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Controversy exists about the safety of soy formula, with the main concern relating to potential estrogenic effects of soy protein. Since estrogens influence early brain development, we compared behav-

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ioral development and cortical responses (event-related potentials; ERPs) to speech sounds in infants fed either breast milk or formula (milk- or soy-based). Across-groups ERP measures were generally similar and behavioral measures were within normal ranges, suggesting no important influences of soy formula on behavioral development and brain function during the study period. Analyses relating ERP and behavioral measures revealed diet- and gender-specific emphases that may reflect differences in developmental trajectories of brain–behavior relationships.

Early nutrition plays a critical role in brain and behavioral development (Georgieff, 2007; Rosales & Zeisel, 2008; Wainwright & Colombo, 2006). Studies have reported that children breastfed as infants perform better on cognitive tests than those who were formula fed (e.g., Pollock, 1994; Taylor & Wadsworth, 1984). Similarly, Pivik, Dykman, Jing, Gilchrist, and Badger (2007) reported advantages for breastfed infants in the development and processing of language stimuli. However, no studies of brain function have been published in children fed the three major infant diets, breast milk, milk-based formula, and soy-based formula. The American Academy of Pediatrics (AAP; 1998) and other health organizations (American Dietetic Association, 2005; World Health Organization, 2004) currently recommend exclusive breastfeeding during the first 6 months of age, but the majority of U.S. infants are presently fed formula during this period. It has been reported that about 18% of all infants in the United States were fed soy formula during some period during the first year of life (Bhatia & Greer, 2008).

Recently, the safety of soy formula has been questioned because of concerns regarding possible estrogenic effects of soy isoflavones (Munro et al., 2003). Isoflavones function as selective estrogen modulators and under some conditions have weak estrogenic activity, which is of potential concern because estrogens are known to affect brain development and function (Hines, 2002; Knickmeyer & Baron-Cohen, 2006). Other than one retrospective survey study which reported no difference in intelligence quotient (IQ) of 9–10-year-old children fed soy-formula exclusively versus as a supplement to breastfeeding during infancy (Malloy & Berendes, 1998), we are unaware of any studies examining the immediate and long-term health and cognitive effects of this infant diet.

We employ event-related potentials (ERPs) and behavioral measures to study early diet influences because behavioral assessments alone may not be sensitive and specific enough to detect early central nervous system (CNS) effects (Uauy & Peirano, 1999). ERP recordings can provide correlates of neural and cognitive development very early in life (Johnson et al., 2001; Picton & Taylor, 2007) and are especially useful in investigating central sensory processing in infants for whom behavioral methods provide rather limited information about brain processes related to their perceptual abilities. For example, ERP methodology has demonstrated that breastfed infants have faster nervous system maturation than those fed formula [e.g., shorter latency brainstem auditory evoked potentials at 1 year (Khedr, Farghaly, Amry, & Osman, 2004) and better visual acuity at 8 months (Makrides, Neumann, Simmer, & Gibson, 2000)].

Among important CNS processes undergoing organization during infancy are those related to language development. Perception and discrimination of syllables are critical aspects of human language development, and cortical ERPs to syllables in infants are thought to reflect neural activity related to these processes (Kurtzberg, Stone, & Vaughn, 1986; Novak, Kurtzberg, Kreuzer, & Vaughn, 1989; Thierry, 2005). Early ERP components have been associated with sensory registration of auditory stimulus attributes and later components with language-specific processing and attention (Dehaene-Lambertz & Dehaene, 1994; Kurtzberg, Hilpert, Kreuzer, & Vaughn,

1984; Novak et al., 1989). Variations in these responses to syllables have differentiated infants with and without risk for later language-related difficulties (Friedrich, Weber, & Friederici, 2004; Leppänen, Pihko, Eklund, & Lyytinen, 1999) and have predicted such problems later in development (Guttorm et al., 2005; Molfese, 2000).

The present study investigated the influence of the three most common diets—breast-milk, milk-based formula, and soy-based formula—on infant cognitive and behavioral development and on cortical ERPs to speech stimuli during the first 6 months of life. The study focus on the auditory processing of language sounds was prompted by a growing literature relating non-invasive measures of brain function and language development in infants, and is not meant to imply that early nutrition influences are either restricted or unique to the auditory system or processes related to language development.

Based on indications of early advantages for breastfed infants in cognitive (Anderson, Johnstone, & Remley, 1999; Rey, 2003) and motor (Sacker, Quigley, & Kelly, 2006) development, we expected scores on the Bayley Mental and Motor scales would be higher for these infants than formula-fed infants. With respect to electrophysiological measures, ERP studies reporting that the development of sensory processing (Khedr et al., 2004; Makrides et al., 2004) and syllable processing and discrimination (Pivik et al., 2007) are enhanced in breastfed relative to milk-formula fed infants suggested that breastfed infants would show greater ERP response amplitudes and shorter response latencies to speech sounds than formula-fed infants. These effects were expected to be greatest at 6 months when there had been longer exposure to the various diets. It was further hypothesized that previously noted developmental changes in ERP response parameters (i.e., reduced response amplitudes and latencies from 3 to 6 months) would be greater in breastfed infants. In the absence of evidence indicating differences in cognitive development or performance between formula-fed groups, it was expected that these groups would show similar outcomes on both behavioral and ERP measures. In view of the potential estrogenic effects of soy formula, a particular interest was to determine whether this infant formula would be associated with gender differences in behavioral and/or cortical responses during this early developmental period. However, gender differences specific to soy formula were not expected.

METHOD

Participants

Data are reported on 130 healthy full-term infants drawn from participants in a longitudinal study examining the effects of infant diet on physical and cognitive development (the Beginnings study; Table 1). Infants selected had adequate artifact-free electrophysiological data and complete behavioral test batteries and included: 40 (20 males) breastfed (BF); 51 (29 males) fed milk-based formula (MF); and 39 (18 males) fed soy-based formula (SF). Parents determined whether to breast feed and formula feeders selected from among major brand formulas fortified with DHA (docosahexaenoic acid) and AA (arachidonic acid). Infants had been on the same diet at least since they were 2 months old, remained on the same diet through the 6-month study period, and took no additional nourishment except water through 4 months. Three day food records were obtained monthly to ensure adherence to diet restrictions. Critical inclusion criteria were: no soy intake during pregnancy; no alcohol or other drugs or medications that would affect gestation or fetal development; normal and unmarkable pregnancy and delivery; birth weight; normal infants

TABLE 1
Study Population Characteristics by Group (Mean ± SD)

Variable	*BF (N = 40)*		*MF (N = 51)*		*SF (N = 39)*		*F(2,127)*	*p*	η^2
Gestation (weeks)	39.43	± 1.15	38.84	± 1.14	38.87	± 0.93	3.84	.024[s]	.06
Birth Weight (kg)	3.57	± 0.36	3.52	± 0.40	3.42	± 0.43			
Birth Length (cm)	51.89	± 2.20	51.48	± 2.22	51.18	± 2.07			
Mom's IQ[1]	110.68	± 10.00	107.45	± 9.64	103.36	± 10.69	5.23	.007[t]	.08
SES[2]	50.86	± 11.22	45.10	± 10.25	46.92	± 10.09	3.43	.035[u]	.05
PROCESS 3mon[3]	76.40	± 5.65	73.94	± 4.69	76.66	± 5.07	3.96	.021[v]	.06
PROCESS 6mon[3]	77.03	± 4.98	75.63	± 4.06	76.80	± 4.81			

[s]BF > SF ($p < .05$); [t]BF > SF ($p < .01$); [u]BF > MF ($p < .05$); [v]SF > MF ($p < .05$).

