

The Neonatal Behavioral Assessment Scale as a Biomarker of the Effects of Environmental Agents on the Newborn

by Edward Z. Tronick*

The organization of the newborn's brain and the nature of the effects of toxins and pollutants conspire to produce complex and difficult problems for the assessment of the behavioral effects of environmental agents. The newborn's brain can be characterized as relatively undifferentiated, and more vulnerable to, but potentially more capable of recovery from, the effects of environmental agents specific to this time period than it will be later in development. Environmental agents tend to have nonspecific, possibly subtle, effects that invade many areas of newborn functioning. These characteristics of the newborn and the behavioral effects of teratogens make assessment at this point in development difficult. Further exacerbating this difficulty is the nature of development. Development is critically dependent on the care the newborn receives. Distortions of a newborn's behavior can produce disturbances in the caretaking environment, and these caretaking disturbances can amplify the original behavioral distortion and produce other distortions. Attention to these types of effects must be built into an assessment.

These considerations lead to the conclusion that an apical assessment of newborn behavior is required. The most standardized, valid, and reliable instrument currently available is the Neonatal Behavioral Assessment Scale developed by Brazelton. It assesses the integrated actions of the infant that function to regulate simultaneously the infant's internal state and exchanges with the animate (caretaking) and inanimate environment. The scale uses a set of reflex and behavioral items to assess the critical domains of infant functioning (e.g., the infant's ability to control his states of consciousness). It has been found to be sensitive to the behavioral effects of known teratogenic agents (e.g., PCBs) and to the potential disturbances in caretaking produced by them. However, because no single assessment is likely to be sufficient, a strategy may be needed in which the effects detected by repeated application of the Neonatal Assessment are followed up with more specific assessments of those effects, such as acoustical cry analysis.

Introduction

The transient and somewhat undifferentiated organization of the newborn's brain and the typically nonspecific and overlapping effects of different environmental agents on the newborn conspire to produce complex and difficult problems for marking the effects of environmental agents on the newborn. These problems can, in part, be overcome by using newly developed instruments for assessing the newborn's behavior. In this paper, I will briefly present characteristics of the newborn brain as well as characteristics of the effects of environmental agents that create assessment problems. Second, I will describe the behaviors of the newborn and the use of the Neonatal Behavioral Assessment Scale (1) to resolve some of the problems of assessment. Third, I will suggest a general strategy for correcting some of the problems remaining after application of this assessment scale. I focus on assessment techniques. This paper is not a comprehensive review of the effects of environmental agents, but to some extent an attempt to broaden the definition of what is considered a teratogenic effect.

The Problem of Assessment

The newborn brain, compared to the older brain, is less differentiated and integrated (2). It is thought to have considerable redundant structure or capacity—a capacity that decreases with maturation (3). The newborn brain is as unique to the newborn period as it is to any developmental period (3). Indeed, many of its structures, forms of organization, and functions are thought to be transient and characteristic of this and no other period of development (4). One reason for the uniqueness is that brain maturation is not simultaneous in all areas. Rather, maturation proceeds at different rates for different areas depending on which areas are necessary for performing the functions characteristic of a specific developmental period. This means that as it develops, the brain undergoes qualitative changes such as the presence but later disappearance of radial glial cells that function as a guiding framework for migrating neurons, or the presence of supernumerary synaptic

*Department of Psychology, University of Massachusetts, Amherst, MA 01003.

contacts and axons and their later reductions (5–8). Additionally, the uniqueness of the newborn brain is the result of the fact that inputs must take place during limited periods of time to have their normal effects. Finally, a critical reason for this uniqueness is that the brain's normal functioning and development is under the control of internal processes as they interact with environmental input (9). Obviously, the environmental input of special importance is that provided by the caregiver. Caregiving must be precisely adapted to the properties of the newborn so that it too has a form in the newborn period that is different from the form it will have in other periods (6,10).

These features of the infant's brain appear to create a number of problems of assessment. The newborn is likely to present fewer specific biomarkers to assess than its older counterpart. Some of the available biomarkers are transient and may hold little importance for later functioning. Others certainly are the precursors of later functions, but their transformation during development is unknown. The biomarkers available are likely to be more difficult to quantify than are those of the older child. This makes it difficult to assess subtle and sometimes even large distortions in their form, their time of appearance, and their coordination with other function. Last, because their form and timing are modified by the environment, the quality of the environment may need to be assessed if one wants to predict their developmental outcome.

