The Development of Human Fetal Eye Movement Patterns

Abstract. *The eye can be visualized ultrasonically in more than 90 percent of fetuses 16 through 42 weeks of gestational age. Slow eye movements are present by 16 weeks. Rapid eye movements begin at 23 weeks and become more frequent between 24 and 35 weeks. Eye inactivity becomes more common after 36 weeks and is associated with sustained diaphragmatic excursions implying a "quiet sleep" state. Pathologic eye movements were seen in four fetuses with dysmorphic brain structure.*

Ultrasound imaging is used in clinical obstetrics for noninvasive visualization of human fetal anatomy. Recent developments in instrument technology have improved image detail and provided the additional capability for studying fetal neuromotor behavior. Distinct movement patterns have been correlated with gestational age (*1*), and particular attention has been directed toward defining the developmental sequence, incidence, and external modification of "respiratory" chest wall excursions (*2–4*). I have been able to visualize fetal eyes and to recognize separate eye movement patterns during the second half of pregnancy through the use of a newly developed instrument.

Ultrasound imaging was performed with a sector scanning device (Advanced Technology Laboratories) operated at 3.0 MHz center frequency with an average 0.8 mm axial and 2.7 mm lateral resolution in the 5- to 10-cm focal depth region. The field of view was a 90° sector of 20 cm maximum depth. The imaging rate was 30 frames per second. Scan conversion and display processing were implemented digitally. The probe was applied to the maternal abdomen, coupled to the skin with a thin layer of water-soluble gel. The fetal position was determined, and a coronal cranial–facial imaging plane was selected. Probe orientation was readjusted during continuous viewing until an annular structure was visualized within the anterior portion of the orbit (Figs. 1 and 2). The eyelids were seen with scan planes directed more anteriorly (Fig. 3).

Examination of the orbits was incorporated into clinical examinations, and a viewing epoch of some 30 seconds was selected arbitrarily. Studies were performed midmorning and midafternoon, and none of the subjects had fasted or were taking medications other than iron and vitamin supplements. Subjects in labor were excluded. Videotape recording of the ultrasound sequence was optional.

The eye margin was visualized in 53 of 57 consecutive examinations (93 percent) of clinically healthy women with pregnancies of 16 through 42 weeks gestational age (postmenstrual dating equal to conceptual age plus 2 weeks, with term at 40 weeks). The eye margin could not be visualized in four cases with prone fetal position at 23, 28, 29, and 37 weeks. Eye movements were noted in 33 of the 53 visualized cases (62 percent). Additional observations were made in a nonconsecutive group of 223 subjects without immediate or subsequent evidence of congenital anomaly, growth retardation, or compromised fetal condition.

Four types of eye movement were recognized: type I—single, transient, linear deviation, usually from a midposition to a lower, outer orbital margin, followed by a (slightly slower) return to the initial position; type II—prolonged, but single deviation to a medial or lateral position; type III—complex sequence of deviations including rotatory components, without apparent spatial or temporal periodicity; these movements were typically brisk and jerky; and type IV—repetitive or nystagmoid deviations.

The incidence of these eye movement patterns with gestational age is given in Fig. 4. Type I movements were present by 16 weeks. Vestibular nuclei believed necessary for ocular movements are differentiated by 13 weeks (*5*), and downward eye movements were noted by Hooker in one $12^1/_2$-week fetus immediately after delivery (*6*). Type III movements were observed after 23 weeks and seemed to increase in incidence (and duration) from 24 to 30 weeks. Differences in the gestational age distributions of types I, III, and IV movements are significant ($P < .001$, *t*-test of independent measures).

Fig. 1 (left). Coronal facial view with probe positioned superior to the brow showing both lenses, 16 weeks gestational age. Fig. 2 (right). Coronal facial view with lateral probe position, 30 weeks gestational age.