[1] Mom's IQ: indexed by Wechsler Abbreviated Scale of Intelligence (WASI) full scale IQ.

[2] SES: Social Economic Status measured by Hollingshead (1975) Four-Factor Index of Social Positions.

[3] PROCESS 3mon/6mon: Pediatric Review of Children's Environmental Support and Stimulation data collected at 3 and 6 month visits.

Abbreviations: BF, Breastfed; MF, Milk Formula; SF, Soy Formula.

without medical diagnoses. Three families (1, SF; 2, BF) reported the presence of dyslexia in the family histories. The protocol was approved by the Institutional Review Board of the University of Arkansas for Medical Sciences. Informed consent was obtained from parents.

Procedures

This report deals with data gathered in the same infants at ages 3 and 6 months. Study visits were scheduled for the morning and during each visit behavioral testing was administered by licensed psychological examiners and ERP recordings were obtained in response to speech sounds. Variables considered other than those related to ERP analyses are listed in Table 1. ERP responses were determined from electroencephalogram (EEG) activity (bandpass 0.1–100 Hz, sampling rate 250 Hz; impedances maintained below 50 kΩ) using 128 channel electrode nets (Electrical Geodesics, Inc.) recorded in electrically shielded, sound-attenuated, and dimly lighted testing rooms. Two naturally produced and recorded consonant-vowel syllables were presented through speakers placed 5 ft. in front of and above the infant's seated position [/pa/ and /ba/, 300 msec; ISI (onset-to-onset): 2,250 msec; 2 or 3 blocks of 90 trials with inter-block rest periods of ~5 min; randomized occurrence: /pa/ (80%), /ba/ (20%)]. Stimulus intensity at the infant's head was 72 dB SPL. The mean number of trials used to generate ERPs was comparable for groups at each visit [3 month: SF ($N = 133.3$); MF ($N = 135.5$); BF ($N = 139.4$); 6 month: SF ($N = 139.6$); MF ($N = 150.9$); BF ($N = 129.2$; all $p > .05$]. During recordings, infants were awake and seated in an infant chair or on their parent's lap. Silent videos were played to engage attention.

EEG Recordings and Analyses

Offline, single-epochs of 1,100 msec were baseline corrected relative to a 100 msec pre-stimulus interval, filtered at 0.3–30 Hz, and subjected to an automatic artifact rejection algorithm. Accepted epochs were separately averaged for each type of syllable, and initial vertex referenced recordings were re-referenced to linked mastoids. This report deals with responses to the frequently

presented syllable (/pa/) only. This provides high signal-to-noise ratios for group comparisons of ERP correlates of syllable processing. This strategy was used by Novak et al. (1989) in their developmental ERP studies. Data on syllable discrimination are not presented in this report.

Analyses of ERP responses focused on the same anterior cortical areas reported to be involved in processing language sounds in infants (Čeponienë, Lepisto, Alku, Aro, & Näätänen, 2003; Novak et al., 1989). Thus, responses from individual electrodes (9-10/area) within anterior frontal (F), central (C), and temporal (ATL) areas and within hemispheres were clustered to produce 6 region-related values: anterior Frontal Left (FL) and Right (FR), Central Left (CL) and Right (CR), Anterior Temporal Left (ATL) and Right (ATR), respectively (Figure 1). Figure 2 presents topographic maps based on grand average responses of all groups from 124 electrodes referenced to linked mastoids showing the voltage distribution of response components at 3 and 6 months relative to these electrode clusters.

We employed grand averages to identify three responses of interest occurring at ~200 msec, ~250 msec, and ~350 msec (Figure 1), which have been routinely observed in infant ERP studies of syllable processing. At 6 months more complex waveforms were elicited. Relative to 3 month responses, the first positive peak emerged earlier (at ~150 msec), the negative inflection at 250 msec increased, and the second positive peak markedly decreased in amplitude. The late slow wave differentiated into an early negative component at ~450 msec and a small positive inflection peaking at ~ 600 msec followed by a slow negative wave. Components were labeled according to their latencies, and this report will focus on components reliably present at both assessment times, that is, the P_i150, N_i250, P_i350 (in this report the subscript "i" is used to indicate infant responses to avoid confusing infant components with corresponding adult components that may not be functionally equivalent) and late slow wave (LSW). Using recommended procedures for ERP analyses (Picton et al., 2000), peak amplitudes and latencies of the P_i150, N_i250, and P_i350 at 3 and 6 months were determined from 50–240 msec, 180–275 msec, and 270–450 msec windows, respec-

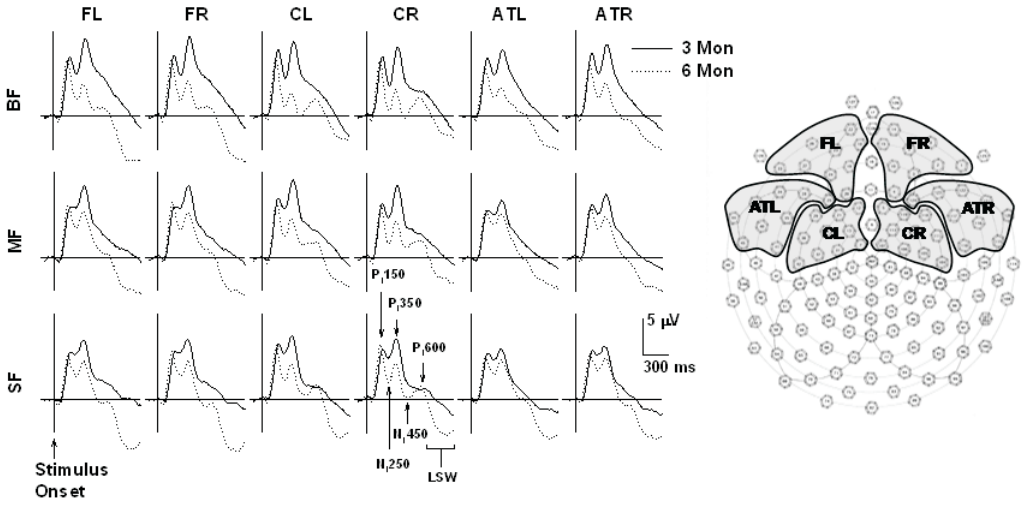

FIGURE 1 Regional event-related potential (ERP) averages in response to the syllable /pa/ for each group with 3- and 6-month waveforms superimposed. Labels in the mid-lower panel identify response components. Brain regions (F, frontal; AT, anterior temporal; C, central) and laterality (L, left; R, right) are as indicated in the diagram. Group abbreviations are: BF, Breastfed; MF, Milk Formula; SF, Soy Formula.