Unfortunately, what we know of the nature of the effects of environmental agents on the newborn does not help us to resolve these issues. If we knew the unique specific effect or even the general effects of different environmental agents on the newborn's functioning, then we could look for that effect with some disregard for other problems (11). However, our knowledge suggests that the effects of different agents are likely to be overlapping, subtle, and invasive of many areas of integrated functioning of the newborn (12–15). For example, the most studied environmental agents are the pain-killing agents used in obstetric procedures (15). The hospital-based use of these agents gives us access to a large number of subjects, some control over their experience, and more detailed information on the history of the subject's exposure and other confounding variables (16). Analgesic agents such as the various barbituates have been found to modify electrophysiological characteristics of the brain, disrupt the infant's sleep-wake cycles, disorganize their sucking patterns, decrease their responsiveness to environmental events, and produce overactivity, excessive crying, and hypertonicity (17–21). Many similar effects are seen when the obstetric medication is one of the anesthetic agents such as lidocaine (15,16,21,22). Some differentiation is possible between the effects of these drugs; for example, barbituates tend to produce hypertonia with decrements in alertness, whereas lidocaine tends to produce hypotonia without associated effects on alertness. But, for the most part, their effects are similar and generalized. Moreover, modifications of each of these behaviors has been found

to affect the caretaking the infant receives (10,15,18,23–26).

The first point, then, is that assessment of the teratogenic effects of environmental agents on the newborn's development is a complicated and difficult task because of the nature of development and the nature of the toxic effects. Furthermore, the importance of caretaking to normal development suggests that the definition of teratology may need to be expanded once again (16,27). According to the history of this field, the definition of teratology was easily expanded from the mortal effects of different agents to morphological effects. Later, with some difficulty, it was expanded to encompass functional effects. I think now we may need to add distortions of the infant's behavior that alter the caregiver's behavior (27,28).

Newborn Behavioral Capacities

What type of test can we use to assess the newborn? Before we can answer this question, we need to know what capacities of the newborn we can assess. Recent research has demonstrated that newborns possess a rich and complex set of behaviors for regulating his internal states and his exchanges with the environment (16). These behaviors provide a good basis for assessment.

A fundamental self-regulatory capacity of the newborn is its ability to organize five different behavioral states: two kinds of sleep states, two kinds of awake-alert states, and one kind of distress state (3,29–31). Each of these states is made up of a qualitatively different and coherent organization of physiologic systems, such as respiration and heart rate; electrophysiologic systems, such as EEG; and behavioral systems, such as motor tone and motility (32). These states are conceptualized as reflecting changes in the mode of activity of the nervous system. They function to change the nature of the input-output relations between the newborn and the environment by modifying the responsiveness of the newborn to different stimuli. For example, the infant's auditory responsiveness is greater in state 2 sleep than in state 1 sleep, whereas most of its proprioceptive reflexes are greater in state 1 sleep than in state 2 sleep (33). Visual responses are available only in the two awake states (33). An infant who was unable to organize his states or was unable to control their sequencing would be unable to set up reliable relations between himself and the environment.

The infant has two abilities for selectively modifying his responsiveness within behavioral states. The first is habituation, the ability not to respond to an environmental stimulus that is either disrupting the newborn's state organization or has no functional significance to the newborn (16). Habituation is sometimes thought to be a primitive form of learning. For example, infants are able to inhibit their motor responses and startle responses to repeated disturbing sounds. An infant whose capacity for habituation was disturbed would be at the mercy of disruptive environmental stimuli.

The second selective capacity is the infant's ability to orient to and process information from the environment. Infants can look, listen, smell, touch, and taste with amazing facility (16,34-37). Infants can make coordinated head and eye movements and visually locate and discriminate among different targets (36). They can turn their heads toward and localize a sound (16). They can discriminate among different tastes and differentiate the odor of their mother's milk from the odor of another mother's milk (38). They are capable of coordinating information between different perceptual systems and between perceptual and motor systems. For example, newborns are able visually to identify an object that they have previously sucked on but not seen, or imitate another person's facial expression (39).

Clearly, the infant's behavior is not simply a compilation of reflexes. For example, the exploratory behavior of the infant's head and mouth as it searches for the nipple and its latching onto it when it is found, followed by the coordination of breathing with sucking and swallowing is indicative of complex motor control systems (40). So is the change in the infant's neutral facial expression to an expression of interest when he turns toward and sees the source of a sound he has been searching for when he finally locates it (1). Importantly, many of the infant's behaviors, including facial expressions, cries, tremors, and startles, and even behavioral states function to change and guide the behavior of the newborn's caretaker (16,24). An infant who is fussy and moving in a disorganized fashion receives different caretaking from a newborn who is awake and alert with relaxed, fluid movements. This suggests the possibility that the infant in part controls his own development by modifying the caretaking he receives.

The infant thus displays an impressive array of behavioral capacities that lend themselves to functioning as biomarkers in the form of an apical assessment. Apical assessments are procedures that assess the overall ability of the organism to adapt to its situation (13). An apical assessment is a comprehensive test that examines a variety of functions. Successful performance requires the integration of intact subsystems. To be effective, an apical assessment must be quantifiable, able to detect subtle differences in performance, and reliable. This means assessing the newborn's integrated actions that function to regulate its internal state and its exchanges with the environment, primarily the animate environment of caregivers.

