the expression of the noradrenergic phenotype in these embryonic neuroblasts. The reserpine effect appeared to be mediated by the maternal pituitary-adrenal axis and release of maternal glucocorticoids since it was (i) mimicked by hydrocortisone administration; (ii) blocked by dexamethasone, which inhibits the stress-induced increase in plasma glucocorticoids; and (iii) diminished by mitotane. It is likely that maternal steroids directly affected the embryos, since steroid hormones can cross the placenta (*19*).

The precise mechanisms responsible for the persistence of catecholamines in these embryos remain to be defined. Glucocorticoid hormones exert a complex variety of actions on developing neuronal tissue, including prolonged survival of degenerating extra-adrenal chromaffin tissue in vivo (*20*), preferential selection of noradrenergic traits in cell populations expressing more than one neurotransmitter phenotype in vitro (*21*), and effects on the cell cycle that alter the sequence of neuronal genesis during development of the central nervous system (*22*). Although it is unclear which of these actions is relevant to the noradrenergic gut cells, several tentative conclusions may be warranted. Glucocorticoids probably do not simply enhance survival of catecholaminergic cells in the gut, since previous work has suggested that the cells normally persist even after losing most noradrenergic characters (*6, 7*). Moreover, reserpine probably causes other noradrenergic characters (such as the catecholamine biosynthetic enzymes) to persist, since these traits appear and disappear simultaneously under normal circumstances (*6*).

Regardless of the intracellular mechanisms involved, it is clear that maternal experience can affect phenotypic expression in developing embryonic neurons. Specifically, our studies indicate that maternal hormones, such as glucocorticoids, may significantly influence the developing nervous system. In addition to regulating normal neurologic development, it is entirely possible that maternal steroids, directly or indirectly, contribute to abnormal development and birth defects when they are present in increased concentration. The presumptive neuroblasts in the embryonic gut may be a valuable system for studying these issues.

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Differential Development of Brainstem Potentials in Healthy and High-Risk Infants

Abstract. *Maturation along the brainstem acoustic pathway, as well as the integrity of these structures, has been shown to be reflected in brainstem evoked potential recordings. Trajectories formed from repeated sequential measurements of several brainstem response variables reveal distinct developmental curves for healthy and high-risk infants. Longitudinal analysis offers a means of determining temporary or permanent maturational effects on the central nervous system in early life.*

The infant born at "high risk" for central nervous system (CNS) damage is more likely to manifest neurological and intellectual deficits in early childhood (*1*). Certain brainstem structures along the auditory pathway are preferentially vulnerable to many of the perinatal conditions that compromise the infant (*2*). Subtle impairments to these subcortical regions may go unnoticed until blatant behavioral defects become apparent in later life. In this regard the brainstem auditory evoked potential (BAEP) technique offers a sensitive index of brainstem maturation and function (*3*). A strong relationship between altered BAEP's and specific or generalized sensory and neurological disorders has been documented in adults (*4*). The diagnostic value of BAEP recordings has recently been extended to newborns (*5*). Yet aberrant BAEP's at one point may or may not imply clinical significance for a later stage of development (*6*). By establishing longitudinal trajectories based on multiple observations of both healthy and sick infants, we show that the maturational curve not only differs for selected measures of the BAEP between the two groups but continues to distinguish the risk population at 1 year of age. In addition, we demonstrate the utility of the longitudinal approach in determining exactly when an individual begins to depart from the expected developmental pattern.

A total of 342 infants participated in this study. All subjects were seen at least twice, but most were seen on three or more occasions from birth to 1 year of age (corrected for prematurity). Of these, 245 were full-term normal babies born without incident. The remaining 97 subjects had been kept in the intensive care nursery (*7*). These infants sustained various complications of birth or pregnancy and were judged to be at risk for CNS involvement. Most were born prematurely and had suffered respiratory distress, some form of oxygen deprivation (asphyxia, hypoxia, and so forth), or both.

All normal babies were tested in open cribs, and most high-risk infants in iso-

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lettes (*8*). The BAEP's were obtained from gold disk electrodes attached to the vertex (Cz) of the scalp and referred to either earlobe (A_1 and A_2). Bioelectric activity was amplified (Grass P-511) and filtered (Krohn Hite 3700). The auditory stimulus consisted of clicks of moderate intensity (approximately 60 dB above normal adult hearing levels) presented binaurally (*9*) through commercial stereophonic earphones at a rate of 15 per second. The potentials (N = 2048) were automatically averaged by sampling 80 μsec per point with a special-purpose computer (Nicolet 1072).

The latency and amplitude of BAEP waves I, III, and IV-V (*10*) were digitized on-line. Latency was taken as the time from stimulus onset to the maximum (peak) of each wave. Amplitude was measured from the positive peak to the succeeding negativity (*11*). Developmental trajectories were constructed separately for amplitude and latency. Each dependent variable was modeled by simply fitting straight line segments to the consecutive observed values for each subject. This provides an estimate of change in the dependent variable between the minimum and maximum ages for which each subject supplied data. The composite curve is derived from averaging these estimates over all subjects for a given age (in days) (*12*).