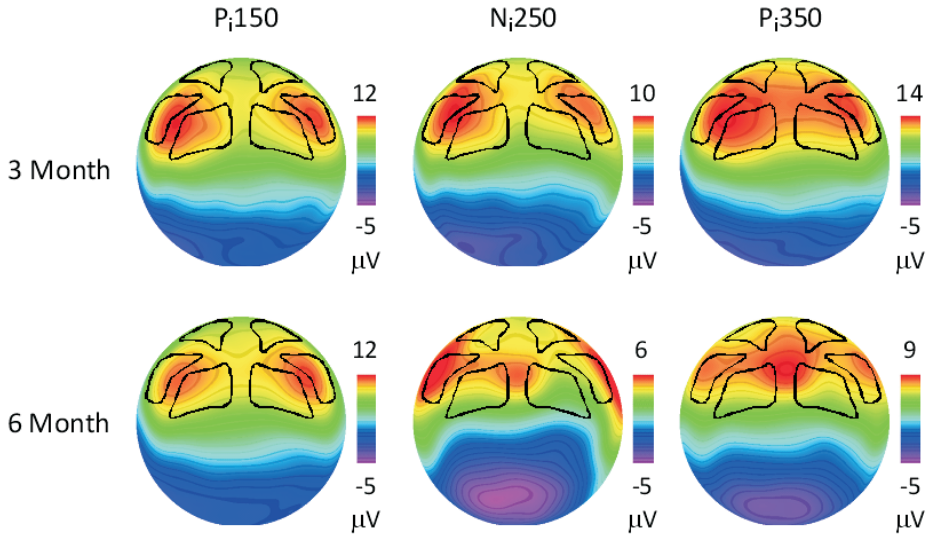

FIGURE 2 Topographic maps based on grand average responses of all groups from 124 electrodes referenced to linked mastoids showing the voltage distribution of response components at 3 and 6 months relative to the electrode clusters used in analyses. (Figure is available in color online)

tively. Average LSW amplitudes were measured within 600–995 msec for both ages. These windows were based on grand average responses and reflect the large inter-subject variability characteristic of infant populations.

Analysis of variance (ANOVA) procedures and *t*-tests using Bonferroni corrections for unplanned contrasts were used to examine group and gender differences in participant characteristics and behavioral assessment variables. Unless otherwise noted, at each age repeated-measure ANOVAs were conducted for response component amplitudes and latencies with feeding group, gender, area, and hemisphere as independent variables. To explore developmental changes, amplitudes and latencies of components across visits were compared using repeated-measure ANOVAs with area, hemisphere, age and feeding group as independent variables. Greenhouse-Geisser adjustments were applied when indicated. Pearson product moment correlation coefficients were computed to describe relationships among study variables and multiple regression analyses were conducted to further assess relationships among infant background variables, ERP response components and measures of behavioral development. For all analyses, a value of $p \leq .05$ was considered statistically significant.

RESULTS

Participant Characteristics

Significant group differences for variables in Table 1 included: longer gestation in BF than SF infants; higher mother's IQ for BF than SF infants; higher socioeconomic status (SES) scores in BF

than MF infants; and, higher scores on the home environment Process scale for SF than MF infants at 3 months.

Gender influences contributed to these group effects. The longer gestation for BF than formula-fed infants was evident in males only [$F(2, 64) = 5.91$, $p = .004$, $\eta^2 = .16$; BF > SF, $p = .004$]. Length of gestation did not differ significantly between males and females in the BF and MF groups, but was longer in SF females than males ($t = 2.07$, $p < .05$). Significant differences related to mother's IQ were only evident for females [$F(2, 60) = 5.48$, $p = .007$, $\eta^2 = .16$; BF > SF ($p = .007$)]. Also both the SES [$F(2, 60) = 3.64$, $p = .032$, $\eta^2 = .11$; BF > MF, $p = .03$) and 3 month Process score [$F(2, 59) = 3.89$, $p = .026$, $\eta^2 = .12$; BF > MF ($p = .043$) effects were most prominent in females. At 6 months families of BF females provided more environmental support and stimulation than those of the males [$F(1, 38) = 6.07$, $p = .018$, $\eta^2 = .14$).

Syllable Processing

No diet group differences and group by gender interactions were observed for P_i150 and N_i250 amplitudes at 3 or 6 months (Figure 3). There were, however, diet group differences in hemi-

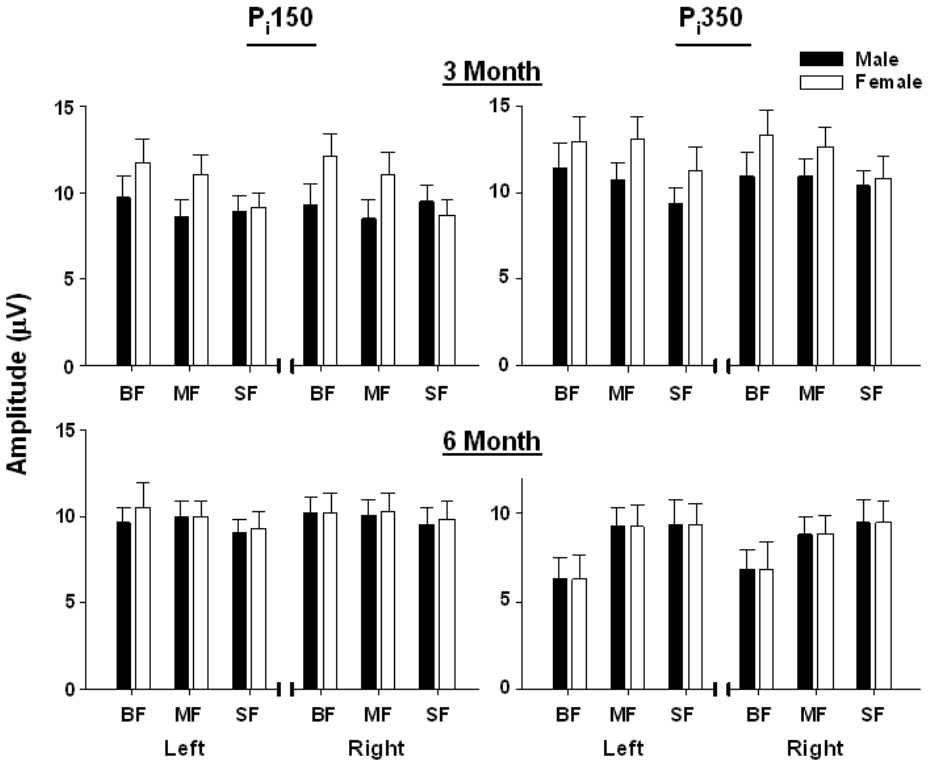

FIGURE 3 Amplitude variations in P_i150 and P_i350 responses at 3 and 6 months as a function of group and gender. Responses are averaged across regions within each hemisphere (indicated as Left and Right). Significant gender-related interactions were present at both ages (see text), but all within-group, between-gender comparisons were non-significant. Group abbreviations are: BF, Breastfed; MF, Milk Formula; SF, Soy Formula.

spheric N_i250 latency measures at 3 months. BF infants' latencies were longer than those of formula-fed infants in both hemispheres, with left hemisphere differences being most pronounced [left hemisphere: BF (245.42 msec); MF (227.78 msec); SF (226.84 msec); BF > MF ($t = 2.40$) and SF ($t = 2.28$), both $p < .05$; right hemisphere: BF (239.46 msec); MF (228.82 msec); SF (222.65 msec); BF > SF, ($t = 2.08$), $p < .05$].

At 3 months group-related effects were present for the later occurring P_i350. Amplitudes for this component were higher over F and C than AT areas for formula-fed groups [$F(4, 248) = 3.27$, $p = .013$; $\eta^2 = .05$; group comparisons all $p \leq .001$); Figure 3], but for BF infants F amplitudes were higher than those in C and AT areas (both $p < .02$). A hemisphere by feeding group by gender interaction [$F(2, 248) = 3.22$, $p = .043$; $\eta^2 = .05$] was not accompanied by significant post-hoc differences. The P_i350 peaked later in the left hemisphere and a significant effect of feeding group [$F(2, 124) = 6.70$, $p = .002$; $\eta^2 = .10$] was based on a longer latency for BF than formula-fed infants (BF: 361.63 msec; MF: 339.53 msec; SF: 334.91 msec; all $p < .02$).

