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Research Report

Developmental appearance and disappearance of cortical events and oscillations in infant rats

Adele M.H. Seelke, Mark S. Blumberg*

Department of Psychology and Delta Center, Program in Behavioral and Cognitive Neuroscience, The University of Iowa, Iowa City, IA 52242, USA

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ABSTRACT

Until recently, organized and state-dependent neocortical activity in infant rats was thought to commence with the emergence of delta waves at postnatal day (P)11. This view is changing with the discovery of several forms of cortical activity that are detectible soon after birth, including spindle bursts (SBs) and slow activity transients (SATs). Here we provide further evidence of surprisingly rich cortical activity patterns during early development and document, in P5–P13 rats, the appearance, disappearance, and transient expression of three cortical events and oscillations. EEG activity in frontal, parietal, and occipital cortices was recorded in unanesthetized, head-fixed subjects using 16-channel laminar silicon electrodes and Ag–AgCl electrodes. In addition to SATs, we identified two novel forms of activity: cortical sharp potentials (CSPs) and gamma bursts (GBs). SBs were not observed in these areas. CSPs, defined as discrete, biphasic events with a duration of 250 ms, exhibited an inverted-U developmental trajectory with peak prevalence at P9. In contrast, GBs, defined as brief bursts of 40-Hz activity, increased steadily in prevalence and duration from P5 through P13. The prevalence of SATs decreased steadily across the ages tested here. Furthermore, both CSPs and GBs were more likely to occur during sleep than during wakefulness. Because SATs, CSPs, and GBs exhibit different developmental trajectories and rates of occurrence, and can occur independently of each other, they appear to be distinct patterns of neuronal activity. We hypothesize that these diverse patterns of neurophysiological activity reflect the instantaneous local structure and connectivity of the developing neocortex.

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1. Introduction

In adult mammals, periods of sleep and wakefulness can be distinguished electrographically using measures of cortical (i.e., EEG) and muscle (i.e., EMG) activity (Rechtschaffen and Kales, 1968). In early infancy, especially in rats and other altricial species at ages before the emergence of highly organized EEG activity, EMG measures coupled with behavior have proven reliable for distinguishing behavioral states (Karlsson and Blumberg, 2002; Seelke and Blumberg, 2005; Seelke et al., 2005). Accordingly, the emergence in rats of slow-wave or delta activity around postnatal day (P)11 (Frank and

* *Corresponding author*. 1544 Newton Court, Center for Neuroscience, The University of California, Davis, Davis, CA 95618, USA. Fax: +1 530 757 8827.
E-mail address: amseelke@ucdavis.edu (A.M.H. Seelke).

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Heller, 1997; Gramsbergen, 1976; Jouvet-Mounier et al., 1970; Seelke and Blumberg, 2008) has been considered an important indicator of cortical maturation.

Recently, however, the identification of two new forms of cortical activity is changing our view of cortical organization during the early postnatal period. First, slow activity transients (SATs), first identified in premature human infants, are low-frequency (0.1 Hz), high-amplitude events that are difficult to detect using conventional EEG filter settings (Vanhatalo et al., 2005a). Analogous events were observed in infant rats as early as P9; these SATs were biphasic, high-amplitude events with a frequency of 0.1–0.2 Hz (Seelke and Blumberg, 2008). Second, brief bursts of 15-Hz activity, called spindle bursts (SBs), have been identified in primary somatosensory, barrel, and visual cortices (Hanganu et al., 2007; Khazipov et al., 2004; Marcano-Reik and Blumberg, 2008; Minlebaev et al., 2007). SBs are generated in response to spontaneous or evoked sensory stimulation of the limbs, whiskers, and retina. Both SBs and SATs appear to be transient features of early development, decreasing in prevalence across the early developmental period.

As SBs and SATs were being discovered and reported, we were searching for developmental precursors of delta activity in the medial dysgranular cortex within the frontal, parietal, and occipital lobes of infant rats. Although we did not find evidence of SBs along the cortical midline, SATs were apparent in these cortical areas before the emergence of delta waves. In addition, we found evidence of two novel forms of activity that had not previously been reported: a discrete event that we designate a cortical sharp potential (CSP) and a brief 40-Hz oscillation that we designate a gamma burst (GB). Here we describe the developmental trajectories of these events and oscillations and establish their relationship with sleep and wakefulness.