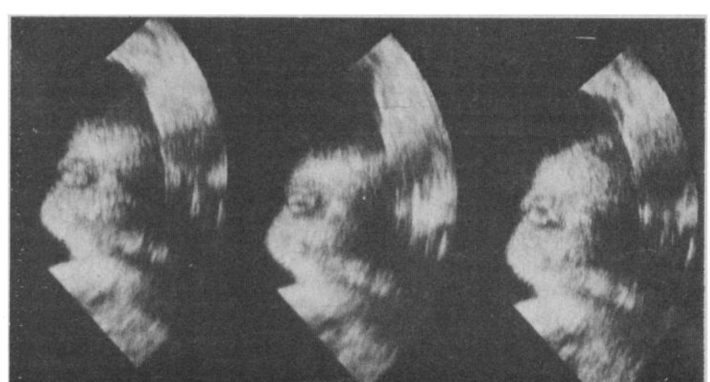

Fig. 3. Serial coronal facial views showing eyelid opening, 35 weeks.

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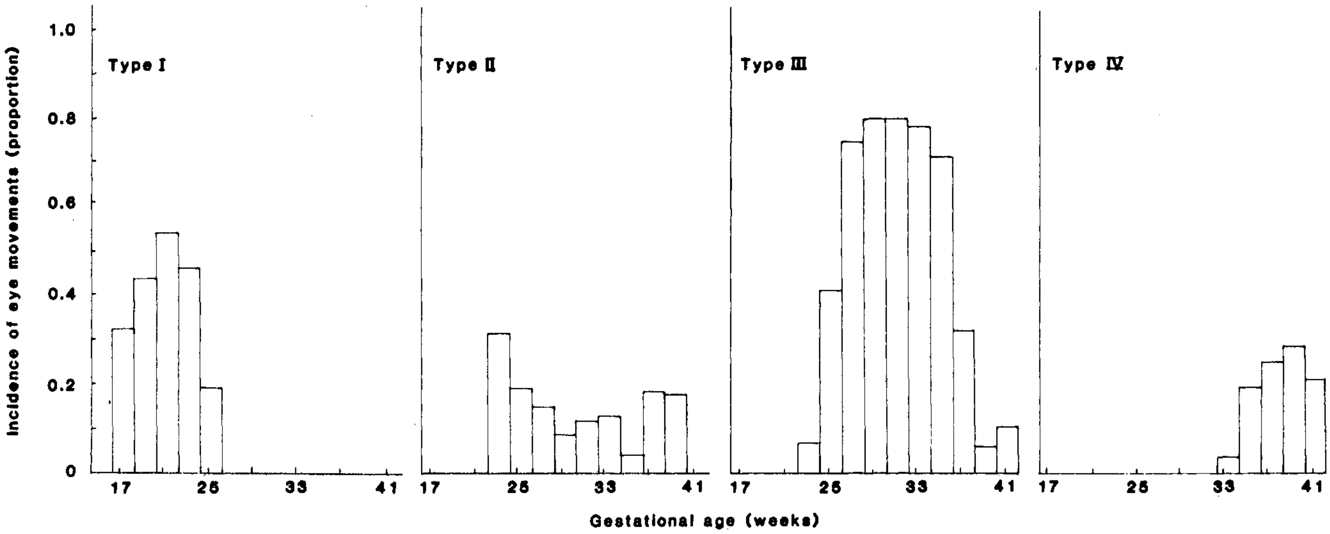

Fig. 4. Distributions of eye movement pattern and gestational age.

In four cases with simultaneous viewing of both eyes after 30 weeks, bursts of type III movements were synchronous and conjugate, while type II movements were disjoint. Type II movements often preceded or followed types III or IV movements. Types I and II movements seem to correspond to slow eye movements and types III and IV to rapid eye movements (REM) as described by direct observation and electro-oculographic study of newborn infants (*7*).

A short viewing epoch is sufficient to demonstrate the occurrence of REM activity, although detailed study of the time statistics of these movements is necessary for understanding the developmental sequence of the process. To my knowledge, no unequivocal adverse biological effect of pulse-echo ultrasound imaging has been reported that would contraindicate lengthy and repeated monitoring of eye movements.