The group-related latency effects observed for the N_i250 and P_i350 prompted an examination of between-component latency relationships. At 3 months the P_i150 occurred earlier and the N_i250 and P_i350 responses later in breastfed relative to formula-fed groups resulting in longer P_i150–P_i350 response intervals for breastfed infants [$F(2,127) = 7.46$, $p = .001$; $\eta^2 = .11$, Figure 4; BF > MF ($p = .01$) and SF ($p = .001$); interval means ± *SD*: BF (170.96 ± 49.88 msec); MF (141.11 ± 46.56 msec; SF (130.60 ± 49.80) msec].

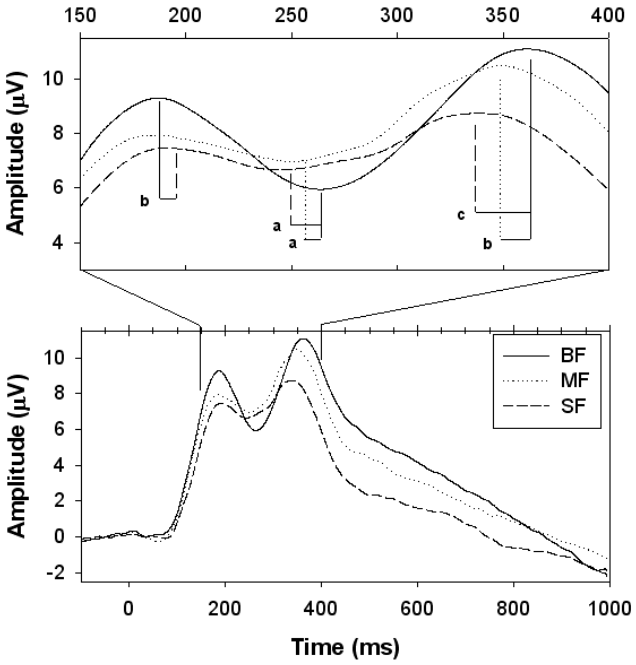

FIGURE 4 Responses averaged across regions illustrating latency differences among feeding groups for P_i150, N_i250, and P_i350 components at 3 months. Significant component-related between-group differences are indicated in the insert ($^a p < .05$; $^b p < .01$; $^c p < .001$). Group abbreviations are: BF, Breastfed; MF, Milk Formula; SF, Soy Formula. See text for discussion.

Amplitude comparisons across groups of the LSW component did not show significant group or group by gender effects at 3 months.

At 6 months none of the amplitude comparisons for the response components significantly differentiated groups. With the exception of an area by feeding group by gender interaction for the N_i250 [$F(4, 248) = 2.81$, $p = .028$; $\eta^2 = .04$) for which post-hoc analyses were non-significant, group comparisons on component latency measures were similarly unremarkable.

Developmental Effects: 3 to 6 Months

The general similarity of groups on response measures at 3 and 6 months suggest the groups would not differ in developmental changes in ERP measures occurring between these assessment times. This was generally confirmed in analyses comparing amplitude and latency measures across visits although significant variations were present for all components evident at both ages. These developmental variations included the following: (a) P_i150 amplitude remained stable across visits but latencies decreased at 6 relative to 3 months across groups [$F(1, 127) = 67.18$, $p < .001$); $\eta^2 = .35$]. This decrease was greatest in AT areas [age by site interaction: $F(2, 126) = 5.51$, $p < .01$; $\eta^2 = .08$]; (b) the N_i250 was more negative-going at 6 than 3 months across groups [$F(1, 127) = 42.52$, $p = .001$; $\eta^2 = .25$]. There was a greater amplitude decrease centrally compared to other areas [age by area interaction: $F(2, 126) = 18.05$, $p = .001$; $\eta^2 = .23$]; N_i250 latency did not change significantly from 3 to 6 months; (c) a decrease in P_i350 amplitude from 3 to 6 months [$F(1, 127) = 32.56$, $p = .001$; $\eta^2 = .20$]. The decrease was greatest centrally [age by area interaction, $F(2, 126) = 18.64$, $p = .001$; $\eta^2 = .23$]. There was no significant age effect for P_i350 latency; and (d) the LSW component became more negative-going at 6 than 3 months [$F(1, 127) = 59.62$, $p = .001$; $\eta^2 = .32$], and the decrease was most apparent frontally [age by area interaction: $F(2, 127) = 38.28$, $p = .001$; $\eta^2 = .35$].

Behavioral Assessments

It should be noted that not all LPEs were blinded to treatment groups. All test results for all groups were within the normal range. No significant group differences were found on Bayley Mental scores at either 3 or 6 months (data not shown). BF infants' Bayley Motor scores were slightly higher compared to MF and SF infants at 3 months [$F(2,127) = 3.00$, $p = .05$, $\eta^2 = .05$; BF: 102.40; MF: 100.27; SF: 99.38], and BF and MF infants scored higher than SF infants on this scale at 6 months [$F(2, 127) = 3.93$, $p = .022$, $\eta^2 = .06$; both $p < .05$; BF: 108.43; MF: 108.06; SF: 103.00). Increases in behavioral assessment scores from 3 to 6 months occurred in all groups.

Correlation and Multiple Regression Analyses

Gestation length, mother's IQ, and SES differentiated groups and these measures were correlated with behavioral and ERP measures at 3 and 6 months. In addition, multiple regression analyses were conducted to evaluate influences among background, behavioral, and ERP measures at the two assessment periods.

Population characteristics and behavioral assessments. At 3 months: longer gestation was associated with higher Bayley scores for formula-fed infants [Mental: MF ($r = .33$, $p <$

.02); SF ($r = .33$, $p < .05$); Motor: MF ($r = .35$, $p < .02$); SF ($r = .33$, $p < .05$)]; Bayley Mental scores were related to mother's IQ for SF infants ($r = .38$, $p < .02$); and, BF infants from higher SES families had lower Bayley Mental scores ($r = –.46$, $p < .01$).

There were only two significant correlations at 6 months. One represented a continuation of relationships present at 3 months [SF: mother's IQ and Bayley Mental ($r = .35$, $p = .03$)] and the other indicated higher Bayley Motor scores in BF infants with longer gestation periods ($r = .38$, $p < .02$).

Multiple regression analyses indicated this set of background variables (i.e., gestation length, mother's IQ, and SES), was significantly related to Bayley Mental scores for all groups at 3 months [BF: $F(3, 36) = 3.42$, $p = .027$, $R = .47$; MF: $F(3, 47) = 2.87$, $p = .046$, $R = .39$; SF: $F(3, 35) = 2.909$, $p = .048$, $R = .45$], but only for BF infants at 6 months [$F(3, 36) = 3.53$, $p = .024$, $R = .48$]. Similar analyses using Bayley Motor scores as the dependent variable showed only one significant result, that is, for MF infants at 3 months [$F(3, 47) = 2.98$, $p = .05$, $R = .39$]. However, as a group these variables were only weak ($R > .20$, $\leq .40$) to moderate ($R > .40$, $\leq .60$) predictors of these developmental scores.

