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Relationship between brain activity and voiding patterns in healthy preterm neonates

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Summary

Introduction
It remains controversial as to whether the brain affects voiding control in preterm newborns. Constant bladder volume has previously been thought to induce bladder voiding in neonates, with no influence from the brain. Lately, there has been distinct evidence for an existing connection between the central nervous system and bladder voiding in preterm infants, as the voiding reflex arouses neonatal children. Video electroencephalography (EEG) is useful for recording bioelectrical activity of the cerebral cortex and exploring its relationship with voiding patterns in preterm neonates.

Objective
The objective was to investigate the relationship between voiding patterns and brain activity in healthy preterm neonates by using video-EEG.

Study design
Forty-seven healthy preterm neonates (16 females) with a mean postconceptional age (PCA) of 34.1 ± 1.8 weeks were divided according to PCA into three groups: Group I (31–33 weeks, $n = 13$); Group II (33–35 weeks, $n = 14$); and Group III (35–37 weeks, $n = 20$). Video-EEG data from eight cortical regions were recorded from 08:00–12:00, along with 4-hour free voiding patterns and status at voiding (awake/sleep).

Results
In Group I, the voiding frequency (VF) was significantly higher and the voiding volume (VV) was significantly lower than in the other groups. There were no significant differences in bladder capacity (BC), bladder capacity/birth weight (BC/BW), postvoiding residual/bladder capacity (PVR/BC), or urinary flow rate (UFR) among the three groups. The Fp1-T3 and Fp2-T4 lead amplitudes significantly differed in Group I and Group II at 5 s before (pre-5), during, and after voiding (post-5). The Fp2-C4 total and theta band lead amplitudes significantly differed across all urination states among the groups. There were no significant differences in electroencephalography frequency among the groups in any urination state.

Discussion
There were no significant differences in BC, BC/BW, PVR/BC, or UFR among the three groups, indicating slow bladder function development in preterm neonates. In this study, the EEG amplitude changed in certain pairs of electrodes. These changes might indicate the degree of bladder sensor maturation along with an increasing PCA. This study further suggests that the brain changes in preterm neonates during quiet sleep voiding prominently occur in the right prefrontal cortex and central region.

Conclusions
In preterm neonates, bladder voiding during quiet sleep was accompanied by cortical arousal that might have emanated from a lower center.

Table Four-hour voiding observations in the three groups.

	Group I	Group II	Group III	*P*
BW (kg)	1.41 ± 0.28	1.70 ± 0.36	1.90 ± 0.49*	0.00
VF (times)	4.43 ± 0.98*	3.29 ± 0.49	2.79 ± 1.19	0.01
VF/QS (times)	2.46 ± 1.05	1.64 ± 1.08	1.00 ± 0.92*	0.00
VV (ml)	6.34 ± 4.15*	9.39 ± 5.30	9.18 ± 6.28	0.04
BC (ml)	9.08 ± 4.61	10.58 ± 5.36	11.50 ± 6.15	0.42
BC/BW	7.14 ± 4.35	5.53 ± 2.37	6.59 ± 3.17	0.43
PVR/BC	0.24 ± 0.17	0.19 ± 0.18	0.17 ± 0.15	0.31
UFR (ml/sec)	2.41 ± 1.60	1.65 ± 0.96	1.99 ± 1.26	0.26

Postconceptional ages: Group I, 31–33 weeks; Group II, 33–35 weeks; Group III, 35–37 weeks.
BC/BW, bladder capacity/birth weight (BC was defined as the sum of VV and PVR); BW, birth weight; PVR/BC, postvoiding residual volume/bladder capacity; UFR, urinary flow rate; VF, voiding frequency; VF/QS, voiding frequency/quiet sleep; VV, voided volumes.
*$P < 0.05$.

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Introduction

It remains controversial as to whether the brain affects voiding control in preterm newborns. Constant bladder volume has previously been thought to induce bladder voiding in neonates, with no influence from the brain [1]. Lately, there has been distinct evidence for an existing connection between the central nervous system and bladder voiding in preterm infants, as the voiding reflex arouses neonatal children [2]; additionally, previous studies have yielded similar results [3–5]. However, it remains unclear as to whether the brains of preterm neonates similarly affect voiding control during quiet sleep (QS), as no direct records of brain activity during voiding are available in the literature. Recently, video electroencephalography (EEG) has made it possible to record whether the cerebral cortex or other areas of the brain are aroused during voiding [6–8].

Electroencephalography is often used in neonates to quantify rapid changes in cerebral cortex bioelectrical activity that is characteristic of brain maturation [9], or to detect brain injury and dysfunction [10]. Video-EEG allows the real-time recording and playback of physical activities and EEG waveforms.

