Pediatr. Res. *16:* 30–34 (1982)

Power Spectral Analysis of the Neonatal Primate Electroencephalogram during Acute Hypoxemia

R. D. GUTHRIE,[26] T. A. KNAUSS, C. M. HABERKERN, S. M. SUMI, AND D. E. WOODRUM

Departments of Pediatrics and Neurology, University of Washington, School of Medicine, and Department of Neurology, Group Health Cooperative Hospitals, Seattle, Washington, USA

Summary

The effect of acute graded hypoxemia on the electroencephalogram (EEG) of five prematures and five full term *Macaca nemestrina* in the neonatal period was determined using power spectral analysis—a technique that obviates the limitations of visual inspection. The EEG of selected epochs was analyzed by a Fast Fourier Transform program (POWER) during the 20 min of each trial of hypoxemia and compared with simultaneous arterial oxygen tensions. Levels of hypoxemia were graded as profound (Pa_{O_2} = 15–25 Torr); severe (Pa_{O_2} = 26–35 Torr), moderate (Pa_{O_2} = 36–50 Torr), or mild (Pa_{O_2} = 51–75 Torr). The EEG during normoxemia had a band width of 0.5 to 10 Hz and a peak power at 1–3 Hz. During mild hypoxemia, an increase in power in the delta range (0–3.5 Hz) occurred in the oldest animals. At moderate hypoxemia, the youngest animals showed a depression of absolute power in the delta band. A slowing of the EEG and decrease in power in the theta frequency range (4–8 Hz) followed when severe hypoxemic levels were reached. During profound hypoxemia, all animals at each postnatal age exhibited a significant decrease in EEG power at the delta and theta frequencies ($P < 0.025$) except 3-wk-old full term animals in which there was no significant change in the delta band. These results clarify and extend previously reported effects of hypoxemia on the neonatal EEG.

Speculation

The hypoxic-induced sequence of changes in the frequency and amplitude of the neonatal primate electroencelphalogram occur as a consequence of "neurotransmitter failure." At the isoelectric threshold, hyperpolarization from hyperkalemia results in electrical silence.

Recurrent episodes of hypoxemia are common in premature human infants with respiratory distress or apnea and these insults are linked to the significant mortality and morbidity associated with these conditions (21, 23). Although there is extensive data on the effects of hypoxemia on the electroencelphalogram (EEG) of adult man and animals, there is controversy concerning the level and duration of hypoxemia at which EEG changes and neuropathologic damage occurs in the neonate. A significant decrease in voltage of the premature human infants electroencephalogram has been correlated with arterial PO_2 levels below 40 Torr (19) whereas others have reported that neither hypoxemia (Pa_{O_2} = 20–46 Torr) nor severe acidosis (pH = 7.02–7.20) affected the EEG of neonates between 28 and 40 wk gestational age (16). In order to clarify this issue, we examined the effects of graded levels of acute hypoxemia on the EEG of premature and full term newborn monkeys using power spectral analysis—a technique that obviates the limitations of visual analysis of the EEG.

MATERIALS AND METHODS

Five premature *Macaca nemestrina* at a gestational age of 150 ± 2 days and five full term animals at a gestational age of 168 ± 2 days were studied serially in the first 3 wk of life. Study animals from timed conceptions (±1 day) were obtained by cesarean section at the desired postconceptual age and were raised in a neonatal primate nursery. On postnatal days 2, 7, and 21, the unanesthetized animals were restrained in the supine position in an incubator at environmental temperatures within the neutral thermal range (34°C at days 2 and 7; 31°C at day 21). Sleep state was determined from simultaneous recording of electroencephalogram, electrooculogram, electromyogram, heart rate, and respiratory pattern on a Beckman Accutrace Electroencephalograph (7). EEG was recorded from right and left fronto-central and centro-occipital leads and from one biparietal lead (time constant 1.0 sec; impedance less than 4000 ohm) using Beckman disc electrodes applied with paralodian. This time constant setting attenuated EEG activity less than 0.16 Hz which is below the range of experimental interest. The five channels of EEG were stored in a magnetic tape recorder (Honeywell 5600C) for later analysis. Electrooculogram was recorded from electrodes placed diagonally over the outer canthus of each eye and electromyogram was recorded from posterior neck muscles.