There were few significant relationships between individual predictors and dependent variables in these analyses. BF infants showed negative relationships between SES and Bayley Mental scores at 3 ($\beta = –.21$, $p = .004$) and 6 ($\beta = –.17$, $p = .05$) months and a positive influence of mother's IQ on Bayley Mental scores at 6 months ($\beta = .21$, $p = .037$). For MF infants there were positive relationships between gestation and Bayley Mental ($\beta = 1.54$, $p = .014$) and Motor ($\beta = 1.79$, $p = .012$) scores at 3 months.

Population characteristics and ERP measures. These analyses were limited to ERP responses occurring within 500 msec after syllable presentation since aspects of components within this time period had shown group differences. There were few significant associations between ERP measures and population variables, that is, 3 involving amplitude and 7 involving latency measures, and these did not indicate strong relationships (all < .40). Amplitude findings consisted of positive correlations at 3 months between gestation length and ATR P_i350 responses (SF: $r = .38$, $p < .02$) and between SES and CR N_i250 responses (BF: $r = .36$, $p = .02$), and at 6 months a negative relationship between SES and FR P_i150 responses (BF: $r = –.32$, $p < .05$). Variables associated with latency measures at 3 months included SES [BF: CR P_i150 ($r = .31$, $p = .05$); left ($r = .37$, $p = .02$) and right ($r = .31$, $p = .05$) AT P_i150] and mother's IQ (SF: CR P_i150, $r = –.35$, $p < .02$). At 6 months shorter gestation in MF infants was related to longer P_i150 latencies in CL ($r = –.26$, $p = .05$) and ATL ($r = –.36$, $p = .01$) areas and in BF infants higher mother's IQ predicted earlier occurrence of CR N_i250 responses ($r = –.37$, $p < .02$).

ERP–behavioral relationships. To investigate relationships between brain activity during syllable processing and behavioral development, correlations were computed (Tables 2 and 3) and multiple regression analyses conducted (Tables 4 and 5) between ERP responses in the 500 msec after syllable presentation and Bayley assessments at each visit.

Amplitude relationships: 3 months. Significant correlations between response amplitudes and behavioral measures at 3 months were largely limited to BF infants (Table 2) for whom higher amplitude P_i150 responses across brain areas were associated with higher Bayley scores. Significant correlations with amplitudes of later components were limited to positive relationships be-

TABLE 2
Correlations Between ERP Amplitudes and Bayley Scales of Infant Development

3 Months					
Behavioral Measure:	Bayley Mental	Bayley Motor			
ERP Component:	P_i150	P_i150	N_i250	P_i350	
Group:	BF	BF	BF	BF	MF
Region					
FL	.41[c]	.51[c]			
FR	.35[c]	.47[b]			
CL		.45[b]			–.27[a]
CR					–.29[a]
ATL	.35[a]	.48[b]	.32[a]	.35[a]	
ATR	.38[a]	.42[b]			

6 Months		
Behavioral Measure:	Bayley Mental	Bayley Motor
ERP Component:	P_i150	P_i150
Group:	BF	BF
Region		
FL	.32[a]	
CL	.32[a]	.32[a]
ATL	.32[a]	

[a]$p < .05$; [b]$p < .01$; [c]$p < .001$.
Abbreviations
ERP, event-related potential.
Group: BF, Breastfed; MF, Milk Formula; SF, Soy Formula.
Region: FL, FR—Frontal Left and Right; CL, CR—Central Left and Right; ATL, ATR—Anterior Temporal Left And Right.

tween Bayley Motor scores and AT N_i250 and P_i350 measures in BF infants, and negative relationships between this scale and C P_i350 amplitude in MF infants.

Regression analyses (Table 4) indicated the set of ERP component amplitudes was a generally weak to moderate predictor of Bayley Mental scores at 3 months, with significant model effects present only for BF infants. Component-specific relationships for these infants showed a consistent pattern associating increases in P_i150 (across sites) and N_i250 (frontal and central) amplitudes with higher Bayley Mental scores. However, for MF infants only the P_i350 component was significant, with lower amplitude responses at frontal and central sites predicting better Mental scores.

ERP component amplitudes predicted Bayley Motor scores at 3 months for BF and MF groups with *R*s in the moderate to strong ($> .60, \leq .80$) range. Significant model effects were present for BF infants at left hemisphere sites and ATR, and for MF infants at all sites. Significant individual component predictors of Bayley Motor performance differed for these groups. For BF infants the most consistent finding indicated increases in P_i150 amplitude with increases in Motor scores, whereas for MF infants decreases in P_i350 amplitude predicted increases in these behavioral scores.

Amplitude relationships: 3 months—Gender effects. At 3 months significant gender-specific amplitude-behavioral relationships were present only for BF infants and all were positive. For males higher amplitude P_i150 responses across sites ($r = .46$) and P_i350 AT responses (left: $r =$

TABLE 3
Correlations Between ERP Latencies and Bayley Scales of Infant Development

3 Months

	Bayley Mental		Bayley Motor			
	N_i250	P_i350	P_i150	N_i250		P_i350
Region	BF	BF	SF	BF	SF	SF
FL	.31[a]				.44[b]	
FR	.38[a]		–.41[b]		.36[a]	
CL			–.38[a]	.41[b]	.31[a]	
CR			–.37[a]		.38[a]	
ATL				.35[a]	.41[b]	
ATR	.35[a]	–.32[a]	–.33[a]			.32[a]

6 Months

	Bayley Mental		Bayley Motor		
	P_i150	N_i250	P_i150	N_i250	P_i350
Region	MF	SF	MF	SF	BF
FL	–.32[a]	.44[b]	–.32[a]		
FR		.42[b]	–.31[a]		
CL	–.35[b]	.32[a]	–.29[a]		–.40[b]
CR	–.30[a]	.43[b]		.33[a]	
ATL		.33[a]			
ATR		.35[a]			–.32[a]

[a]$p < .05$; [b]$p < .01$.
Abbreviations
ERP, event-related potential.
Group: BF, Breastfed; MF, Milk Formula; SF, Soy Formula.
Region: FL, FR—Frontal Left and Right; CL, CR—Central Left and Right; ATL, ATR—Anterior Temporal Left and Right.

.47; right: $r = .45$; all $p < .05$) were associated with higher Bayley Mental scores. Better Bayley Motor performance was related to higher P_i150 amplitude across sites for females ($r = .60, p < .01$) and higher ATR P_i350 responses for males ($r = .45, p < .05$).

Within-groups, regression analyses[1] relating ERP response amplitude to Bayley Mental performance indicated higher multiple *R*s for BF females (moderate to strong) than males (moderate) and for MF males (moderate) than females (weak) , but similar values (weak to moderate range) for SF males and females. The few significant model effects at this age were present for BF females [FL, FR: both $F = 3.82, p = .031$; CL ($F = 4.81, p = .014$] and MF males [ATR: $F = 3.54, p = .029$]. Only these infants had significant beta coefficients for individual component measures at this time. For BF females higher Bayley Mental scores were associated with increases in P_i150 amplitudes at FL (.65), FR (.64) and CL (.61) and N_i250 amplitudes at FL (–.65) and CL (–.60). For MF males Bayley Mental scores increased with increases in P_i150 amplitude [CR (.52), ATL (.61), and ATR (.52)] and with decreases in P_i350 amplitude [FL (–.54), FR (–.53), CR (–.64), ATL (–.91), and ATR (–1.06)].

