Clinical Implications for Behavioral Assessment of Sleep/Wake States in Neonates: Augmenting Medical Diagnostic Evaluations

Author: DeSantis, Darlene T, PhD

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Full Text: Headnote ABSTRACT: The use of behaviorally defined sleep and wake states for detecting or predicting abnormal development in high risk newborn infants is addressed. One case of a relatively low risk 32-week gestation infant is used to illustrate that immediate subjective impressions by a trained observer may reveal information useful to the medical staff without having to wait for the lengthy computer analyses usually performed with this assessment technique. A second case illustrates a situation in which sleep/wake assessment by a trained observer assisted the medical team in confirming their diagnosis of massive brain damage and loss of function in an anencephalic newborn. The use of sleep variables in evaluating other behavioral and medical conditions in the young infant is also discussed. The literature demonstrating the usefulness of sleep/wake patterns to predict or evaluate medical and behavioral problems in newborns has grown steadily over the past three decades. Such varied disorders as aplastic anemia, behavior disorders (possible Attention Deficit Disorder with Hyperactivity), developmental delays on standardized tests in infancy, Down's Syndrome, high bilirubin levels (liver problems), high riskness accompanied by clear signs of Central Nervous System (CNS) dysfunction, mental development at one year, prenatal exposure to drugs, prenatal exposure to maternal stress and seizure disorders have been predicted or immediately diagnosed as a result of sleep/ wake evaluation (Becker &Thoman, 1981; Dinges, Davis &Glass, 1980; Prechtl, Theorell &Blair, 1973; Thoman, Denenberg, Sievel, Zeidner &Becker, 1981). Perhaps the greatest volume of support for the predictive validity of neonatal sleep patterns concerns Sudden Infant Death Syndrome (Guilleminault, Ariagno, Souquet &Dement, 1976; Harper, Leake, Hoffman, Walter, Hoppenbrouwers, Hodgman &Sterman, 1981; Thoman et al., 1981). While most of these studies used polygraphic means to determine states, a few added behavioral criteria and another group used solely behavioral criteria. Behavior-only sleep-wake assessment of infants shares some commonality in its definitions with the pioneering work of Wolff (1966). However, users of the behavioral technique have varied in amount of observation time (from one to several hours), length of epoch defining a state (from 10s to 3 or more minutes), the specific states used and their defining criteria, and the statistical variables analyzed (Prechtl, 1977). This has made cross-laboratory comparison difficult for research purposes but need not be a serious obstacle to making clinical inferences. The infants described below were observed with a behavior-only method that has demonstrated predictive validity (Waite, DeSantis, Thoman &Denenberg, 1977), reliability (Thoman, Waite, DeSantis &Denenberg, 1979), and sensitivity to experimentally induced differences (DeSantis, Waite, Thoman &Denenberg, 1977) in animal models. The animal model version was deliberately chosen so that investigators could go back and forth between species in order to obtain both empirical and clinical information. It was modified for species-specific human behaviors before application to preterm and fullterm infants (DeSantis, in review) but otherwise is applicable to at least developing rabbits and rats as well as to infants. METHODS The procedure for the two infants to be described involved one hour of observation immediately following a feeding (in the case of the anencephalic, the entire interfeeding interval was covered, or 3.5 hours). States were defined based on a 10s epoch signalled to the observer through a tone delivered through an earpiece. The observation was entirely naturalistic, involving no intervention or disturbance to the infant (and thus making the procedure useful in a variety of settings). Specific designations of waking used were Quiet Alert and Waking Active. For sleep, Active Sleep ("REM Sleep" in polygraphic studies) and Quiet Sleep ("NonREM Sleep" in polygraphic studies) were the main designations. Briefly, Active Sleep is