Tidal volume and respiratory frequency were measured using nasal prongs and a hot wire anemometer (7). Arterial blood gases were sampled from umbilical arterial or femoral arterial lines placed under local anesthesia. Blood pressure was recorded from these lines using a Statham pressure transducer (model 23 DB). A constant infusion of 10% dextrose at 1 ml/hr was maintained through the arterial lines during the experiments.

Each animal was randomly given 15, 10, and 5% oxygen in nitrogen to breath for 20 min during non-REM sleep after a room air baseline period. Experiments were started in non-REM sleep in order to obtain stable respiratory measurements and artifact free power spectra. Each experimental trial was performed in duplicate. Arterial blood gases were sampled during room air breathing and 2, 5, 7, 10, 15, and 20 min after the onset of inhalation of each gas mixture. Levels of hypoxemia were classified as profound (Pa_{O_2} = 15–25 mm Hg), severe (Pa_{O_2} = 26–35 mm Hg), moderate (Pa_{O_2} = 36–50 mm Hg), or mild (Pa_{O_2} = 51–75 mm Hg). Epochs interrupted by arousal and movement artifacts which occurred most frequently when older animals were breathing O_2 were not included in the data analysis. Between experimental trials 15–30 min were allowed for the animal to recover and any metabolic acidosis was corrected with infusion of $NaHCO_3$.

Selected 21 second epochs of EEG were obtained at the specified time periods when arterial blood gases were sampled and band pass filtered between 0.5 and 30 Hz and digitalized at 256 samples/channel/second. The digitalized signals were stored on magnetic tape and epochs which were free of artifact were analyzed off line on a PDP-15 computer. Power spectra were generated using a Fast Fourier Transform program (POWER) (5). The selected epochs of EEG were analyzed for peak frequency, band width and power; the integrated power at 0–3.5 and 4–8 Hz under immediately preceding room air and subsequent hypoxemic trials were determained at the different levels of hypoxemia and at the specified time intervals and statistically compared by the paired *t* test.

At either 8 or 24 hr after the final episode of induced hypoxemia and subsequent recovery four animals were sacrificed and their brains fixed by intracardiac perfusion of buffered glutaraldehyde-paraformaldehyde fixative under "Inovar" anesthesia. After removal from the skull, the brains were kept in the same fixative for several days and subsequently sectioned in the coronal plane. Multiple sections were embedded in paraffin and stained with hematoxylin and eosin, and other sections were embedded in gelatin, sectioned on a freezing microtome, and stained with oil-red-O and hematoxylin (3).

RESULTS

The EEG during normoxemia (Pa_{O_2} = 62 ± 2 mm Hg—day 2; 87 ± 3 mm Hg—day 7; 93 ± 6 mm Hg—day 21) had a band width of 0.5 to 10 Hz and peak power at 1–3 Hz (Fig. 1 *left* and Table 1). In the premature infants, the absolute power of the EEG increased in both the delta and theta bands with increasing postnatal age. In full term animals only theta band power increased with postnatal maturation. Premature animals had significantly less power than full term animals in the delta band at 2 and 7 days of age and in the theta band at 7 days of age.

EEG changes during the various levels of hypoxemia did not differ between premature and full term animals except as specifically noted and the results reported below are for all the animals combined.

During mild hypoxemia, 3-wk-old animals all demonstrated an increase in power in the delta band (normoxemia: 3826 ± 324 μv^2/Hz, mild hypoxemia: 4146 ± 443 μv^2/Hz; $P < 0.025$ by paired t test). Most animals at one week of age demonstrated a similar increase in amplitude at 0–3.5 Hz but this change did not reach statistical significance ($P = 0.2$).

