PHYSIOLOGY

Gamma Oscillations in the Somatosensory Cortex of Newborn Rats

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Here we addressed a question of whether gamma oscillations previously described in the whisker-related barrel cortex are a universal pattern of activity in the somatosensory cortex of newborn rats. Intracortical recording of local field potentials and action potentials in neurons using multisite silicon electrodes in 2-7-day-old rats showed that mechanical stimulation of single fingers or specific areas on the plantar or back side of the foot evoked early gamma oscillations followed by spindle-burst oscillations in the corresponding regions of the somatosensory cortex. Early gamma oscillations had maximum amplitude in layer IV of the somatosensory cortex and effectively synchronized action potentials in layer IV neurons. It was concluded that early gamma oscillations evoked by activation of the topographic sensory input are a universal activity pattern of the entire somatosensory cortex of newborn rats.

Key Words: *electroencephalogram; newborn; somatosensory cortex; sensory responses; gamma oscillations*

CNS development is characterized by unique patterns of early activity contributing to the formation of specific synaptic connections between neurons [1,2,4]. Two main patterns of oscillatory network activity are described in the somatosensory cortex of newborn rats during the so-called critical periods of the development of sensory thalamocortical maps [12]: early gamma oscillations (EGO) and α - β oscillations (spindle oscillations, SO), which differ by dominating oscillations in corresponding frequencies [3,5,8-11,13,14]. EGO and SO mediate opposite mechanisms of plasticity, long-term potentiation and depression, in the thalamocortical synapses, thus contributing to the formation of thalamocortical maps [10]. In the cortical barrels that receive sensory inputs from whiskers, EGO and SO are evoked by stimulation of whiskers corresponding to these barrels [10,13]. At the same time, in other areas of the somatosensory cortex, *e.g.* in upper and lower limb projection zones, only SO were described as sensory responses [5-7,14], and the question whether EGO are the pattern specific for developing barrel cortex or EGO are the universal pattern of activity in all the somatosensory cortex in the early stages of development remains unsolved.

Here we studied whether gamma oscillations previously described in the whisker-related barrel cortex are a universal pattern of activity in the somatosensory cortex of newborn rats.

MATERIALS AND METHODS

Experiment was performed on rat pups during the first week after birth (postnatal days 2-7). The ani-

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Fig. 1. Sensory responses induced in the somatosensory cortex of newborn rats. *a*) traces of the responses evoked by stimulation of the finger II of the forelimb and recorded with an extracellular electrode in layer IV of the primary somatosensory cortex (CC1) corresponding to the projection area of the finger II of the forelimb; action potentials are indicated above each electrogram by vertical lines. *b*) averaged LFP. *c*) histogram of the distribution of action potentials (pooled data from 100 responses); shoulder of gamma oscillations is indicated by arrows. *d*) power spectral frequency of responses evoked by sensory stimulation (300 msec; solid line); power spectral density of basal activity: dotted line (300 msec). *e*) plot of coherence between action potentials and LFP during responses evoked by sensory stimulation.

mals were anesthetized with 1.5% isoflurane, skin and soft tissues were removed from the skull with a scalpel. Neck muscles were cut off from the occipital bone. The cranial surface was treated with Gemostab to stop capillary bleeding. A small area on the right side of the skull in the projection of the somatosensory cortex was washed from hemostatic fluid with saline using a cotton swab. The exposed cranial surface except for projection of the somatosensory cortex was covered with a thin layer of cyanoacrylate glue and dental cement, to which two plastic tubes were later attached (horizontal one, to occipital bone and vertical one, to the frontal bone) for subsequent fastening in a stereotaxic apparatus. Silver chloride electrode was inserted into the cerebellum and visual cortex to a depth of 2-3 mm, fixed to the surface of the cortex with cyanoacrylate glue, and served as the combined earth and reference electrodes. After surgery, the pups were injected with 0.5-1 g/kg urethane, placed into a recording chamber on the thermal pad (37-38°C) and wrapped with cotton. The head was fixed in a stereotaxic apparatus using plastic tubes previously fixed to the head. Recordings of local field potentials and multiple action potentials were performed using a 16-channel silicon-based probe (Neuronexus) with 100- μ distance between the detection electrodes. The probe was introduced into the somatosensory cortex (±1 mm from bregma, 1.5-3 mm lateral) perpendicular to its surface to a depth of 1400 μ , which provided simultaneous recording across all layers of the cortical column. All recordings were amplified (×1000, frequency band 0.3 Hz to 5 kHz), digitized at 10 kHz, saved in computer memory for later analysis, and then analyzed with Matlab. Sensory stimulation was performed with short (5-20 msec) touch of a metal rod (diameter 0.4 mm, displacement amplitude up to 0.5 mm fixed to the piezoelectric plate) to the skin surface.