characterized by several facial and body movements (i.e., behavioral activity), vocalizations, and none to dense Rapid Eye Movements (REMs). Three categories are distinguished based on the amount of REMs: none, some (less than 5s), and dense (more than 5s). Quiet Sleep signals behavioral quiescence except for the occasional occurrence of isolated twitches, Moro-like startles and rhythmic mouthing. Additional categories recorded include Drowse (transition between wake and sleep), Transitional, (when the subject's state cannot be classified) and Q-State (believed to be a primitive or abnormal form of Quiet Sleep). For more extensive descriptions of recording criteria see DeSantis (in review) and Thoman et al., (1979). Analysis of state data yields information on frequency, amount, duration, latency and sequencing of states or desired clusters of states plus indication of overall organization or patterning. The latter is used most often to describe aberrant development. This procedure requires several computer runs, thus often considerably delaying the time between when the observation is done and when the results are obtained. An additional procedure was used with the infants to be discussed whereby the observer summarized, in a very subjective fashion and with no formal analysis, her impressions of the child's state organization, quantitative estimates for each state, qualitative evaluations of state expression (e.g., how intense was the twitching, where was it located, were any unusual behaviors noted) and anything she felt was unusual about the observation. It is these so-called clinical comments, obtained at the time of the observation, that will be discussed. Two cases are presented which illustrate two CNS disorders not previously related to early state patterns. The first is prospective, in which the infant was judged to be relatively low risk for his gestational age but showed an atypical state picture in the clinical evaluation at 29 hours of age. His computer results are compared to those from the larger study of state development in preterm and fullterm infants between 24 and 48 hours of life (see DeSantis, in review). The second infant was born anencephalic. Not part of a research study, the neonatologists requested a state observation of him as well as administration of the Brazelton Neonatal Behavioral Assessment Scales (NBAS) which assesses auditory and visual habituation during sleep, response to auditory and visual stimuli during Quiet Alert, and capacity for social interaction and bonding during Quiet Alert. This request came after the mother reported behaviors and states occurring during feeding that the medical staff did not think were possible given his diagnosis. RESULTS Case A: Preterm Newborn Prenatal and labor/delivery history: Maternal history included mild preeclampsia beginning 6 months prior to labor (highest blood pressure was 160/90 with all others borderline and negative urine tests) and a pre- or early pregnancy history of genitourinary infection. This 19 year old mother was a primagravida. There were no other problems until 32 weeks, at which time labor began spontaneously for no apparent reason. When attempts to stop labor with medication failed, the mother was helicoptered to the facility of observation. These drugs were administered 16 hours prior to delivery. Three hours prior to delivery the mother was given 25 mg Demerol for pain. Delivery itself was normal, vaginal and in the vertex position. Immediate neonatal problems: Apgar scores were 7 (normal) at one minute dropping to 6 (borderline) at 5 minutes as respiratory problems began. Initial heart rate was good (100 beats per minute), cry effort fair, respiratory effort problematic with flaring and grunting. At this point the infant was suctioned to clear airways. Following suctioning heart rate decelerated to 50 (distress) and resuscitation with oxygen by bagging was required. Now stable, the infant was transferred to the Level III Neonatal Intensive Care Unit (NICU). There the pediatric exam found partial Moro and grasp reflexes, no sucking reflex, capability to move all extremities, normal color and skin tone, and a normal (mature) lung function test. The initial diagnosis was early Respiratory Distress Syndrome (RDS) with possible narcosis secondary to maternal medication during labor. This Caucasian male was judged to be 32.5 weeks gestational age based on the Dubowitz modified exam (Ballard, Novak &Driver, 1979; Dubowitz, Dubowitz &Goldberg, 1970). Birthweight, length and head circumference were all appropriate-for-gestational age on the Colorado Growth Charts. He was placed on a two-hour feeding schedule via oragastric tube. Problems at time of observation (29 hours of age): Prior to observation the charts of infants in the preterm study were reviewed for an update on problems, lab results and changes in diagnosis. They were also scored for cumulative risk status using the Perinatal Problem Oriented Risk Assessment