This study aimed to use video-EEG to assess the relationship between brain bioelectrical activity and voiding patterns in preterm neonates during a 4-hour period of QS. It is believed that this is the first study to report the relationship between voiding patterns and brain bioelectrical activity in preterm neonates using video-EEG monitoring.

Patients and methods

Forty-seven healthy preterm neonates (31 males, 16 females) were recruited for this study at the First Affiliated Hospital of Zhengzhou University, China. Postconceptional age (PCA) was defined as gestation plus postnatal age [11]. The mean PCA was 34.1 ± 1.8 weeks, with a mean birth weight (BW) of 1.7 ± 0.4 kg. According to the PCA, the preterm neonates were divided into three groups: Group I (31–33 weeks, $n = 13$); Group II (33–35 weeks, $n = 14$); and Group III (35–37 weeks, $n = 20$). All preterm neonates were selected according to the following criteria: 1-minute and 5-minute Apgar scores >8, no urinary tract pathologies or abnormal symptoms (e.g. hematuria, edema, abnormal urine routine, and abnormal blood urea nitrogen and serum creatinine levels), and no congenital or ultrasonographic abnormalities. The present study was approved by the Ethics Commission of the First Affiliated Hospital of Zhengzhou University and performed according to the Declaration of Helsinki. The parents of all neonates provided informed written consent.

Neonates were placed in incubators set to optimal temperatures (according to weight). Video-EEG (Nicolet EEG v32, CareFusion Corp., San Diego, CA, USA) was used to record eight cortical regions per neonate between 08:00 and 12:00. Artificial feedings were given at odd-numbered time points (e.g. 07:00, 09:00, and 11:00). Flash lamps were used to indicate urination: one end was placed under the neonates' hips to respond to urine, and the other end was placed 1 meter away from the incubators to avoid waking the sleeping infants. At the 4-hour recording period, the neonates were undressed to observe the urinary stream during a single void.

Four EEG electrodes were applied to each side of the neonates' heads, as follows, to correspond with the 10–20 system as modified for neonates: Fp1-2 (frontal), C3-4 (rolandic or central), O1-2 (occipital), and T3-4 (temporal) [12]. The left-side (Fp1, C3, O1 and T3) and right-side electrodes (Fp2, C4, O2 and T4) were used for symmetric recording. Self-adhesive disposable electrodes and adhesive paste were used. At least two voiding episodes were included in the 4-hour recordings and were indicated by the above-described flash lamps. The recording speed was 20 mm/s, with a sensitivity of 7 μV/mm. No medication (sedative) was administered before or during the recording periods. Data were analyzed using the Nicolet EEG v32. Amplitude was defined as the square root of the EEG power. The frequency was divided into four bands: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz).

Diapers were weighted using a microelectronic balance (PL602-S, [accuracy: 0.1 g]; Mettler-Toledo Incorporated Company, Mesa, AZ, USA); the voiding volume (VV) was defined as the difference in diaper weight from before to after voiding. The urine volume was calculated according to the urine density (1 g/ml) and weight; the VV was accurate to 0.1 ml. The postvoiding residual volume (PVR) was measured 1 min after each voiding (more than a few ml but excluding some drops of urine) by using an ultrasound meter (LOGIQ400 [accuracy: 0.3 mm]; General Electric Company, Riverside, CA, USA). The PVR was calculated by multiplying the three dimensions (length × width × thickness × 0.5) [13]; the PVR was accurate to 1 ml. Bladder capacity (BC) was defined as the sum of the VV and PVR. The recorded parameters included voiding frequency (VF, the total number of voids during 4 h); VV (ml); voiding time (VT, hour:minute:second); urinary flow rate (UFR); PVR; consciousness at voiding (sleeping/awake); intermittent voiding and the percentage of intermittent voiding (PIV). The UFR was calculated based on the VV/VT. Intermittent voiding was defined as two or three small voids within 10 min, with the lowest residual urine after the last episode [14]. The PIV was defined as the percentage of intermittent voids from among the total number of voids. Micturition occurred two or three times in 10 min, which was defined as one intermittent voiding and one voiding episode. Preterm neonates observed to have an interrupted stream were the same ones with intermittent voiding.

Quiet sleep (QS) was defined as the state characterized by closed eyes, negative eye movements, negative body movements, and regular respiration. Wakefulness was defined as the state characterized by open or slightly open eyes [11].

Data were analyzed using the SPSS 17.0 software package (SPSS, Inc., Chicago, IL, USA). One-way analysis of variance (ANOVA) was used to compare the mean BW, VF, VF/QS, VV, BC, BC/BW, PVR/BC, and UFR values obtained in the three groups. Whenever differences were significant at a level of $P < 0.05$, a post hoc Bonferroni test was used to check for differences between the groups. The EEG parameters in each group and among the three groups were analyzed using the Friedman and Kruskal–Wallis tests [15]. *P*-values <0.05 were considered to indicate significant differences.

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