strongly suggests that complement is not crucial in bringing about the nerve lesion. The demonstration of a potentially pathogenic role of m-IgG in myeloma neuropathy may have implications for the management of patients with this disorder (*17*).

As in myasthenia gravis (*18*), a humorally mediated autoimmune disease of the neuromuscular junction, antibody depletion therapy by plasma exchange might prove beneficial.

Note added in proof: After submission of this manuscript, Latov *et al.* (*19*) described a human monoclonal antibody to peripheral nerve myelin in a patient with IgM_{Kappa}-monoclonal gammopathy. The patient's polyneuropathy improved after treatment with plasma exchange, steroids, and cytotoxic drugs. As in the mice used in our experiments, the patient's nerves showed segmental demyelination.

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20. Nerve conduction velocity of the tail nerve was measured in a paraffin bath maintained at 30°C by a pair of subcutaneous tungsten microelectrodes at the proximal end of the tail. Supramaximal stimuli of 0.1-msec duration were applied at the distal end of the tail by another pair of electrodes with a Grass S 88 stimulator connected to SIU 5. The distance between stimulating and recording electrodes was measured by caliper and was 5 to 6 cm. Recordings were made with a differential amplifier, displayed on a Tektronix 5103 N storage oscilloscope, and photographed by Polaroid film. All measurements were made at least three times on the same day with different electrode positions. The coefficient of variation of these multiple measurements ranged from 1.5 to 6.4 percent in individual mice.
21. We thank D. B. Drachman for providing the idea that stimulated us to carry out this investigation. We thank B. v. Specht for discussion on immunology, J. Newsom-Davis and W. I. McDonald for reviewing the manuscript, and J. Witthöft, S. Luh, and P. Becker for technical assistance.
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Periodicity of Sleep States Is Altered in Infants at Risk for the Sudden Infant Death Syndrome

Abstract. *The normal succession of sleep and waking states through a night is disturbed in infants at risk for the sudden infant death syndrome. Compared with normal infants, siblings of the sudden infant death syndrome victims have longer intervals between active sleep epochs at particular times during the night in the newborn period and a decreased tendency to enter short waking periods at 2 and 3 months of age. The latter finding is interpreted as an increased tendency to remain asleep, or a relative failure to arouse from sleep in infants at risk.*

Sleep is a focal point for studies of the sudden infant death syndrome (SIDS), since victims of this syndrome succumb at times when they would be expected to be asleep (*1*). We report here that the organization of sleep states is disturbed in infants at risk for SIDS. Sleep in the infant is composed of two distinct states: a quiescent, or quiet sleep (QS) state, characterized by regular respiration and a slow wave encephalographic (EEG) pattern, and an active sleep (AS) state, accompanied by irregular respiration, activated EEG, and phasic muscle activity (*2*). Episodes of QS and AS, intermixed with waking (AW) periods, follow each other in succession throughout the night. This temporal sequencing, rather than the total amount of time spent in each state, is disturbed in infants at risk for SIDS. The importance of this finding is that arousal from sleep may be necessary to restore respiration after certain challenges to the infant (*3*), and an inability to switch from sleep to waking might lead to total respiratory failure.

Twenty neurologically normal infants and 20 infants who were subsequent siblings of SIDS victims (SSIDS) participated in this study. All infants were of conceptional ages between 37 and 44 weeks, and all had 1-minute Apgar scores between 8 and 10. Subsequent siblings of SIDS victims were chosen as a risk group since they have a three- to fourfold higher risk for SIDS than the general population does (*4*). The SSIDS and normal infants were matched according to the educational level of their parents in order to equate for socioeconomic background. Birth weights ranged from 2878 to 4111 g for the normal infants and from 2301 to 4593 g for the higher risk infants. Each infant was admitted to the sleep laboratory at 1700 hours for an all-night monitoring session (range, 10 hours and 40 minutes to 12 hours) during the first week of life and subsequently at 1, 2, 3, 4, and 6 months of age (*5*). The parents were informed of the nature and objectives of the study, and written permission was obtained before participation.