At moderate hypoxemic levels, no consistent EEG changes were seen. Older animals tended to show an increase in delta and theta power whereas the youngest animals showed a significant decrease in delta band amplitude (Table 2). When arterial oxygen tensions reached 26–35 Torr (severe hypoxemia), a slowing of the EEG was observed. As can be seen in Table 3 and Figure 2, a significant decrease in EEG power occurred in the theta band at all postnatal ages.

During profound hypoxemia, premature and full term animals at each postnatal age exhibited a significant decrease in power at 0–3.5 and 4–8 Hz ($P < 0.025$) except animals at 3 wk of age in which there was no significant change in the power at the delta

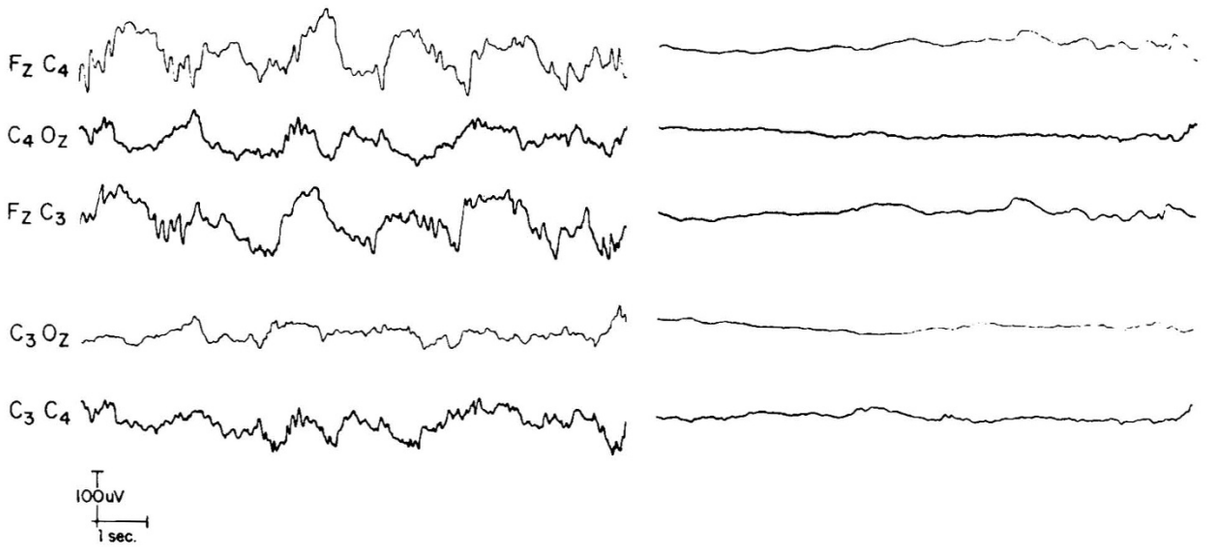

Fig. 1. Effects of profound hypoxemia on the EEG of a premature monkey. *Left*, represents the various leads of EEG in a 2-day-old premature monkey during normoxemia. *Right*, demonstrates slowing a a decrease in amplitude in all leads after 5 min of profound hypoxemia in the same animal.

Table 1. *EEG changes with maturation*[1]

Postnatal age (days):	2		7		21	
EEG frequency Hz:	0–3.5	4–8	0–3.5	4–8	0–3.5	4–8
Premature	1851 ± 681	12 ± 6	3976 ± 760	21 ± 4	4588 ± 634[2]	82 ± 32[2]
Full term	4772 ± 1884[3]	16 ± 8	5237 ± 862[3]	105 ± 23[3]	5059 ± 755	74 ± 4[2]

[1] Integrated absolute power during normoxemia is shown as mean ± 1 S.D.
[2] The absolute power is significantly greater than the respective power at day 2 at $P < 0.005$.
[3] The power at the respective EEG frequencies is greater in the full term than in the premature infant at the same postnatal age at $P < 0.01$ or better.