The developmental trajectories (Fig. 1) address the question of whether deviations in the BAEP detected early in infancy persist throughout the first year of life. The longitudinal curves for the individual BAEP components not only display unique maturational characteristics but also show that healthy and high-risk infants follow different developmental trends.

For example, the latency of wave I in the high-risk population parallels but does not equal the normal values even at 1 year of age. Wave III latency seemingly fails to differentiate the two groups until beyond the first year. Wave V shows a pattern similar to wave I through the third month of life; by the fifth postnatal month, however, normal and high-risk subgroups are no longer distinguishable with respect to latency. The discrepancy in wave I latency between the two groups is not passively relayed to all succeeding waves. This result suggests that the delay in wave I latency in the risk population may be due primarily to peripheral factors. A separate analysis of the latency difference between waves I to V, often taken as a measure of central conduction, revealed no difference between the high-risk and healthy infants (*13*).

The greatest latency differences between term and preterm infants can be attributed to gestational age (Fig. 1). This result agrees with earlier findings showing prolonged BAEP's in premature infants (*14*) and suggests that nerve conductile processes, although delayed in maturation in many high-risk infants, do approximate normal values with increasing age (*15, 16*).

In contrast to BAEP latency, the amplitude trajectories for high-risk and healthy infants progressively diverge during the latter part of the first year. Waves III and IV-V, in particular, seem to approach asymptote by the third to sixth postnatal month (Fig. 1), at a time when the magnitude of the normal response is still increasing sharply (*17*). It is not until 1 year of age that the respective curves markedly separate for wave I amplitude (*18*).

Whether this disparity in BAEP amplitude represents differences in synaptic efficacy, neural synchrony, or simply a delay in development is not yet known. Notwithstanding, response amplitude best differentiates the developmental time course for high-risk infants. Although the morbidity for gross CNS disturbances (cerebral palsy, mental retardation, and so forth) among babies that had been in the intensive care nursery has been drastically reduced in recent years, the incidence with which children showing generalized cognitive impairments and neurological soft signs present histories of unfavorable perinatal events is still formidable (*19*). Focal brainstem and thalamic lesions may account for a variety of childhood disorders, including infantile autism and minimal brain dysfunction (*20*). Indeed, abnormal BAEP's have been reported in a group of children manifesting autistic traits, minimal brain dysfunction, and psychomotor retardation (*21*).

Because the infant born at risk is, by definition, predisposed to insults of the CNS (discrete, diffuse, or both) it becomes of paramount importance to be able to identify instances of transitory (reversible) versus permanent injury.

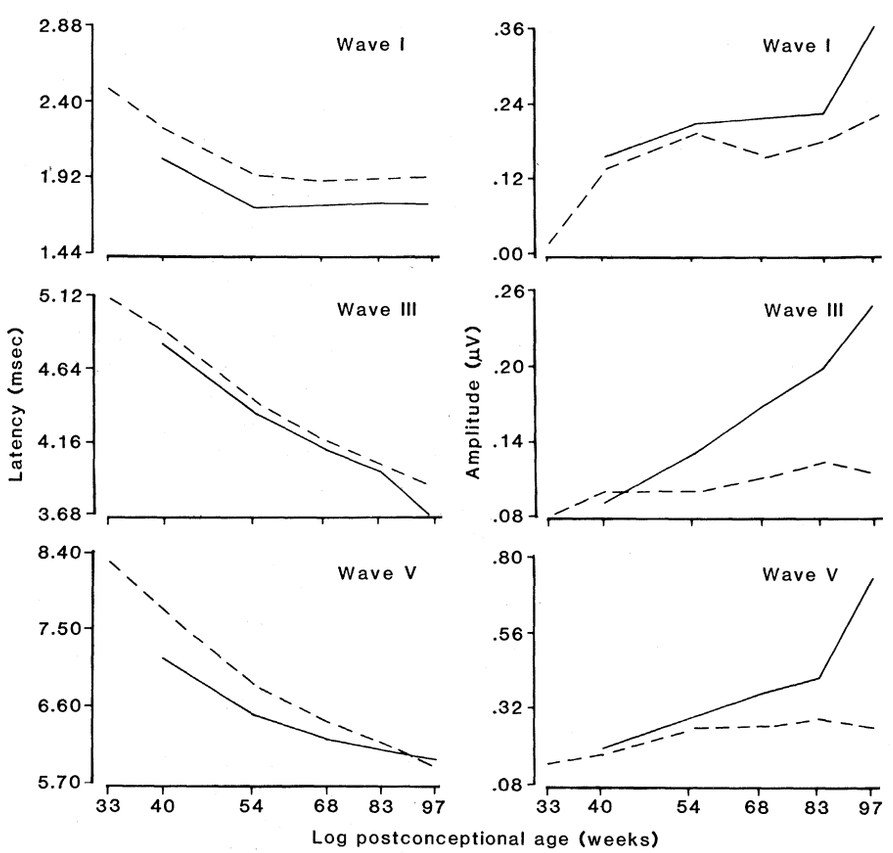

Fig. 1. Trajectories for BAEP latency and amplitude of waves I, III, and V for healthy (solid lines) and high-risk (dashed lines) infants as a logarithmic function of postconceptional age.