Increasing phases of eye inactivity late in the third trimester imply the development of inhibitory mechanisms (*8*). Of 53 fetuses beyond 36 weeks, 11 had regular, sustained diaphragmatic excursions without any eye movement, which occurs with "deep sleep" (*9*). This pattern was not seen in any normal subject prior to 35 weeks, but was observed in one case of diabetic pregnancy with hyperglycemia at 33 weeks and in one growth-retarded subject at 34 weeks, possibly indicating accelerated neuromotor maturation with stress (*10*). A similar pattern was seen in a 31-week fetus sensitized to rhesus factor 2 weeks after intrauterine transfusion (*11*). Rapid eye movements were seen 24 hours and 1 week after transfusion. Intrauterine death occurred 12 hours after the 31-week study and was not explained anatomically by autopsy. While the deep sleep pattern before 32 weeks might be interpreted as an analog of coma, there is considerable lability in the association of eye movements and other indicators of behavioral state in the preterm infant (*12*), so that diagnostic inferences from apparent dissociative behavior must be deferred until more detailed fetal data are accumulated.

Observations from eight additional subjects with dysmorphic brain structure are summarized in Table 1. Pericentral movements were repetitive, rapid, and had excursions of small amplitude. No seizure-like activity of the limbs was observed in these cases. Transitional movements were solitary, like type I or II, but as brisk as type III. Subject 4 was one of twins. Typical type III movements were identified in the normal twin at 29 and 32 weeks, and a quiet sleep pattern was present at 38 weeks.

Table 1. Eye movements in subjects with dysmorphic brain structure. The minimum observation periods were 3 minutes.

Subject	Diagnosis	Gestational age (weeks)	Eye movements
1	Encephalocele	16	0
2	Hydrocephalus (forking defect)	24	Pericentral
3	Massive right porencephaly	31	Rare, transitional
4	Microcephaly	29	0
	Hydranencephaly	32	Transitional
	Midline facial defect	38	0
5	Hydrocephalus Microphthalmia	32	Pericentral
6	Advanced hydrocephalus (aqueductal stenosis)	36	Pericentral
7	Advanced hydrocephalus	39	Pericentral
8	Advanced hydrocephalus	38	III + quiet sleep phases

Rapid eye movement activity during sleep in infants was described in the first quarter of the century (*13, 14*) and rediscovered by Aserinsky and Kleitman (*15*). Since the work of Wolff (*16*), Prechtl (*17*), and others, eye movement has become a consistent indicator of behavioral state. Observation of combined eye and breathing patterns in the newborn seems a sensitive predictor of the functional development of the central nervous system (*18–20*). A similar assessment may be possible antenatally as a means of defining physiologic neuromotor patterns and recognizing abnormal developmental conditions.

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Phenomenological Space-Time: Toward an Experiential Relativity

Abstract. *Subjects observing differently scaled environments undergo systematic shifts in the experience of time. The experience of temporal duration is compressed relative to the clock in the same proportion as scale-model environments being observed are compressed relative to the full-sized environment. This research suggests that spatial scale may be a principal mediator in the experience of time.*

The experience of time and temporal duration is central to mood, feeling, and emotional states (*1*); is often symptomatic of a range of emotional pathologies (*2*) and learning disorders (*3*); and is related to information processing (*4*). Despite numerous studies dealing with temporal experience (*5*), a coherent theory consistently integrating major aspects of previous research findings has not been developed (*6*).

This research suggests that spatial scale—the size of an environment relative to the size of an observer—is a principal mediator in the experience of time and temporal duration; and that for large samples the relationship between spatial scale and temporal experience is subject to precise theoretical formulation.

Spatial scale as defined here is based on the linear dimension, not volume. A wall 12 m long represented by a model in which the wall is 1 m long yields a linear scale of 1/12, while the volumetric reduction is 1/1728 ($1/12^3$).