The results of gender-related regression analyses examining the influences of response amplitude on Bayley Motor performance at 3 months generally mirrored those for the Bayley Mental for BF and SF groups, but showed strengthened associations for MF females. In these results, sig-

TABLE 4
Results of Regression Analyses Relating ERP Response Amplitudes With Bayley Scales of Infant Development

Bayley Mental

	3 Month							*6 Month*		
	BF				*MF*		*SF*	*BF*	MF	SF
	Model		β		*Model*	β	*Model*		*Model*	
Region	*R*	*F(3,36)*	P_i150	N_i250	*R*	P_i350	*R*		*R*	
FL	.52	4.51[b]	.61[c]	–.37[a]	.32	–.33[a]	.28	.37	.09	.23
FR	.52	4.42[b]	.59[c]	–.34[a]	.32	–.32[a]	.33	.29	.12	.20
CL	.45	3.03[a]	.48[b]	–.33[a]	.27		.29	.33	.08	.26
CR	.49	3.02[a]	.47[b]		.30	–.30[a]	.28	.22	.07	.27
ATL	.39		.48[a]		.29		.16	.36	.24	.18
ATR	.47	3.48[a]	.62[b]		.36	–.48[a]	.28	.21	.21	.21

Bayley Motor

	3 Month								*6 Month*		
	BF			*MF*				*SF*	*BF*	MF	SF
	Model		β	*Model*		β		*Model*		*Model*	
Region	*R*	*F(3,36)*	P_i150	*R*	*F(3,47)*	P_i150	P_i350	*R*		*R*	
FL	.54	5.01[b]	.59[b]	.52	5.65[b]	.62[a]	–.60[c]	.09	.28	.11	.30
FR	.51	4.30[b]	.54[b]	.50	5.25[b]	.51[a]	–.58[b]	.07	.24	.14	.24
CL	.49	3.76[a]	.52[b]	.43	3.55[a]			.18	.34	.16	.16
CR	.33			.51	5.45[b]	.44[a]	–.57[c]	.20	.26	.16	.19
ATL	.49	3.77[a]	.48[a]	.43	3.62[a]		–.62[b]	.19	.16	.10	.28
ATR	.47	3.43[a]	.60[b]	.47	4.41[b]		–.72[b]	.11	.19	.12	.17

[a]$p < .05$; [b]$p < .01$; [c]$p < .001$.
Abbreviations
ERP, event-related potential.
Group: F, Breastfed; MF, Milk Formula; SF, Soy Formula.
Region: L, FR—Frontal Left and Right; CL, CR—Central Left and Right; ATL, ATR—Anterior Temporal Left and Right.

nificant model effects were present for BF females [FL: $F = 4.38$, $p = .02$, $R = .67$; FR: $F = 3.79$, $p = .032$, $R = .65$] and MF females [FL: $F = 4.80$, $p = .013$, $R = .67$; FR: $F = 4.64$, $p = .014$, $R = .66$] and males [CR: $F = 3.36$, $p = .036$, $R = .54$; ATR: $F = 4.17$, $p = .016$, $R = .58$]. Significant component-related beta coefficients were limited to these subgroups. For BF females and both MF females and males increases in P_i150 amplitude were related to increases in Motor scores [BF: FL (.69), FR (.66), CL (.63); MF females: FL (1.16), FR (1.08); MF males: CR (.60)]. Increases in Motor scores were also related to N_i250 amplitude increases in MF males, and to P_i350 amplitude decreases in MF males [FL (–.63), FR (–.67), CL (–.79), CR (–.89), ATL (–1.06), ATR (–1.35)] and females [FL (–.67), FR (–.71), CL (–.37), CR (–.51)].

TABLE 5
Results of Regression Analyses Relating ERP Response Latencies With Bayley Scales of Infant Development

Bayley Mental

	3 Month						*6 Month*					
	BF				*MF*	*SF*	*BF*	*MF*			*SF*	
	Model		β		*Model*	*Model*	*Model*	*Model*		β	*Model*	β
Region	*R*	*F(3,36)*	N_i250	P_i350	*R*	*R*	*R*	*R*	*F(3,47)*	P_i150	*R*	*F(3,35)*	N_i250
FL	.33				.31	.20	.13	.39	2.74[a]	–.06[a]	.33	2.88[a]	.07[b]
FR	.43		.06[a]		.30	.25	.16	.31			.44		.06[a]
CL	.32				.27	.20	.22	.40	2.91[a]	–.08[b]	.38		.06[a]
CR	.32				.15	.25	.19	.34		–.07[a]	.51	4.05[a]	.07[b]
ATL	.32				.28	.20	.22	.20			.33		
ATR	.49	3.77[a]	.05[a]	–.05[a]	.11	.17	.27	.28			.43		.06[a]

Bayley Motor

	BF		*MF*		*SF*				*BF*		*MF*		*SF*			
	Mod.	β	*Mod.*	β	*Model*		β		*Mod*	β	*Mod*	β	*Model*		β	
Region	*R*	N_i250	*R*	P_i150	*R*	*F(3,35)*	P_i150	N_i250	*R*	N_i250	*R*	P_i150	*R*	*F(3,35)*	N_i250	P_i350
FL	.19		.34		.47	3.21[a]		–.07[a]	.13		.32	–.09[a]	.40			
FR	.26		.30		.50	3.83[a]	–.06[a]		.08		.34	–.09[a]	.33			
CL	.43	–.06[a]	.36		.48	3.49[a]	–.05[a]		.40	–.06[a]	.30	–.09[a]	.33			
CR	.20		.26		.43				.18		.27		.45	2.92[a]	.10[a]	–.05[a]
ATL	.41	–.06[a]	.35	–.06[a]	.50	3.91[a]		–.08[b]	.32		.2		.22			
ATR	.34		.23		.42				.37	–.06[a]	.25		.34			

[a]$p < .05$; [b]$p < .01$.

Abbreviations

ERP, event-related potential.

Group: BF, Breastfed; MF, Milk Formula; SF, Soy Formula.

Region: FL, FR—Frontal Left and Right; CL, CR—Central Left and Right; ATL, ATR—Anterior Temporal Left and Right.

Amplitude relationships: 6 months. Only BF infants had significant amplitude–behavioral associations at 6 months (Table 2). These remained concentrated on P_i150-related relationships, were all positive and were present only for left hemisphere sites, that is, Bayley Mental (all left hemisphere sites) and Motor scores (CL).

Predictive relationships between ERP amplitude measures and developmental scores were generally reduced relative to those at 3 months (Table 4). Regression analyses did not indicate any significant relationships between ERP amplitude measures—considered either as a set or as individual variables—and Bayley measures at this age.

Amplitude relationships: 6 months—Gender effects. Significant group-related gender relationships at 6 months (all $p < .05$) were limited to BF males [CL P_i150 amplitude with Bayley Motor scores ($r = .47$)] and MF males and females [P_i350 amplitude with Bayley Mental (females: left ($r = .50$) and right ($r = .54$) AT; and Bayley Motor scores (males: CL ($r = –.37$)].

Regression analyses indicated that predictive relationships between ERP component amplitudes and Bayley Mental and Motor performance were generally weak at this age with no significant model effects. The only significant individual component effects present were for MF females [positive relationships between P_i350 amplitudes [ATL ($\beta = .78$), ATR ($\beta = .80$) and Bayley Mental scores] and MF males [positive relationship between P_i150 amplitude [ATL ($\beta = 2.55$) with Bayley Motor scores].

