals as those found during the first day of experiment. Spindle activity was emphasised.

V day of experiment

Stimulation of 60% of animals with combinations of electrical stimulus parameters used those in previous days triggered changes in bioelectrical activity in all animals. Registered frequency corresponded to electrical stimulus intensity, with amplitude of 50 to 110 mV. Regardless of electrical stimulus parameters we found waves, covering over basic activity, with frequency of 7 to 9 cps and amplitude of 50 to 100 μV with emphasized synchronizated activity and single spindle activity in the left sensory-motor cortex. There was no activity changes in the right sensory-motor cortex in the context of low frequency waves in the stimulation rhythm, but only slow wave and low frequency activity of 6-8 cps frequency and 40-70 μV amplitude with single spindle activity. Single spindle activity of lasting 1 to 3 sec was registered during the stimulation regardless of electrical stimulus parameters and the day of experiment. By increasing intensity and with the every next day of experiment, the spindle activity became more emphasized and the duration became more extensive up to 2 sec and in some parts up to 3 sec. Low frequency high amplitude and high frequency low amplitude activity were expressed during stimulation. Regularity in transforming one into the other was absent. During the first day of experiment synchronous and desynchronous activity were presented equally. With every next day synchronization became more expressed and slight increase in amplitude was registered. Low amplitude and slightly lower frequency were found in the contralateral cortex when compared to ipsilateral cortex. The difference was more expressed during the stimulation. If the stimulation had fallen during the period of synchronous activity there would have been no visible response in the stimulation rhythm, although that response was achieved with lower electrical stimulus parameters earlier.

Discussion

The main aim of our study was investigation of functional relations in neural circuit cortex - striatum-palidus-motor nuclei of thalamus-premotor cortex. Other authors have studied morphological, functional and biochemical aspect of organization of these structures, particularly their integrational functions in sensory-motor aspect of programming motor activity (1, 6, 7). The striatum has two routes by which it is able to control the activity of basal ganglia output neurones. The first of these is the 'direct pathway' through which striatopallidal and striatonigral neurones will directly induce the inhibition of medial pallidal or pars reticulata neurones. This mechanism has been shown to operate in experimental electrophysiological studies in primates where basal ganglia output neurones associated with a particular body part or muscle group show a pause in their action potential discharge during movement of that region. Since medial pallidal and pars reticulata output neurones are themselves inhibitory, this leads to disinhibition of target neurones including those of the motor thalamus. The resulting increase in the activity of thalamic neurones causes excitation of the cells of the cerebral cortex. The effect of activation of the direct pathway is, therefore, to support or facilitate ongoing movements (8). The second route by which striatal neurones can influence the output of the basal ganglia is the so-called 'indirect pathway' via the subthalamic nucleus. Efferents from the striatum terminate in the lateral pallidal segment and their activation induces inhibition of lateral pallidal neurones. The principal efferent projection of the lateral pallidum is to the subthalamic nucleus which, therefore, becomes disinhibited. The resulting increase in discharge of subthalamic neurones causes activation of medial pallidal and nigral neurones and, in turn, inhibition of thalamic and cortical cells. This has the effect of inhibiting unwanted movements (9, 10). Our study indicated that by increasing electrical stimulus parameters, the number of animals reacting to them increased as well. This indicates the selectivity in treshold level when using treshold intensities from 4 to 10V. In our study the lowest intensity of elecrical stimulus of 3 V led to change in basic bioelectrical activity at 20 to 30% of animals. In the first day after stimulation with 5V we found change in basic bioelectrical activity at 50% of animals, and in every next day we found change in more animals, i.e. 70% during the secod day and 90% during the third day. The first change of bioelectric activity was recorded in ipsilateral sensory-motor cortex and with the higher intensity of the stimulus the changes overtook the contralateral sensory-motor cortex. Some authors suggested a greater number of pathways of nc. Caudatus with ipsilateral cortex than with contralateral. Projections from cortex into caudatus and putamen are ipsilateral, except those from areas 4, 6 and 8 which are bilateral (8, 10). We noticed that stimulation of caudatus led to appearance of slow waves in stimulation rhythm as a well organized response added on basic activity with the same frequency as stimulation frequency, with amplitude of 80 to 150 μV that is increasing with increasing of intensity and with every next day of experiment. In some investigation, stimulation of caudatus with single threshold intensity electrical stimuli give two respons-