RESULTS

Local mechanical stimulation of fore and hind limb fingers evoked complex responses in the topographic locus of the somatosensory cortex in newborn rats (2 to 7 postnatal days; n=10; Fig. 1, a). Early component (sensory potential) was presented by a negative shoulder with maximum amplitude in cortical layer IV. It was featured by multiple action potentials in layer IV neurons arising with a short time delay. The mean sensory action potential amplitude in cortical layer IV was $1170\pm387 \mu$ V, latent period was 68 ± 24 msec, and rise time 4.5 ± 0.8 msec (n=10). The sensory potential was followed by EGO lasting about 100-150 msec, which were temporarily stimulus-dependent. Thus, EGO could be detected even in average responses during the analysis of local field potentials (LFP) and in the

histograms of extracellularly recorded action potentials (Fig. 1, b). Frequency analysis of responses evoked by sensory stimulation revealed EGO peak at a frequency of 51±6 Hz and power of 48±6 µV²/Hz. Analysis of EGO at different cortical depth levels showed that EGO have maximum amplitude in cortical layer IV, *i.e.* at the same depth as the sensory potential. Analysis of neuronal excitation during EGO also demonstrated maximum activity at the depth of layer IV and moderate excitation of neurons in the supra-and infra-granular cortical layers. Neuronal action potentials were modulated by EGO, which was manifested in the high coherence between action potentials and local field potential at gamma frequency (Fig.1, d). These data indicate that thalamic gamma oscillator is essential for the generation of cortical EGO as was previously shown in the thalamocortical barrel system [10]. The frequency of EGO and oscillatory activity decreased with time to α - β frequencies characteristic of SO.

Our results suggest that EGO are a characteristic pattern of oscillatory activity in the somatosensory cortex corresponding to limb projections and are triggered in these areas by stimulation of the topographic sensory inputs. Comparison of the results with those obtained in the barrel cortex [3,10,13,14] suggested that EGO are universal pattern of activity encoding topographic sensory inputs not only in the barrel cortex, but also in the other areas of the somatosensory cortex. Thus, they are a versatile tool for the formation of thalamocortical somatosensory topographic maps. Moreover, since EGO evoke long-term potentiation of thalamocortical synapses [8], we can assume that EGO are involved in potentiation and subsequent stabilization of topographic synapses. The findings are also important for future studies of the relationship between cortical activity and myoclonic jerks, which are known to trigger the emergence of cortical oscillations of in the newborn rats [5].

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REFERENCES

- A. G. Blankenship and M. B. Feller, *Nat. Rev. Neurosci.*, **11**, No. 1, 18-29 (2010).
- M. Colonnese and R. Khazipov, *Neuroimage*, **62**, No. 4, 2212-2221 (2012).
- M. T. Colonnese, A. Kaminska, M. Minlebaev, et al., Neuron, 67, No. 3, 480-498 (2010).
- 4. L. C. Katz and C. J. Shatz, Science, 274, 1133-1138 (1996).
- 5. R. Khazipov, A. Sirota, X. Leinekugel, et al., Nature, 432, 758-761 (2004).
- A. J. Marcano-Reik and M. S. Blumberg, *Eur. J. Neurosci.*, 28, No. 8, 1457-1466 (2008).

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- 7. A. J. Marcano-Reik, T. Prasad, J. A. Weiner, and M. S. Blumberg, *Behav. Neurosci.*, **124**, No. 5, 600-611 (2010).
- M. Minlebaev, Y. Ben-Ari, and R. Khazipov, *Cereb. Cortex*, 19, No. 3, 688-696 (2009).
- M. Minlebaev, Y. Ben-Ari, and R. Khazipov, J. Neurophysiol., 97, No. 1, 692-700 (2007).
- M. Minlebaev, M. Colonnese, T. Tsintsadze, *et al.*, *Science*, 334, 226-229 (2011).
- E. J. Mohns and M. S. Blumberg, J. Neurosci, 28, No. 40, 10,134-10,144 (2008).
- 12. H. Van der Loos and T. A. Woolsey, *Science*, **179**, 395-398 (1973).
- J. W. Yang, S. An, J. J. Sun, et al., Cereb. Cortex, doi: 10.1093/ cercor/bhs103 (2012).
- 14. J. W. Yang, I. L. Hanganu-Opatz, J. J. Sun, and H. J. Luhmann, J. Neurosci., 29, No. 28, 9011-9025 (2009).