Table 2. *EEG power during moderate hypoxemia*[1]

	Integrated power (μv^2/Hz)					
Postnatal age (days):	2		7		21	
EEG frequency Hz:	0–3.5	4–8	0–3.5	4–8	0–3.5	4–8
Normoxia	4844 ± 2823	13 ± 6	3054 ± 1390	56 ± 31	5276 ± 1800	64 ± 20
Moderate hypoxemia	4335 ± 2664[2]	15 ± 7	3303 ± 1326	67 ± 34	4430 ± 378	91 ± 41

[1] Integrated power at delta and theta frequencies is shown as mean ± 1 S.D. expressed as μv^2/Hz.
[2] EEG power is significantly decreased at $P = 0.05$ by the paired t test.

Table 3. *Changes in EEG power during severe hypoxemia*[1]

	Integrated power (μv^2/Hz)		
Postnatal age (days):	2	7	21
EEG frequency (Hz):	4–8	4–8	4–8
Normoxemia	23 ± 7	91 ± 54	67 ± 23
Severe hypoxemia	16 ± 5[2]	20 ± 22[2]	47 ± 19[2]

[1] Integrated power at 4–8 Hz is shown as the mean ± 1 S.D. expressed as μv^2/Hz.

[2] EEG power is significantly depressed at $P < 0.05$.

frequencies (Table 4 and Fig. 1 *right*). The EEG became isoelectric in many instances. The power spectra in Figure 3 demonstrates the EEG changes seen when the arterial PO_2 is between 15 and 25 Torr; the power in the delta and theta bands is significantly diminished at both frequencies. Premature animals at 3 wk of age all demonstrated a decrease in integrated power during severe hypoxemia {normoxemia: 4588 ± 634 (μv^2/Hz), severe hypoxemia: 1967 ± 740 (μv^2/Hz); $P < 0.1$. Full term animals demonstrated a variable change in power in the delta frequencies [normoxemia: 5059 ± 755 (μv^2/Hz); severe hypoxemia: 5637 ± 708 (μv^2/Hz)].

All of the above described changes occurred beginning 5 ± 2

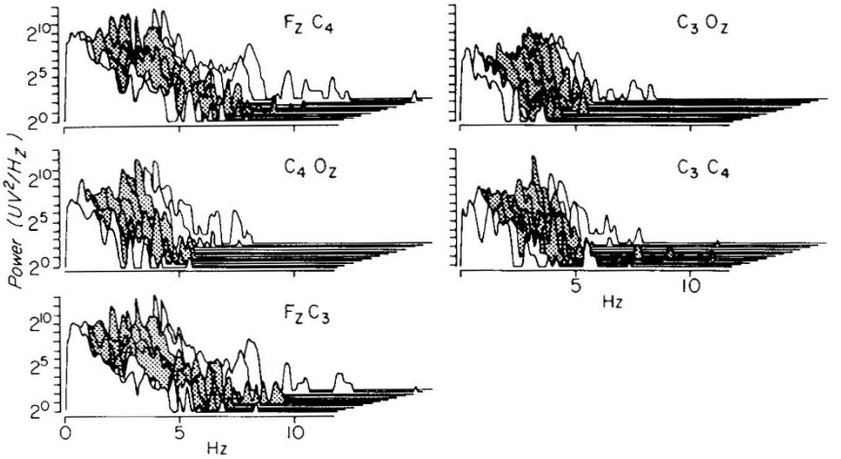

Fig. 2. Power spectral analysis of the premature monkey EEG during moderate to severe hypoxemia. The *unshaded areas* are the power spectra of a 2-day-old premature monkey during normoxemia—room air control behind, room air recovery foremost. The *shaded areas* are the power spectra at 2, 4, 7, and 10 min after the onset of moderate to severe hypoxemia (Pao_2 = 26 to 40 Torr). Each spectra represents data from 21-sec epochs. A significant decrease in power at 4–8 Hz from 122 μv^2/Hz to 37 μv^2/Hz is seen during hypoxemia.