In experiment 1, adult subjects (*7*) observed different scale-model environments 1/6, 1/12, and 1/24 of full size. Scale-model environments representing small lounges were constructed with cardboard partitions and chipboard furniture as well as scale figures. Subjects were familiarized with the model environments, asked to move the scale figures through them, to imagine themselves the scale figure, and to identify activities appropriate for the space. They were then instructed to imagine themselves the scale figure in the space, to engage in one of the activities previously identified, and to inform the investigator when they subjectively felt (not thought) the scale figure had been engaged in the activity in the scale-model environment for 30 minutes (*8*).

The sample exposed to the 1/24 scale environment was also exposed to the 1/12 environment in order to derive a cross-checking index for scale effects on the experience of temporal duration. Presentation in this sample was counterbalanced. Data consisted of elapsed stopwatch times (T) associated with the experiential duration of 30 minutes (E) (Table 1).

In order to minimize potential investigator bias, the data for the 1/12 sample were collected in subsamples by 16 different investigators, and the data for the 1/24 sample were collected in subsamples by 13 investigators. The range of compression ratios (CR = T/E) across subsamples (1/7.3 to 1/19.5 for the 1/12 model and 1/12.3 to 1/23.2 for the 1/24 model) makes unlikely a systematic, distorting bias attributable to investigator cuing.

Experiment 2 was performed to eliminate potential bias in conjunction with testing in the 1/24 environment. In that environment, large portions of the subject's peripheral visual field were outside the model environment and were stimulated by the surrounding full-sized environment. To eliminate this visual mixing

Table 1. Elapsed time (T) associated with experiential duration (E) of 30 minutes in differently scaled environments. The compression ratio (CR) is T/E. S.E.M., standard error of the mean.

Condition	Model scale	N		Elapsed time (min) ($\bar{X}$ ± S.E.M.)	Elapsed time (min) Range	CR*
Experiment 1 (unmasked)						
Single exposure	1/6	20		4.15 ± 0.630	1.73 to 13.83	1/7.23
	1/12	166		2.52 ± 0.170	0.62 to 11.33	1/11.9
Exposure to two scales (same sample)	1/12	124		2.64 ± 0.133	0.35 to 9.75	1/11.36
	1/24			1.57 ± 0.085	0.17 to 4.92	1/19.10
Experiment 2 (masked)						
Multiple exposure, same scale (independent samples)	1/6	11	1	5.48 ± 0.619	1.0 to 8.15	1/5.47
			2	5.46 ± 0.561	1.28 to 7.37	1/5.49
			3	5.35 ± 0.501	1.55 to 7.42	1/5.60
	1/12	10	1	2.72 ± 0.417	1.35 to 5.47	1/11.03
			2	2.43 ± 0.453	1.33 to 6.17	1/12.34
			3	2.83 ± 0.531	0.68 to 6.87	1/10.60
	1/24	10	1	1.44 ± 0.274	0.42 to 2.78	1/20.83
			2	1.56 ± 0.312	0.37 to 3.72	1/19.23
			3	1.48 ± 0.255	0.45 to 3.05	1/20.27
Exposure to three scales (random order, same sample)	1/6	27		3.85 ± 0.357	0.98 to 8.58	1/7.79
	1/12			2.60 ± 0.204	0.72 to 5.55	1/11.54
	1/24			1.55 ± 0.179	0.25 to 3.45	1/19.35
Experiment 3 (masked)						
Group F						
Single exposure	1/12	23		2.89 ± 0.434	0.19 to 8.75	1/10.38
Exposure to two scales (same sample)	1/12	9		2.44 ± 0.448	0.48 to 5.75	1/12.30
	1/24			1.46 ± 0.280	0.20 to 3.23	1/20.55
Group A†						
Single exposure	1/12	32		8.20 ± 0.635	3.85 to 18.2	1/3.66
Exposure to two scales (same sample)	1/12	10		7.36 ± 1.167	4.18 to 15.0	1/4.08
	1/24			6.02 ± 1.58	2.78 to 18.75	1/4.98

*Theoretically CR should equal model scale [$E = x(T)$]. †Sample characterized by acoustic interference, internal auditory timing, or both.