es, primary of 10 sec in duration, and secondary that is characterised as caudatal spindle. Some experiments suggested that electrostimulation of caudatus with threshold electrical stimulus parameters led to caudatal spindle in the cerebral cortex. Enter emphasise that stimulation of caudatus lead to inhibitory effect, resulting in appearance of caudatal spindle. The caudatal spindles are often blocked with physiological and artefi-cial stimuli (attention) and are more expressed at sleepy and tranquil animals. Forming of caudatal spindles require an intact pathway of caudatus with VA nuclei of thalamus (caudatal cross-road). Researchers indicated the double role of caudatus, i.e. together with thalamus participate in creating an inhibitory influence on cortex and simultaneously inhibit overactivity of thalamus. After destruction of caudatus there is anh expressed high amplitude and epileptiform activity on EEG because of deficit of upstream inhibition on cortex. Destruction of caudats leads to aggressive behaviour, hyperactivity and motor agitation at animals. This study did not find any difference in morphology between spontaneous spindle activity at calm animal and express caudatal spindle in the period after stimulation. Caudatal spindle in the period after stimulation is expressed more frequently and for a longer period (9,10). In animals with no changes in bioelectrical activity during stimulation in the form of slow wave activity in stimulation rhythm, there was period of slow wave and high amplitude activity or high wave and slow amplitude activity, with slower frequency when compared with period before the stimulation. During the first day of experiment we found both activities: high amplitude activity and high wave and slow amplitude activity in the similar manner. Each next day increasing synchronisation activity was found.

Conclusion

Results of our study indicate that caudatus belongs to structures which have synchonisation effects on bioelectrical activity of cerebral cortex in rats.

Threshold values of electric stimulus intensity from 3 to 5 V, frequency from 3 to 5 Hz, duration from 3 to 5 ms, lead to the change in basal bioelectric activity of cerebrum through the stimulation of the head of nucleus caudate in rats. The change of bioelectric activity is firstly recorded in equilateral cortex and with the higher intensity of the stimulus the changes overtake the contra lateral cortex.

Stimulation of the nucleus caudate head in rats lead to the appearance of slow waves in the stimulation rhythm in the form of well organized activity added on basic bioelectrical activity. This response follows the rhythm of the frequency of electric stimulation of nucleus caudatus.

The changes in bioelectrical activity were registered in 30% of animals with intensity of electrical stimulus of 3 V in the first day of experiment while after stimulation with 5 V they were registered in 50% of animals. With every next day we registered changes in bioelectrical activity in more animals with higher intensity of electrical stimuli used. During the second day of experiment the changes in bioelectrical activity were registered in 70% animals after electric stimulation with intensity of 5 V while during the third day these changes were registered in 90% animals which continued until the end of experiment.

In the group of animals with no changes in bioelectrical activity during the period of stimulation in the form of slow waves in the stimulation rhythm there were periods of slow wave and high amplitude activity or high wave and slow amplitude with lower frequency when compared to period prior to the stimulation. Study found that with the accentuation of intensity of electrical stimuli there was accentuation of amplitude in ipsilateral sensory-motor cortex from 80 to 150 μV and from 70 to 140 μV in contralateral sensory-motor cortex each day of the experiment.

From the middle of the experiment there was an increase in the proportion of caudatal spindle activity superimposed on slow waves that occured in the stimulation rhythm, with frequency of 7 to 8 cps and amplitude approx 80 μV which is more expressed in ipsilateral sensory-motor cortex.

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