Table 4. *EEG power during normoxemia and profound hypoxemia*[1]

	Integrated power of EEG (μv^2/Hz)					
Postnatal age (days):	2		7		21	
EEG frequency Hz:	0.5–3.5	4–8	0.5–3.5	4–8	0.5–3.5	4–8
Normoxemia	3312 ± 1090	14 ± 5	4606 ± 589	63 ± 19	4857 ± 570	77 ± 14
Profound hypoxemia	1846 ± 812[2]	3 ± 2[2]	3314 ± 722[2]	6 ± 4[2]	3801 ± 959	7 ± 5[2]

[1] Integrated power at the respective frequencies is the mean ± 1 S.D. expressed as (μv^2/Hz).

[2] EEG power is significantly different at $P < 0.05$ compared to the respectively normoxemic baseline.

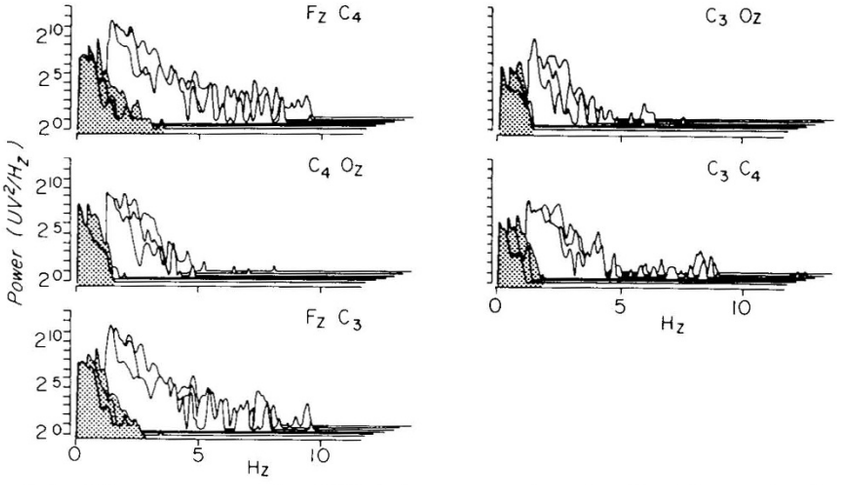

Fig. 3. Power spectral analysis of the premature monkey EEG during normoxemia and profound hypoxemia. The *unshaded area* in each lead represents the EEG of the premature monkey during room air breathing as shown on the *left*. The *shaded area* is the power spectra after 5 min of profound hypoxemia. Each spectral array represents averaged data from successive 21-sec epochs. Slowing of the EEG and a marked decrease in amplitude is clearly seen.

min after onset of the hypoxic stimulus and persisted for the full 20 min of the stimulus. Changes in the power spectra were similar in each of the five cortical leads and there was no asymmetry.

At the earliest age studied, minute ventilation increased from eucapnic levels of 346 ± 18 to 441 ± 35 ml/min/kg by 1 min after onset of hypoxemia and decreased toward eucapnic values 5–7 min after onset. Six of eight animals became apneic (5–20 sec) during profound hypoxemia at day 2; the EEG was simultaneously isoelectric. Variable changes in heart rate were seen but cardiac arrest did not occur. By 3 wk of age, a sustained increase in minute ventilation to values 22 to 32% above eucapnic levels occurred during hypoxemia even when the EEG was isoelectric; one of eight animals developed short (≃5 sec) apneic episodes. A further analysis of the ventilatory data is presented elsewhere (24).

Blood pressure during normoxemia ranged between a mean of 55 ± 6 mm Hg on day 2 to 83 ± 7 mm Hg on day 21. During profound hypoxemia when the EEG changes were most pronounced, blood pressure decreased moderately to 41 ± 2 mm Hg on day 2 and to 70 ± 5 mm Hg on day 21.

Neuropathologic examination of sacrificed brains revealed minor changes which were probably not significant when controlled for perfusion artifacts and compared to eight normal control brains. The hippocampal neurons in all four animals were completely normal, and there was no evidence of neuronal loss. Cortical necrosis of laminar or pseudolaminar type was never seen, even in frozen sections stained with oil-red-O. In all animals there were sudanophile lipid-containing cells in the posterior corpus callosum, splenium, and in the tapetum.