2. Results

Recordings performed using 16-channel laminar Silicon (Si) electrodes revealed a cortex replete with activity, even in subjects as young as P5. The phenomenology and state dependency of three cortical events—CSPs, GBs, and SATs—are described in detail below. Although recordings were performed using Si electrodes in the frontal, parietal, and occipital lobes, only data from the parietal lobe recordings are presented here. Data from all 3 lobes are presented in Supplemental Fig. 1.

2.1. *Cortical sharp potentials (CSPs)*

Fig. 1A (left panel) illustrates a typical Si electrode placement in the parietal lobe of a P9 rat. An enlarged view of the cortex (right panel) shows the electrode track passing through cortical layers I–VI. A representative CSP from this P9 subject is depicted in Fig. 1B. As can be seen, CSPs were discrete, biphasic events. A subset of CSPs exhibited phase reversals across cortical layer IV, indicating that the event was generated locally (i.e., within the cortex) and not passively propagated from elsewhere in the brain or generated by movement artifact. A current source density (CSD) analysis (Fig. 1C) revealed alternating sources and sinks throughout the depth of the cortex, indicating that the entire cortical column is involved in the generation of CSPs (Kandel and Buzsaki, 1997). Only CSPs exhibiting phase reversals are included in the following analyses.

Mean CSP amplitude increased significantly with age, from 141.0±2.7 μV at P5 to 246.2±11.7 μV at P13 ($F_{4,45}=25.9$, $p<.0001$). Mean CSP duration ranged from 0.24±0.01 s at P13 to 0.27±0.01 s at P11; ANOVA revealed a small but significant increase across age ($F_{4,45}=3.5$, $p<.05$).

The mean number of CSPs occurring per minute changed significantly with age ($F_{4,15}=9.7$, $p<.0005$). As shown in Fig. 1D, CSPs exhibited an inverted-U distribution with a peak of 6.7±0.7 per min at P9 and minima of 1.6±0.5 per min and 0.7±0.2 per min at P5 and P13, respectively. Fig. 1D also shows that CSPs were most prevalent during AS at P5, P7, and P9. Following the emergence of delta activity at P11, CSPs occurred predominantly during QS. Across all ages, CSPs occurred more frequently during sleep than expected by chance (Fig. 1E; $t_{29}=3.9$, $p=.0005$).

A representative sleep–wake cycle from a P5 rat is shown in Fig. 1F. Although CSPs are present during periods of wakefulness and QS-related behavioral quiescence at this age, they cluster predominantly during bouts of AS-related phasic activity.

2.2. *Gamma bursts (GBs)*

In Fig. 2A, a typical Si electrode recording site is again shown, this time alongside an example of a GB (Fig. 2B) from a P9 subject. The GB pictured here was embedded in the CSP depicted in Fig. 1B. Much like CSPs, a subset of GBs exhibited phase reversals across cortical layer IV which indicates that GBs, like CSPs, can be generated locally within the cortex. Fig. 2C shows a CSD analysis from a P9 subject, which confirms that GBs are generated within layer IV. Only GBs exhibiting phase reversals are included in the following analyses.

Mean GB amplitude increased significantly with age ($F_{4,45}=11.8$, $p<.0001$), from 33.1±1.4 μV at P5 to 53.5±3.8 μV at P11. Mean GB duration also increased significantly with age ($F_{4,45}=5.8$, $p<.001$), ranging from 0.18±0.01 s at P7 to 0.26±0.01 s at P13. Mean GB frequency remained stable across age ($F_{4,45}=1.7$), ranging from 36.3±0.4 Hz at P9 to 39.1±0.3 Hz at P7.

The mean number of GBs increased significantly with age from 3.7±2.0 per min at P5 to 18.4±7.8 per min at P13 ($F_{4,15}=7.3$, $p<.005$; Fig. 2D). Much like CSPs, GBs were most prevalent during periods of AS-related phasic activity at P5, P7, and P9. Following the emergence of delta activity at P11, GBs occurred predominantly during periods of QS-related behavioral quiescence. Finally, at all ages, GBs occurred more frequently during sleep than expected by chance ($t_{28}=4.21$, $p<.0005$) (Fig. 2E).

A representative sleep–wake cycle from a P5 rat is shown in Fig. 2F. At this age, although GBs are present during periods of wakefulness and QS-related behavioral quiescence, they predominantly cluster during bouts of AS-related phasic activity.

2.3. *Slow activity transients (SATs)*

SATs occur in freely moving P9, P11, and P13 rats (Seelke and Blumberg, 2008). To confirm the presence of SATs in head-