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6. In our ongoing studies on human BAEP development, we have often observed what appear to be "reversals" in classification (normal or abnormal) on successive testing occasions. This is particularly true in the neonatal period and early infancy.
7. Of the 97 high-risk subjects, 55 were seen at Letterman Army Hospital and 42 were tested at the University of California School of Medicine (San Francisco) through the cooperation of the Follow-up Program.
8. Since most high-risk infants were connected to electrocardiogram and apnea monitors, the absence of electrical interference was assured before BAEP recording began. For both groups the ongoing electroencephalogram was continuously monitored for artifacts. In the presence of contamination, from any source, averaging ceased. An attempt was made to record from all subjects only during periods of quiescence.
9. In testing newborns (and particularly premature infants), we have observed that binaural stimulation substantially increases response resolution and waveform reproducibility. This greatly facilitates wave identification in the neonatal period. In contrast, monaural stimulation produces much more variable responses. Although monaural deficits could be obscured in binaural recordings, such effects were minimized through regular audiological evaluations.
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11. Wave V amplitude actually refers to the IV–V complex.
12. All computations were implemented with the university's computer (IBM 370/148) through the aid of the Scientific Computing Service and the SAS statistical package.
13. Six of the high-risk infants initially yielded no measurable BAEP. Two were later confirmed to be deaf. Data from one infant were not usable because of technical problems. Therefore, 90 high-risk infants were actually included in the analyses. Only two of these were found to have mild hearing loss at follow-up. Thus, approximately 8.25 percent of our high-risk population had or were suspected of having some auditory deficit. This figure is in keeping with the expected incidence of hearing loss among intensive-care nursery survivors [R. Galambos and K. E. Hecox, *Otolaryngol. Clin. N. Am.* **11**, 709 (1978)]. By eliminating these subjects, severe congenital hearing loss may be ruled out as a major contributor to the observed group differences.
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18. Multivariate analyses of variance confirmed significant ($P < .01$) differences in the BAEP between normal and high-risk infants at selected ages from birth to 1 year. [A. Salamy, T. Mendelson, W. H. Tooley, E. R. Chaplin, *Early Hum. Dev.* **4** (2), 179 (1980)].
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Goal Orientation by Blindfolded Humans After Long-Distance Displacement: Possible Involvement of a Magnetic Sense

Abstract. *A wide range of animals are able to orient toward home when subjected to displacement-release experiments. When comparable experiments are performed on blindfolded humans, a similar ability emerges. Such goal-orientation does not result from following the complete journey on a mental map, nor is it influenced by cloud cover. Bar magnets worn on the head do seem to exert an influence.*

A wide range of animals are able to orient toward home when experimentally displaced from that home and either released or tested in an orientation cage. Among animals that have been subjected to such displacement experiments and shown able to orient toward home are lobsters, snails, honey bees, fish, amphibians, turtles, rodents, bats, and, of course, birds (*1*). Human subjects are notably absent from this list. This report describes displacement experiments over tens of kilometers on blindfolded humans, in which they demonstrated an ability for homeward orientation.

The major experimental series was carried out in and around Manchester, England. "Home" was Manchester University. Groups of between 5 and 11 university students who had been living in Manchester for 2 years were placed in a Sherpa minibus, blindfolded, and then driven by a tortuous route to a release point between 6 and 52 km from the university (Fig. 1). Subjects were asked not to talk. The first 8 km of the outward journey were always the same and to the south southeast. This initial stage of the journey terminated at a major roundabout which was then driven round three times before a particular exit road was selected. On at least one other occasion during each journey, a similar maneuver was executed at another roundabout, as available. Also, on at least one occasion during each journey, an area of short, twisting roads with frequent junctions (for example, a housing development) was selected and driven through for 5 minutes. Most journeys also involved a section in which the road curved gradually through 50° or more. Backtracking, however, was used only for release site a (Fig. 1).

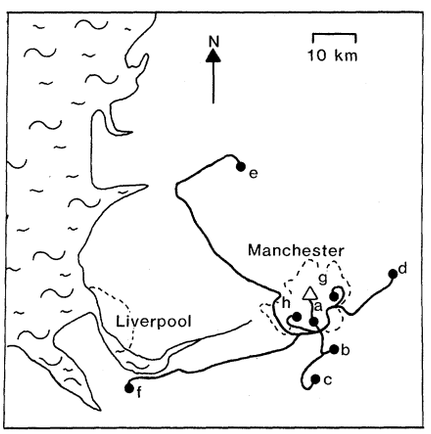

Fig. 1. Release sites and displacement routes during the Manchester experiments. Symbols: ●, release sites (*a* to *h*); △, home (Manchester University).

At the release point for each journey, individuals were removed from the minibus one at a time and, while still blindfolded, asked to state the compass direction (north, southwest, east southeast, and so forth) of the release point from the university. The use of these 16 compass directions to identify direction may generate noise in the data through subjects confusing north and south, or particularly east and west. However, this only makes homeward orientation more difficult to demonstrate.

In all, this first experimental series included ten separate journeys to eight dif-

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