DISCUSSION

The use of power spectral analysis in this investigation provided a more detailed description of the sequence of changes in the EEG of the neonatal primate during hypoxia than has been reported to date. The previous study of Roberton (19) who relied on visual inspection of the EEG demonstrated only a decrease in the amplitude of the human neonates EEG when the Pa_{O_2} was less then 40 Torr. Radvanyi *et al.* (16) found no EEG changes in premature and full term neonates other than differences in sleep cycle organization when Pa_{O_2} was between 20–46 Torr or when pH was between 7.02 and 7.20. In marked contrast to these reports, we observed a progressive sequence of changes in the newborn primate's EEG using power spectral analysis.

First, an increase in EEG amplitude during mild hypoxemia was observed in the delta frequencies in the oldest animals. The youngest animals showed a depressed amplitude in the delta band during moderate hypoxemia. This pattern was followed by a slowing of the EEG and a decrease in power at 4–8 Hz when arterial oxygen tensions reached severe hypoxemic levels (26–35 Torr). Not until arterial oxygen levels reached 15–25 Torr—a level comparable to or below fetal Pa_{O_2} levels (9)—did a significant decrease in EEG power in both the delta and theta frequency bands occur. Even at these profoundly hypoxic levels, the most mature animals (full term animals at 3 wk of age) maintained some power in the delta band.

Maturation influenced the tolerance of the neonatal primate EEG to hypoxia. The youngest animals studied (2 days of age) first demonstrated a decrease in power at the delta frequencies at a higher Pa_{O_2} threshold than did older animals—36–50 *versus* 15–25 Torr. Postconceptual age also seemed to be an important variable since full term animals at 3 wk of age demonstrated no change in the delta band EEG power during profound hypoxemia whereas premature animals all showed decreased EEG power. These findings suggest that tolerance of cortical neuronal function to hypoxemic insults increases with maturation. The mechanism of such a maturational influence on cortical EEG tolerance to hypoxia is unknown.

Tolerance of the primate brain to acute hypoxic insults is even more pronounced in the fetus. At normal fetal arterial oxygen tensions of 26 ± 4 Torr, Martin *et al.* (9) observed normal EEG patterns in the fetal primate rather than the significant changes described above in the newborn at the same oxygen tension. Meyers (13, 14) demonstrated in the partially asphyxiated monkey fetus that the oxygen content of fetal thoracic aorta blood had to be lowered in the range of 0.8 to 1.5 volumes percent for a minimum of 25–30 min before brain injury occurred. Mann *et al.* (10) have similarly shown that the umbilical vein oxygen tension at which the fetal lamb EEG became isoelectric was 4.4 ± 0.4 Torr. This superior tolerance of the fetal brain to anoxic or hypoxic insults is probably a result of lower total cerebral energy consumption following anoxia in the fetus compared to neonates or adults (6, 22).

This pattern of EEG changes after hypoxia in the neonatal primate is similar to the sequence of EEG changes described in adult man and monkeys exposed to hypoxia (1). It also differs in minor ways from the adult sequence by virtue of the relative immaturity of the neonatal primate brain and the specifics of the design of the present investigfation. In adult animals and man, after hypoxia, there is first a latent period in which no EEG changes occur followed by a period of increased amplitude of the predominant alpha pattern (8–13 cycles/sec). Then a slowing and increase in amplitude develops until the predominant frequencies are in the delta and theta ranges. Next, the slowed EEG decreases in amplitude and becomes dysrhythmic. Finally, a prolonged isoelectric state is reached at cortical PO_2 values below 10 mm Hg (12). After a latent period in the newborn monkey, the increased amplitude at 8–13 Hz (α pattern) was not observed because the newborn primate's predominant frequencies are in the delta and theta range (11) and α rhythms do not develop until 24 wk of age (18). Also periods of arousal—which did occur in the older animals during moderate to severe hypoxemia—were excluded from data analysis in order to avoid movement artifacts in the spectral analysis. During mild hypoxemia in the older animals the expected increase in amplitude in the delta range and a tendency toward an increase in the theta range was observed although these changes were no doubt minimized by the fact that the experiments were begun in quiet sleep in order to obtain stable respiratory measures and artifact free-power spectra. Next, during severe hypoxemia, a slowing of the EEG and loss of power in the theta range occurred as reported in adults. Finally, the marked decrease in amplitude of the EEG progressing to the isoelectric state was clearly seen during profound hypoxemia. Thus, the pattern of expression of EEG changes after induced hypoxemia in the neonatal primate is also influenced by the relative immaturity of cortical development in the newborn primate and by differences in experimental design between this study and previous reports in adults. There might also be differences between neonates and adults in the susceptibility of cerebral oxidative metabolism to hypoxic insults (6).