Successive minutes of each record were classified QS, AS, or AW according to criteria described elsewhere (*6*). Sleep scores for each state were then transformed into a binary sequence of 0's and 1's, with 0 representing the absence of a given state and 1 representing the presence. In this manner, 640- to 720-point binary series for QS, AS, and AW were compiled and used to describe the presence or absence of each state in a 12-hour recording. Because of the abrupt transitions associated with binary elements, these three time series for each individual at every age were subjected to a three-term moving filter to reduce high-frequency components (*7*). The smoothed series was then submitted to a fast Fourier transform program to esti-

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mate relative amounts of activity at different frequencies of recurrence of episodes for each state. After the transform, spectra were summed into three broad bands: 0.00 to 0.59, 0.64 to 1.35, and 1.41 to 4.92 cycles per hour. Analysis of variance procedures were used to quantify differences between the state spectra within these bands.

The two groups of infants showed a similar pattern of rather irregular sleep state cycling patterns at 1 week, followed by the establishment of a highly regular hourly rhythm for both QS and AS by 3 to 4 months of age. There were significant group differences in the distributions of sleep-waking states at particular ages, however. At 1 week, the SSIDS had higher power than normal infants in the AS low-frequency band [$F(1, 38) = 9.38$, $P < .005$], corresponding to frequencies slower than 1 cycle every 2 hours (Fig. 1). Further, the awake spectra of the SSIDS at 2 and 3 months showed decreased power in the higher frequency range [faster than 1.4 cycles per hour; $F(1, 38) = 5.84$, $P < .025$ and $F(1, 38) = 4.26$, $P < .05$, respectively], and at 3 months their AW spectral power was also lower at moderate frequencies [approximating 1 cycle per hour, $F(1, 38) = 9.02$, $P < .005$].

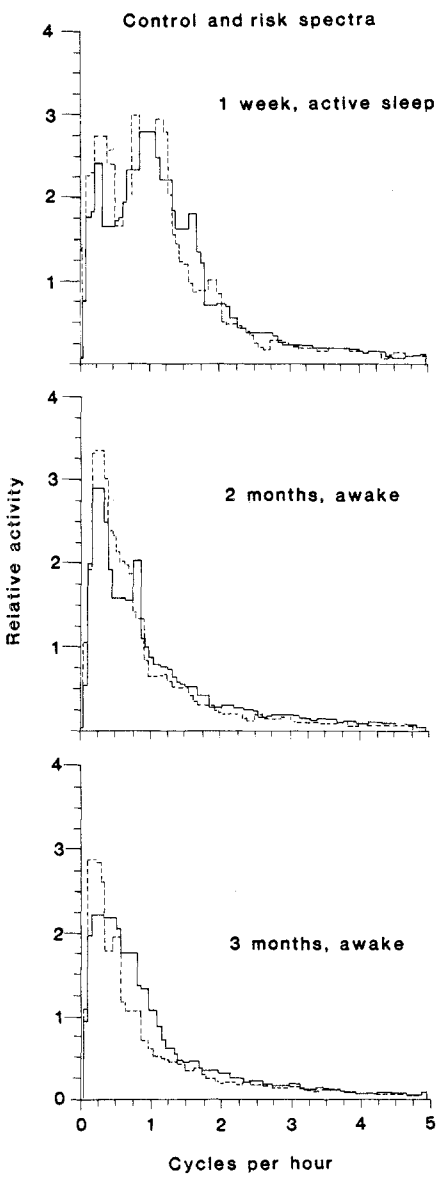

Fig. 1. Averaged autospectral plots of binary state data from control subjects (solid lines) and siblings of SIDS victims (dashed lines). Spectral values have been smoothed by a moving median filter (*7*). Note the increased low-frequency power during active sleep for risk infants at 1 week and the relative shift from higher frequency power to lower frequency power during waking at 2 and 3 months.