System (POPRAS) of Hobel, Hyvarinen, Okada &Oh (1973) as modified by Campbell &Wilhelm (1982) for degree of risk for brain damage. In this system a score of less than 50 indicates low risk while greater than 50 signifies high risk for brain damage. This subject scored 32 and the physician indicated before the observation that the infant was doing well with "the usual problems of prematurity." The diagnosis was now mild RDS with no mention of narcosis. Still on a 2-hour feeding schedule, he was in a warming crib under an oxygen hood (29% oxygen) in NICU. In addition to scoring states for 10s epochs, the observer's immediate impressions of each infant were informally noted in a clinical log at the end of the observation, as mentioned above. For this baby, the observer's notes imply subtle problems in state amounts and patterning and in the intensity of behaviors which may have been relevant to developing problems and/or predictive of his eventual outcome. Compared to other subjects in the 30 to 34.5 week gestational age range (and to young rabbits of comparable brain maturity), this subject displayed excessive Quiet Sleep and Q-State, with Quiet Sleep inappropriately predominating over Active Sleep. Quiet Sleep visits also seemed unusually prolonged. Visits to Active Sleep seemed appropriate in frequency but very brief and deficient in REMs. After Quiet Sleep first appeared in the hour, subsequent visits to Active Sleep were sudden, exceptionally brief, and mild in intensity of twitching and movements. The physician was notified of the unusual results, reviewed the most recent chart notes and confirmed that the medical picture was still one of a healthy and stable infant doing well with anticipated problems. It was decided that the observation would be repeated the next morning. During the night, the infant developed repeated severe episodes of apnea and bradycardia requiring vigorous resuscitation. Before the state observation could be repeated the infant was removed from the nursery for a full neurologic workup (spinal tap, EEG, CT-Scan). By Day 4 of life it was confirmed that he now suffered from severe and large brain hemorrhages (subarachnoid, intraventricular and intracranial). The parents, after meeting with physicians, social workers, clergy and the hospital ethics committee, consented to an order not to resuscitate if any further apnea/bradycardia episodes occurred. All other medical procedures would be continued. For the record, the infant declined in other systems as well: requiring an exchange transfusion for high bilirubin, antibiotics for infection, heart medication, and supplements of metabolites to compensate for various imbalances (he was also placed on artificial breathing apparatus until the decision not to interfere with the respiratory condition was made). He succumbed on Day 9. It should be emphasized that the use of state measures for diagnostic measures is too preliminary for the significance of this subject's results to be evaluated. What is noteworthy, however, is the concordance between the observer's subjective judgments immediately following the observation and the infant's actual quantitative scores relative to his gestational age group when the formal computer analyses had been completed. The subject fell outside standard deviation (SD) limits on a number of measures, including those earmarked by the clinical comments of the observer. The overall pattern was mixed: on some measures he was appropriately immature, on others advanced, and on still others he deviated either in the value of the score or the direction in which it deviated from the group mean. The specific results are as follows: 1. High percentage of Q-State (+2.1 SD). 2. High percentage of Quiet Sleep (+1.8 SD). 3. High frequency of episodes of Q-State (+1.7 SD). 4. High frequency of episodes of Quiet Sleep (+1.9 SD). 5. The Active Sleep results were less remarkable but still matched the observer's clinical notes: -1.2 SD on durations of both Active Sleep and Active Sleep Without REM, and -1.0 SD for frequency of visits to Active Sleep. Case B: Anencephalic Newborn Since this infant was not part of any research study no details were taken from his chart. It is known that he was a Caucasian male, the fullterm product of an uneventful pregnancy to a multiparous mother with no known family history of anencephaly or related genetic disorder (e.g., spina bifida). Anencephaly is a rare genetic disorder in which part or all of the brain does not develop. It is always terminal, although the period of survival varies from minutes to months. This infant was believed to have vegetative functions to at least brainstem level and was maintained on a regular 4-hour oral feeding schedule. He was isolated in the NICU because the anencephaly was complicated by the also rare occurrence of a meningoencephalocele (hernial protrusion of the meningial membranes and brain tissue through a skull defect). Because of this, he was