The mechanism(s) of the hypoxemic induced EEG changes in the neonatal primate is (are) unknown. Although concomitant ischemia cannot be excluded in our study since cerebral blood flow was not measured, hypoxia is known to increase cerebral blood flow in fetal lambs and human infants (4, 15). Preliminary evidence in the newborn puppy also indicates that cerebral blood flow and intracranial pressure increase when the Pa_{O_2} falls to 25 Torr (2, 17). Furthermore, the observed drop in blood pressure of 15 to 25% is modest and would not be expected to result in a decrease in cerebral blood flow is autoregulation is intact as has been shown in puppies (2); if autoregulation is lost during hypoxemia as suggested by others, cerebral blood flow would decrease moderately but still remain above baseline values (17). Parallel studies of cerebral oxidative metabolites in the newborn puppy at comparable levels of profound hypoxemia indicates that cerebral ATP, ADP, and AMP levels are unchanged while lactate and pyruvate concentrations and lactate/pyruvate ratios increase (2). Thus, cerebral energy stores appear to be unchanged during acute profound hypoxemia and anerobic glycolysis is accelerated. "Neurotransmitter failure" characterized by an increase in the excitatory amino acids—glutamate and asparate, an increase in the inhibitory transmitter—GABA—or by decreases in serotonin, the catecholamines and acetylcholine might explain these EEG results (20). Finally, an hypoxemic induced increase in extracellular K^+

and consequent hyperpolarization might account for the observed decrease in cortical EEG power (8). The precise mechanism of these observed effects of hypoxemia on the cortical EEG in the neonatal primate remains to be elucidated.