In order to translate these periodicity differences to differences in sleep-waking state intervals, the raw binary traces for each state were examined at 1 week and at 2 and 3 months. Traces in which the spectra showed the largest deviations from the mean for both normal and risk infants are plotted in Fig. 2. These plots suggest that increased low-frequency AS power in the higher risk SSIDS group at 1 week resulted from both long inter-AS intervals and from AS-free intervals at the beginning and end of recordings belonging to a subset of risk infants. Subsets of infants at risk at 2 and 3 months of age were characterized by long inter-AW periods and an absence of short AW epochs (Fig. 2). These AW spectral findings translate to sustained periods of no waking in certain infants at risk, unlike the rather frequent periods of waking that occur between sleep states in normal infants. Thus, certain infants at risk for SIDS seem to have difficulty in making the normal transition from sleeping to waking states. This difficulty was present at both 2 and 3 months of age, which coincides with the period of maximum risk for SIDS (*8*). Arousal from a sleeping state to waking may be essential for resumption of breathing or correction of respiration after airway obstruction (*9*) or chemical stimulation (*10*). Victims of SIDS exhibit symptoms of asphyxia (*11*) and show signs of having been subjected to chronic hypoxia (*12*). Continued difficulty in making the transition from sleep to waking so as to resume normal respiration might underlie a hypoxic condition and might establish the scenario for terminal apnea. Consequently, this study suggests that an essential element of the syndrome may be a failure to arouse from sleep during a critical transient event, such as an apnea, that might subsequently lead to death. Normally, such an event would result in an awakening and restoration of breathing. It is important to emphasize that we suspect dysfunction in the mechanisms which cause arousal, as opposed to dysfunction of the control of respiration within a state.

Although there is a relative sparing for SIDS during the first month of life (*11*), disturbed sleep state patterning in the SSIDS group was apparent as early as 1 week of age. Abnormally low heart rate variability is also present in risk infants during this period (*13*). This suggests (i) that there is a potential for differentiating those infants who may be at special risk for SIDS before the critical 2- to 3-month age period, and (ii) since the physiologi-

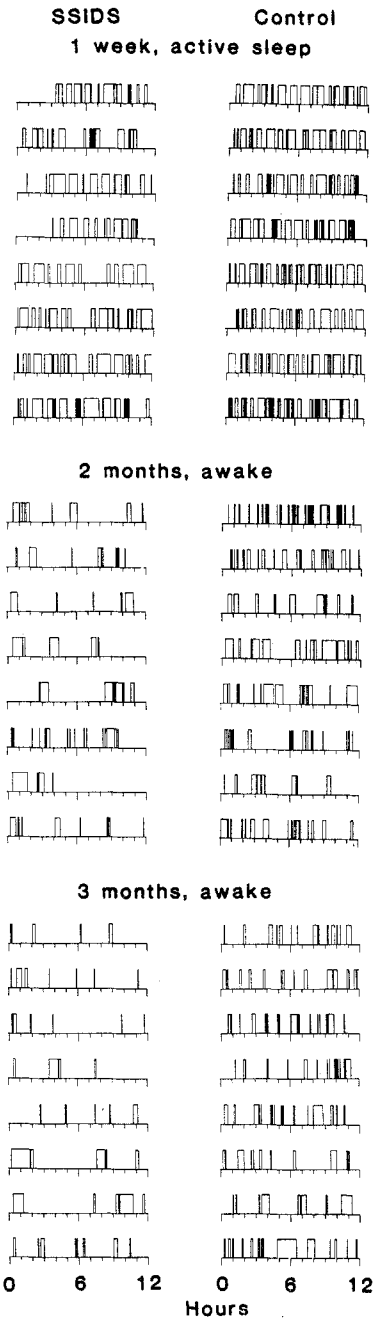

Fig. 2 Plots of binary state sequences from selected risk and control infants. The presence of a state is indicated by a rise from the baseline. Occasionally, the rise is only momentary and results in a short pulse. Absence of a state is indicated by return to zero baseline.

cal signs indicating risk for SIDS are manifested in the newborn, these signs may not be due solely to postnatal environmental influences. Early neonatal deaths and death from SIDS share a variety of common epidemiological factors (*14*). The antecedents of SIDS might therefore lie in a disturbance in fetal development.