Latency relationships: 3 months. Significant correlations between component latencies and behavioral measures occurred in BF and SF groups and were largely related to P_i150 and N_i250 components (Table 3). For BF infants longer N_i250 latencies were associated with better Bayley Mental (F and AT) and Motor (CL and AT) performance, and shorter ATR P_i350 latencies predicted higher Bayley Mental scores. For SF infants shorter P_i150 latencies and longer N_i250 and ATR P_i350 latencies were related to better Bayley Motor performance. Correlations of the P_i150–P_i350 interval with behavioral scores showed significant positive relationships across areas between this measure and SF infants' Bayley Motor scores.

At 3 months regression analyses indicated that component latency measures were weak (formula-fed groups all sites; BF infants left hemisphere) to moderate (BF infants, FR and ATR) predictors of Bayley Mental scores (Table 5). Only BF infants showed significant model (ATR) and component [positive with N_i250 latencies (FR, ATR), negative with P_i350 (ATR)] relationships with this variable at this time.

For all groups the power of the ERP component latency model to predict Bayley Motor scores at 3 months was weak to moderate. Only SF infants showed significant model effects (FL, FR, CL). For formula-fed infants, decreases in P_i150 latency predicted higher Motor scores (MF: ATL; SF: CL, FR). Increases in N_i250 latency were related to better Motor performance for BF (CL, ATL) and SF (FL, ATL) groups.

Latency relationships: 3 months—Gender effects. Group ERP latency–behavioral relationships at 3 months were influenced by gender-specific relationships. For example, only BF females had significant correlations between the Bayley Mental scale and N_i250 [rs = .44 (FR) and .57 (ATR); both $p = .05$] and P_i350 latencies [$r = –.56$ (ATR); $p = .01$]. Both genders showed significant positive N_i250 latency correlations with Bayley Motor scores [males: rs = .55 (CL) and .53 (ATL); both $p < .02$; females: $r = .45$ (ATR); $p < .05$]. For SF infants a positive association be-

tween the N_i250 latency and Bayley Motor scores was reflected primarily in males [*r*s = .54 (FL), .48 (FR), .46 (CR), .49 (ATL), .51 (ATR); all $p = .05$].

Gender effects were also evident in the results of regression analyses of ERP latency–behavioral relationships at this time. As predictors of Bayley Mental scores, latency model *R*s were higher in BF females (generally moderate to strong) than males (generally weak), and only BF females showed significant model [ATR: $F = 5.44$, $p = .007$; $R = .72$] and individual variable (ATR P_i350: –.06) effects. There were no significant regression effects for these measures for formula-fed groups, but latency model power was better for MF males (weak to moderate) than females (very weak to weak), and in the weak range for both SF males and females.

Gender effects were less evident in analyses relating ERP latency measures and Bayley Motor performance. For BF and MF infants model *R*s were generally weak for both genders, but there were significant beta coefficients linking ATL N_i250 latency (.08) with better Motor performance in BF males and higher Motor scores with higher P_i150 amplitudes (CL: .09) in MF females. For SF infants the overall relationships between component latencies and Motor scores were moderate to strong, with females showing a significant model effect [FR: $F = 4.63$, $p = .015$) and significant betas present for males (FL, N_i250: .11) and females (FL, P_i150: –.07).

Latency relationships: 6 months. All groups, ERP components, and behavioral assessments were represented among the significant latency–behavioral correlations at 6 months (Table 3). For BF infants, these correlations reflected a negative relationship between P_i350 latencies and Bayley Motor performance. MF infants showed significant negative relationships between P_i150 latencies and both Bayley scales. SF infants maintained an emphasis on positive associations between behavioral measures and the N_i250 component, however at 6 months earlier relationships were fewer, or related to assessments different from those at 3 months (Bayley Mental instead of Motor**).**

Regression analyses indicated significant effects of the ERP component latency model and Bayley Mental performance for formula-fed groups at this time (MF: FL, CL; SF: FL, CR), but *R* values were weak to moderate (Table 5). Also, only these groups showed significant relationships between individual components and Bayley Mental scores. Higher Mental scores were associated with decreases in P_i150 latency (FL, CL, CR) for MF infants and increases in N_i250 latency (FL, FR, CL, CR, ATR) for SF infants.

At 6 months ERP latency measures were generally weak predictors of Bayley Motor scores. A significant model effect was present for SF infants (CR), and higher Motor scores were related to latency decreases for the P_i150 for the MF group (FL, FR, CL), and for the P_i350 for BF (CL, ATR) and SF (CR) infants.

Latency relationships: 6 months—Gender effects. In BF infants, negative associations of P_i350 latencies with the Bayley Motor [*r*s = –.69 (CL), –.66 (ATL), –.61 (ATR); all $p \leq .01$] were most prominent in males. For females shorter ATR P_i150 latencies were related to higher Bayley Motor scores [$r = –.61$; $p \leq .03$].

In MF infants response latency–behavioral relationships at 6 months were limited to three for males, that is, Bayley Mental with P_i150 [$r = -.40$ (FL), $p < .05$] and Bayley Motor with P_i150 [*r*s = –.51 (FL) and –.49 (FR), both $p < .01$], and one for females [P_i150 and Bayley Mental: $r = –.49$ (CL), $p = .02$]. For SF infants significant correlations were generally similar for both genders, for example, males and females contributed to the positive correlations between the N_i250 latency and Bayley Mental scores [males: *rs* = .47 (FL), .47 (FR), .48 (CL); females: .44 (FL), .44 (CR),

all $p \leq .05$]. A tendency for more pronounced negative correlations between P_i350 latencies and Bayley Motor scores in males than females was evident across brain regions, but significant only frontally [$r = -.51$ (FL), $p = .03$].

At 6 months regression analyses indicated greater latency model *R*s and Bayley Mental performance for BF males than females (very weak to weak), for MF females than males (weak to strong), and for SF males than females (moderate to strong). Significant model effects were present for MF females at CL [$F = 4.28$, $p = .019$; $R = .65$] and CR [$F = 3.40$, $p = .024$; $R = .63$] and SF males at CL [$F = 3.93$, $p = .032$; $R = .63$]. Only these infants showed significant beta coefficients for individual latency variables. For MF females there were negative relationships between Mental scores and latencies for both P_i150 (CL: –.22; CR: –.19) and P_i350 (CL: –.06; CR: –.07) components. For SF males Mental scores showed positive relationships with N_i250 amplitudes at CL (.12) and ATR (.09), and a negative relationship with P_i350 amplitude at CL.

Gender differences in model and individual component effects linking latency measures to Bayley Motor performance at 6 months were evident in all groups, but most prominent in BF and SF infants. BF females had higher *R*s than males, but both genders showed significant model effects at the same sites, i.e., CL [males: $F = 5.84$, $p = .007$; $R = .72$; females: $F = 5.61$, $p = .008$; $R = .72$], ATL [males: $F = 4.98$, $p = .013$; $R = .70$; females: $F = 5.28$, $p = .01$; $R = .71$], and ATR [males: $F = 3.18$, $p = .05$; $R = .61$; females: $F = 6.31$, $p = .005$; $R = .74$]. However, the significant individual component beta coefficients differentiated males and females in this group. For males, these effects were present only for P_i350 latencies and all indicated a negative relationship between these measures and Motor scores (FR: –.07; CL: –.13; ATL: –.11; ATR: –.11). For females, effects included earlier components and associated higher Motor scores with shorter P_i150 latencies (CL: –.18; ATL: –.10; ATR: –.16) and longer N_i250 latencies (FR: .17); CL: .18; ATL: .11; ATR: .11). Unlike males, for females P_i350 latencies were positively related to Motor performance (FR: .07; CL: .10; ATL: .07).