REFERENCES AND NOTES

1. Bostem, E., Naquet, R., Vuillon-cacenrrolo, C., and Bimar, J.: Spectral analysis of the EEG in the monkey *Papio papio*. Effects of anoxia. Electroenceph. Clin. Neurophysiol., *27:* 451 (1969).
2. Casciotti, M. S., Hernández, M. J., Cannucci, R. C., Bowman, G. S., and Brennan, R. W.: Cerebral blood flow and oxidative metabolism in the hypoxic newborn dog. Physiologist, *22:* 18 (1979).
3. Chiffelle, R. L., and Putt, F. A.: Propylene and ethyleneglycol as solvents for Sudan IV and Sudan Black B. Stain Technol., *26:* 51 (1951).
4. Cooke, R. W. I., Rolfe, P., and Howat, P.: Apparent cerebral blood-flow in newborns with respiratory disease. Develop. Med. Child. Neurol., *21:* 154 (1979).
5. deJong, R. H., and Thomas, J. E.: POWER: 8 channel version. DECUS, 15 (1977).
6. Duffy, T. E., Kohle, S., and Vannucci, R. C.: Carbohydrate and energy metabolism in perinatal rat brain: Relation to survival in anoxia. J. Neurochem., *24:* 271 (1975).
7. Guthrie, R. D., Standaert, T., Hodson, W. A., and Woodrum, D. E.: Sleep and maturation of eucapnic ventilation and CO_2 sensitivity in the premature primate. J. Appl. Physiol. Respirat., Environ. Exercise Physiol., *48:* 347 (1980).
8. Kirshner, H. S., Blank, W. F., and Meyers, R. E.: Brain extracellular potassium activity during hypoxia in the cat. Neurology, *25:* 1001 (1975).
9. Martin, C. B., Murata, Y., Petrie, R., and Parer, J.: Respiratory movements in fetal rhesus monkeys. Am. J. Obstet. Gynecol., *119:* 939 (1974).
10. Mann, L. I., Prichard, J., and Symmes, D.: EEG, ECG, and acid-base observations during acute fetal hypoxia. Am. J. Obstet. Gynecol., *106:* 39 (1970).
11. Meier, G. W., and Berger, J.: Development of sleep and wakefulness patterns in the infant rhesus monkey. Exp. Neurol., *12:* 257 (1965).
12. Meyer, J. S., Gotoh, F., Tazaki, Y., Hamaquchi, K., Ishikawa, S., Nouilhat, F., and Symon, L.: Regional cerebral blood flow and metabolism in vivo. Arch. Neurol., *7:* 560 (1962).
13. Meyers, R. E. Threshold values of oxygen deficiency leading to cardiovascular and brain pathological changes in term monkey fetuses. In: Bruley, D. F., and Bicher, H. I.: Oxygen Transport to Tissue: Instrumentation, Methods, and Physiology. pp. 1047–1054 (Plenum Publishing Corp., New York, 1973).
14. Meyers, R. E.: Experimental models of perinatal brain damage: relevance to human pathology. In: L. Gluck: Intrauterine Asphyxia and the Developing Fetal Brain. pp. 37–97 (Year Book Medical Publishers, Inc., Chicago, 1977).
15. Purves, M. J., and James, I. M.: Observations on the control of cerebral blood flow in the sheep fetus and the newborn lamb. Cir. Res., *25:* 651 (1969).
16. Radvanyi, M. F., Monod, N., and Dreyfus-Brisac, C.: Electroencephalogramme et sommeil chez le nouveau-né en d'etresse respiratoire etude de l'influence des variations de al PaO_2 et de l'equilibre acido-basique. Bull. Physiolpath. Resp., *9:* 1569 (1973).
17. Raju, T. N. K., Bhat, R., and Vidyasagar, D.: Intracranial pressure (ICP) changes during acute hypoxemia in neonatal puppies. J. Pediatr., *96:* 1107 (1980).
18. Reite, M., Pauley, J. D., Kaufman, I. C., Stynes, A. J., and Marker, V.: Normal physiological patterns and physiological-behavioral correlations in unrestrained monkey infants. Physiol. Behav., *12:* 1021 (1974).
19. Roberton, N. R. C.: Effect of acute hypoxia on blood pressure and electroencephalogram of newborn babies. Arch. Dis. Child., *44:* 719 (1969).
20. Siesjo, B. K.: Brain Energy Metabolism. pp. 428–438 (John Wiley and Sons, New York, 1978).
21. Stewart, A., and Reynolds, E. O. F.: Improved prognosis for infants of very low birthweight. Pediatrics, *54:* 724 (1974).
22. Vannucci, R., and Duffy, T.: Carbohydrate metabolism in fetal and neonatal rat brain during anoxia and recovery. Am. J. Physiol., *230:* 1269 (1976).
23. Volpe, J.: Intracranial hemorrhage in the newborn: current understanding and dilemmas. Neurology, *29:* 632 (1979).
24. Woodrum, D. E., Standaert, T. A., Mayock, D. E., and Guthrie, R. D.: Hypoxic ventilatory response in the newborn monkey. Pediatr. Res., *15:* 367 (1981).

25. The authors thank Dr. J. E. Heavner for assistance in the PDP-15 computer analysis of the EEG, and Dr. W. A. Hodson for advice and support during this study.

26. Requests for reprints should be addressed to: Dr. Robert D. Guthrie, Department of Pediatrics, RD-20, University of Washington, Seattle, WA 98195 (USA).

27. This research was supported by NIH SCOR Center Grant HL 19187 and Regional Primate Center Grant RR00166.
28. Received for publication February 6, 1981.
29. Accepted for publication May 1, 1981.

0031-3998/82/1601-0030$02.00/0

Printed in U. S. A.