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Neural Control of Swimming in a Vertebrate

Abstract. *An excitatory drive to the spinal cord neurons supplying rhythmic locomotor output in swimming was demonstrated in paralyzed late* Xenopus *embryos. The motor system for a single muscle can independently generate rhythmic motor discharge with the normal swimming cycle period.*

In many groups of animals, including mammals, the basic alternating pattern of motor discharge required for locomotion can be generated within the central nervous system without reflex feedback from the movement itself (*1*). Current hypotheses favor the idea that the rhythmic activity underlying locomotor patterns in vertebrates is generated within the spinal cord. Higher centers are thought to activate and modulate this spinal cord pattern generator by means of a descending tonic excitatory drive. In most hypotheses, reciprocal inhibition between antagonistic motor systems in the spinal cord is crucial, either being fundamental to the rhythmicity of the spinal cord pattern generator (*2*) or being necessary for the coordination of phase relationships between separate, inherently rhythmic motor systems (*3, 4*). Despite the long history of most of these proposals, direct evidence for excitatory drive during locomotion and on the role of reciprocal inhibition is not available for vertebrates. We have therefore sought a simple vertebrate preparation in which to explore the origins of locomotory rhythms and their control by higher centers.

The behavior of embryos of fish and amphibians is limited, and they are neuroanatomically simple. They therefore offer a model system in which to explore fundamental features of nervous organization. We have studied late embryos of the clawed toad (*Xenopus laevis*) at stage 37/38 (*5*) (Fig. 1A). When released from their egg membranes, embryos will swim spontaneously or in response to mechanical stimuli or dimming of the light (*6*); swimming can be stopped by bumping the head or cement gland (*7*). Filming

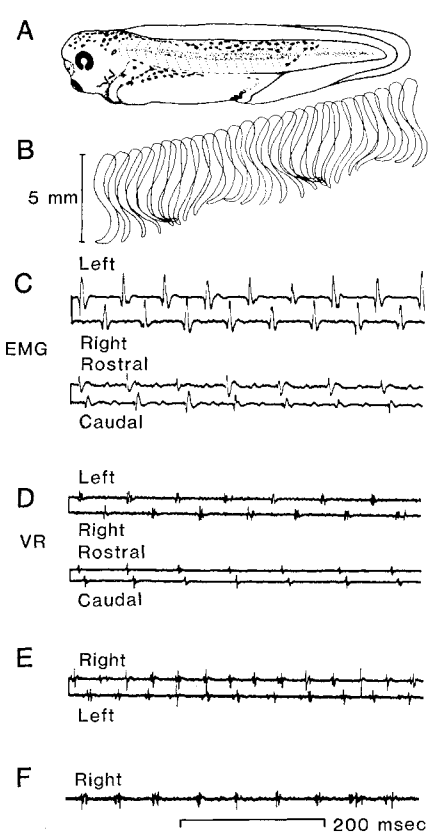

Fig. 1. (A) Side view of a late embryo of *Xenopus laevis* at stage 37/38 (*5*). (B) Tracings of swimming movements from cine films taken at 300 frames per second. Waves of bending pass caudally down the body. (C) Muscle potentials during swimming in restrained embryos were recorded by placing saline-filled suction pipettes on exposed myotomal swimming muscles. Activity on left and right sides of one segment alternated (upper traces). Activity was delayed at the more caudal of two recording sites on the same side, 2 mm apart (lower traces). (D) Motoneuron discharge in the ventral roots (*VR*) of paralyzed embryos (*9*) recorded with suction pipettes placed at the junctions between segmented myotomes where muscle fibers are innervated. Rhythmic discharge, evoked by dimming illumination (*6*), alternated on left and right of one segment (upper traces). Discharge was delayed at the more caudal of two recording sites on the same side, 1.5 mm apart (lower traces). (E) Rhythmic ventral root bursts on both sides of a paralyzed embryo lacked strict alternation when left and right halves of the nervous system were surgically separated caudally from the first postotic myotome (*15*). (F) Rhythmic ventral root bursts recorded from the isolated right half of the hindbrain–spinal cord (*16*).

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