at great risk for infections. The physicians felt strongly that this child could not achieve a waking state and did not have brain function above the thalamic level, if that far. The request to observe state (and to perform the Brazelton NBAS exam, which was done by another staff member) came after the mother reported eye-opening, alertness and possible eye contact during a feeding. Since such an infant had never been observed with behavioral state, it was decided to use the entire interfeeding interval (3 to 4 hours) for observation. This turned out to be necessary to verify the first hour's results since the state patterns were very unusual. Brazelton NBAS findings: The tester found no evidence of responsiveness to auditory or visual stimuli in any state and no evidence of waking during the entire exam (which usually awakens the infant and elicits all wake states including fussing and crying). Behavioral state findings: Two observations were done: the first on Day 18 of life and the second one week later on Day 25. On Day 18 observation no evidence of full waking or alertness was found. During a diaper change the infant did vocalize and show a considerable increase in activity. This was scored as Drowse and was the closest to a waking state the infant ever got in either observation. He also showed periods of activity (limb and torso movements) accompanied by non-cry vocalizations. These were scored as Transitional since it was unclear as to whether the infant was awake or asleep and such behavior is possible in Active Sleep. Active Sleep predominated both observations but it was atypical in that the behaviors (e.g., twitches) were not very intense, eye movements were mild to moderate in intensity and never reached the amount of density expected of a fullterm infant. Quiet Sleep (the more mature of the two major sleep categories and the one expected to dominate as maturation increases) was rare on Day 18 and absent but for 2 epochs on Day 25. Periods of irregular breathing with behavioral quiescence suggested the possible existence of Q-State but were scored as Transitional because they were not clear enough to be designated one of the other states. No computer analyses were done on this infant. The overall impression reported to the physicians was as follows: 1. Definite cycling between "activity" and "quiescence" was seen but the infant never showed any clearly definable state except Active Sleep With REM. 2. The only eye-opening noted was partial, followed a coughing episode, totalled 70 consecutive seconds and occurred during the third hour of the Day 18 observation. It was scored as Drowse and not true waking. 3. The baby was very active at times (eyes closed), even moving himself forward in the prone position. It could not be determined whether this represented spontaneous waking with eyes closed (not a standard characteristic) or reflexive crawling of which most newborns are capable if placed properly in the prone position. 4. Overall, this infant showed abnormal sleep, with the less organized and less mature Active Sleep predominating, REMs were present but atypical for a fullterm infant, Transitional (not definable) was the second most observed state with Quiet Sleep virtually absent although some atypical quiescent epochs were clear enough to give the impression of cycling between "activity" and "quiescence." One might conclude from this consideration of sleep that even the brainstem systems had not completely developed or were adversely affected by the slow but continuous loss from the skull. Finally, neither observation supported the mother's impression of alertness being achieved. The closest to wake seen was the heavy-lidded half to barely open eyed look of Drowse. The infant went home to his parents and siblings soon after the second observation. He survived a total of three months despite severe brain damage. DISCUSSION/SUMMARY The clinical impressions obtained during a formal observation of sleep/wake states appear to have provided immediate information about two medical conditions not previously discussed with respect to behavioral state assessment (i.e., brain hemorrhage and anencephaly) in newborn infants. In the case of the brain hemorrhages, the infant's behavior revealed abnormalities before physiological parameters or medical tests. While such hemorrhages are not uncommon in the first 72 hours of life in preterm infants, what is notable here is that the state assessment (and an experienced observer's immediate interpretation of it) apparently detected a problem before the usual symptoms appeared. The EEG or CT-scan would have detected problems far more accurately, but at the time of the observation there was no medical justification for ordering either test. Whether or not the hemorrhages could have been stopped or the damage minimized had they been detected earlier is not known but is within the realm of possibility (or will be with future technological