There are several assessments that have attempted to meet these criteria (30,41-45). The Neonatal Behavioral Assessment Scale developed by the pediatrician Brazelton is the most successful effort to-date (1,46-50). Brazelton's scale is an integration and systematization of clinical knowledge of the newborn, the nature of the effects of the newborn's behavior on its caregivers, and our increased understanding of the newborn's functioning derived from developmental research. The scale is a valid and reliable instrument (1,46,50,51) that can detect subtle differences in performance. It uses reflexes and 26 behavioral performance items to assess

seven domains of infant functioning (Table 1) (51): habituation, orientation, motor performance, range of state, regulation of state, autonomic regulation, and reflexes. To put this in other words, the Brazelton examination looks inward at an infant's capacities to maintain physiological homeostasis, to organize his states of consciousness, and defend himself against disruptions of these states by external stimulation. The scale also looks outward at the infant's capacities to engage the environment and the effect that the infant's form of engagement might have on the environment. The examination of an infant by a trained examiner takes about 30 to 40 min.

Research with the Brazelton scale has demonstrated its usefulness in detecting deviations in performance as biomarkers produced by environmental agents, most often obstetric medications, but also for PCBs; recreational drugs, including marijuana, tobacco, and caffeine; and other factors such as subclinical and clinical malnutrition (10,12,14,21,25,46,52). For example, Jacobson et al. and Fein (14,18) found abnormal behavioral development in a group of infants whose mothers had chronic exposure to PCBs. The strongest relationships were found between the consumption level of contaminated fish and the infant's organization of behavioral state, motor performance, and physiologic regulation. Specifically, the exposed infants had more jerky, unbalanced, cogwheel motor movements, a greater number of abnormal reflexes, and fewer state changes. No deviations were noted in their orientation performance. These effects remained after likely confounders were

Table 1. Brazelton scale items that are included in the seven *a priori* clusters.

Cluster	Brazelton scale item
Habituation	Response decrement to: light, rattle, bell, pin prick
Orientation	Inanimate visual (red ball) Inanimate visual (rattle) Animate visual (face) Animate auditory (voice) Visual and auditory (face and voice) Alertness
Motor performance	Tonus Motor maturity Pull-to-sit Defensive movements Activity
Range of state	Peak of excitement Rapidly of buildup Irritability Lability of state
Regulation of state	Cuddliness Consolability Self-quieting Hand-to-mouth
Autonomic regulation	Tremors Startles Lability of skin color
Reflexes	Number of abnormal reflexes

From Lester (51).

removed from the data. The results are consistent with the reports in the animal literature (14). These results, along with the results from the effects of obstetric medication, indicate that environmental agents do have disruptive effects on several areas of behavioral functioning and that these effects can be detected by the Brazelton assessment.

I have argued that we consider not only functional disturbances, but also their effects on the caretaking environment as part of evaluation of the teratogenic effects of environmental agents. For example, I found, using the Brazelton examination, that Guatemalan infants who had experienced malnutrition *in utero* had poor motor tone, poorly organized states of alertness, were unresponsive to stimuli, had weak cries, and had a behavioral state characterized by sleep and a lack of distress or even fussiness (10). Because their mothers nursed them in response to their signals of distress, these infants were fed less often and became even weaker and less responsive. In the U.S., I have seen similar behavioral effects in a group of clinically normal but slightly underweight infants and similar effects on the caretaking provided by their parents (46).

Like all apical tests, the Brazelton scale has a number of limitations. It is not specific as to the underlying mechanism causing the developmental distortion because it examines performances based on the integration of many processes. Second, it is susceptible to the intrusion of other factors affecting the performance rather than the one of concern. This may be partially resolvable through the use of statistics and clinical experience. Third, as sensitive and comprehensive as the Brazelton scale is, it is not sufficient. This brings me to my final point in regard to a strategy for assessment.

An assessment strategy should begin with two or three repetitions of the examination during the newborn period. Repeated assessments have been found by Lester to document more subtle effects than a single examination (1). Critically, repeated assessments help us to distinguish transient acute physiological effects from longer term effects on the central nervous system, and they provide some information on the infant's capacity to recover from an insult (48). Then, following these repeated assessments and guided by the results, more sensitive and specific assessments should be attempted. These assessments would be: a full neurological assessment (41,44,47); 24-hr observation of sleep and awake states (41,48); visual attention or auditory attention studies (36); cry analysis when the quality of distress states and the infant's ability to achieve them appear disrupted (51,52); and studies of caretaker-infant interaction to assess the impact of these behavioral distortions on the caretaking environment (23).

Conclusion

The nature of infant development and the nature of the effects of environmental agents conspire to produce great difficulties for the assessment of teratogenic effects. Given what we now know about the behavioral

capacities of the infant, an apical test such as the Brazelton scale resolves some, but not all, of the difficulties. Such a test must be embedded in a larger strategy of assessment. I have argued that the definition of teratogenic effects must be expanded to include the distortion of the caretaking provided to the infant that may be produced by the distortion in his behavior.

I have focused on assessment and not on a presentation of the teratogenic effects of environmental agents on newborn behavior and caretaking. However, animal models and models of the adult, the young child, and even the fetus are not easily applied to the infant. There are few well-worked-out models of such effects on human newborns. Our methods of assessment only begin to evaluate the behavior of the infant; knowledge and research is limited. Yet, it is extremely sobering that whenever we have looked for such effects, we have found them, and we have only begun to look.

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