and pharmacological developments). In the case of the anencephalic infant, once again a CT-scan would have determined the exact amount and location of damage. In this child's case, however, the condition was still terminal, the parents' insurance did not cover the expensive scan, and it is unlikely that the treatment plan would have been altered. The behavioral observation was successful in verifying (or not) the mother's interpretation of the baby's ability to achieve a waking state and also suggested that the brain damage was more extensive than the physicians originally thought (re: the disordered Active Sleep which, of all states, should have been fairly normal if the brainstem were intact). It is also worth noting that the parents' decision to take the baby home (against the strenuous objections of the medical staff) may have contributed to his longevity. By providing a normal, loving environment and allowing parental and sibling relationships to form, they also provided themselves with the opportunity to bond and, upon the infant's death, undergo a normal grieving process with closure. While subjective clinical impressions of behavioral state will not by themselves elucidate sleep/wake development, prematurity or various medical or behavioral problems that may develop later, their inclusion does seem to add useful information to the immediate clinical picture which may ultimately affect outcome. A prerequisite to their successful use is the degree of experience of the observer in normal state parameters in the gestational age groups of relevance. Repeated observations are also recommended, although in some cases (as in the preterm infant studied here) the medical situation may be too urgent for delayed action by the medical staff. It should be emphasized that this procedure is not intended as a diagnostic test in itself but rather as an additional piece of information for the physician to use in deciding his/her medical plan and the need for additional standard diagnostic tests. Finally, it is this author's opinion that it does not matter which particular set of definitions or state categories the observer uses to obtain the information discussed above as long as the observer is very well-versed in the normal versions of his/her assessment system. This remains to be demonstrated by the various laboratories which use behavioral state assessment. References REFERENCES Ballard, J.L., Novak, K.K., &Driver, M. (1979). A simplified score for assessment of fetal maturation of newly born infants. The Journal of Pediatrics, 95, 769-774. Becker, P.T. &Thoman, E.B. (1981). Rapid Eye Movement storms in infants: Rate of occurrence at 6 months predicts mental development at 1 year. Science, 212, 1415-1416. Campbell, S.K. &Wilhelm, I.M. (1982). Developmental sequences in infants at risk for CNS dysfunction: The recovery process in the first year of life. In J.M. Stack (Ed.), An interdisciplinary approach to the optimal development of infants: The special infant. New York: Human Sciences Press. DeSantis, D.T. (in review). From babies to bunnies and back: Application of an animal model of sleep and prematurity. DeSantis, D., Waite, S., Thoman, E.B., &Denenberg, V.H. (1977). Effects of isolation rearing upon behavioral state organization in the rabbit. Behavioral Biology, 21, 273-385. Dinges, D.F., Davis, M.M., &Glass, P. (1979). Fetal exposure to narcotics: Neonatal sleep as a measure of nervous system disturbance. Science, 209, 619-621. Dubowitz, L.M.S., Dubowitz, V., &Goldberg, C. (1970). Clinical assessment of gestational age in the newborn infant. The Journal of Pediatrics, 77, 1-10. Guilleminault, C, Ariagno, R., Couquet, M., &Dement, W.C (1976). Abnormal polygraph findings in near-miss Sudden Infant Death. The Lancet, June 19, 1326-1327. Harper, R.M., Leake, B., Hoffman, H., Walter, D.O., Hoppenbrouwers, T., Hodgman, J., &Sterman, M.B. (1981). Periodicity of sleep states is altered in infants at risk for the Sudden Infant Death Syndrome. Science, 213, 1030-1032. Hobel, C.J., Hyvarinen, M.A., Okada, D.M., &Oh, W. (1973). Prenatal and intrapartum high-risk screenings: I. Prediction of the high risk neonate. American Journal of Obstetrics and Gynecology, 117, 1-9. Prechtl, H.F.R. (1977). Assessment and significance of behavioral states. In S.R. Berenberg (Ed.). Brain: Fetal and Infant. The Hague: Martinus-Nijhoff Medical Division. Prechtl, H.F.R., Theorell, K., &Blair, A.W. (1973). Behavioural state cycles in abnormal infants. Developmental Medicine &Child Neurology, 15, 606-615. Thoman, E.B., Denenberg, V.H., Sievel, J., Zeidner, L.P., &Becker, P. (1981). State organization in neonates: Developmental inconsistency indicates risk for developmental dysfunction. Neuropediatrics, 12, 45-54. Thoman, E.B., Waite, S.P., DeSantis, D.T., &Denenberg, V.H. (1979). Ontogeny of sleep and wake states in the rabbit. Animal Behaviour, 27, 95-106. Waite, S., DeSantis, D., Thoman, E.B., &Denenberg, V.H. (1977). The

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