For MF infants the set of component latencies were weak predictors of Motor scores and generally similar for males and females at all but frontal sites. At these sites *R*s for females were weak (both < .30), but males showed significant model [FL: $F = 3.07$, $p = .05$; $R = .52$; FR: $F = 2.94$, $p = .05$; $R = .51$] and P_i150 component (FL: –.13; FR: –.13) effects.

For SF infants latency model *R*s across sites were moderate to strong for males and weak for females. For males, significant model effects were present at FL [$F = 3.71$, $p = .037$; $R = .67$], CL [$F = 3.83$, $p = .034$], and ATR [$F = 4.06$, $p = .029$; $R = .68$]. Significant component influences for males associated better Motor performance with longer N_i250 latencies (FL: .12; CL: .17; ATR: .16) and shorter P_i350 (FL: –.08; CL: –.11; ATR: –.11) latencies.

DISCUSSION

This study is the first to compare brain measures of information processing as a function of the three major infant diets. Perhaps the most important finding of this study is that all behavioral and electrophysiological results were within the normal range for breast-fed and formula-fed infants. Since the inclusion and exclusion criteria restricted participants to healthy infants and the formulas studied herein have been used for decades, this outcome is not surprising. However, potential safety issues related to soy formula make these findings particularly timely and relevant.

The AAP argues that breastfeeding is the preferred method to provide diet to infants because of several factors, and recommends milk formula where breastfeeding is not possible (Bhatia & Greer, 2008). Breast milk contains many factors not available in formulas that may provide advantages for CNS development (Banapurmath, Banaputmath, & Kesaree, 1996) and the breastfeeding process may facilitate bonding behavior and enhance neurodevelopment (Drane & Logemann, 2000; Stuart-Macadam, 1995). Thus, based on previous findings we posited that breastfed infants would display "better" or more advanced brain function than milk formula-fed infants. Another position taken by the AAP is that "…although studied by numerous investigations in various species, there is no conclusive evidence from animal, adult human or infant populations that dietary isoflavones may adversely affect human development, reproduction, or endocrine function" (Bhatia & Greer, 2008; p. 1063). While the AAP sees no advantages to soy formula over milk formula, it acknowledges that growth and development of infants fed soy formula and milk formula are essentially equal. Thus, our second hypothesis was that brain function and behavior would not differ between these formula-fed groups.

Behavioral assessment scores in the current study were within the normal range for all three diet groups, and as hypothesized BF infants did have higher scores on developmental scales. Within this range scores on the Bayley Motor scale showed group differences at 6 months with higher scores in BF and MF than SF infants. Although motor systems are involved in speech and language processes (Boulenger et al., 2006; Terumitsu, Fujii, Suzuki, Kwee, & Nakada, 2006) and early motor development may influence language development (Viholainen et al., 2006), the very weak effect size ($\eta^2 = .06$) associated with these differences make it seem unlikely they will predict later language development.

Participant Characteristics and Development

Questions regarding the impact of diet and feeding type on infants' cognitive development have proved difficult to answer in part because of other prenatal and postnatal variables—such as gestational length, parental IQ and education, mother's health and diet, and environmental influences—which influence CNS and behavioral development. In this investigation, many of these family and child variables considered significant confounders in previous studies (Anderson et al., 1999; Rey, 2003) were documented and evaluated. Although there were significant group differences for gestational length, mother's IQ and SES—each generally favoring the breastfeeding group—the few significant correlations between these measures and those reflecting either behavioral development or ERP measures were small to moderate in strength and occurred primarily in formula-fed infants. Furthermore, regression analyses indicated that for all groups these variables were only weak to moderate predictors of performance on behavioral scales.

ERP Responses

Documentation of ERPs to spoken syllables in infants as correlates of language development is a relatively new endeavor and the specific measures and their relationships to language variables are still being defined (Thierry, 2005). Infant auditory ERPs involve four commonly observed components: P_i150, N_i250, P_i350, and N_i450 (Dehaene-Lambertz & Dehaene, 1994; Jing & Benasich, 2006; Kurtzberg et al., 1984; Kushnerenko et al., 2002; Novak et al., 1989; , but there is a lack of consensus regarding when various components emerge and how they change with devel-

opment. These differences likely relate to methodological variations among studies as well as individual differences in developmental dynamics among the infants studied. In the present study, all of these components were identified—the first three were present at both 3 and 6 months, and the N_i450 at 6 months.

Developmental changes from 3 to 6 months included a reduction in P_i150 latency without an obvious change in amplitude, a substantial increase in N_i250 amplitude and a P_i350 amplitude decrease. N_i250 latency was slightly longer at 6 than 3 months, while P_i350 latency remained unchanged. By 6 months more complex waveforms developed including a negativity at 450 msec (N_i450) and a positive peak at 600 msec (P_i600), followed by a gradual decrease below baseline lasting until the end of the epoch. The P_i150 latency and amplitude effects, and stable latencies of P_i350 across this time period have been previously described (Kushnerenko et al., 2002). However, the increased N_i250 latency is in contrast with reports that this measure remains stable (Kushnerenko et al, 2002) or decreases (Jing & Benasich, 2006) during this time. Furthermore, the N_i250 amplitude increase and P_i350 amplitude decrease have not been observed by others until after 6 (Kurtzberg et al., 1986; Kushnerenko et al., 2002) or even 9 (Jing & Benasich, 2006) months. These age-related variations may reflect dynamics in the development and interaction of neural networks that form the generators of these events (Jing & Benasich, 2006; Kushnerenko et al., 2002). In summary, there was a general congruence regarding the morphology and early developmental variations of ERP responses to speech sounds observed in this study with those reported in other infant studies using similar methodology.

Diet-Related Effects on ERP Measures of Syllable Processing

The hypothesis that diet-related effects on ERP correlates of syllable processing would indicate developmental advantages for BF compared with formula-fed infants was partially supported by the results, but expectations that group differences would be most evident at 6 months when exposure time to the various diets had been greater were not realized. Developmental ERP response patterns were generally similar across groups. The few significant group differences observed occurred at 3 months, were related more to latency than amplitude measures, and all involved the P_i350 component. A P_i350 amplitude-related difference reflected regional emphases between BF and formula-fed infants, with maximum amplitude at frontal sites for BF and fronto-central sites for formula-fed groups. For all groups, the lowest amplitude responses occurred at AT sites. These results suggest a more selective development at this time of frontal processes related to P_i350 function in BF than formula-fed infants. These results are consistent with reports of advanced development of response amplitude in midline relative to more lateral cortical areas during the first 6 postnatal months (Kurtzberg et al., 1986; Novak et al., 1989). Novak et al. (1989) also reported higher amplitude ERP responses to speech stimuli in infants in frontal-central than AT regions, and based on these amplitude differences inferred more rapid maturation of frontal-central areas.

At 3 months longer N_i250 and P_i350 latencies in BF than formula groups resulted in a significantly longer P_i150- P_i350 interval. If the P_i150 and P_i350 are related to sequential stages of increasingly refined analyses of auditory input (Dehaene-Lambertz & Dehaene,1994), this would indicate that speech processing takes more time in BF infants. This could reflect diet-related differences in extent of myelination occurring during early postnatal development (Paus et al., 2001) and suggests the presence of greater myelination in formula-fed infants at this time. The high

scores for BF infants on behavioral measures at 3 months and the significant positive correlations at this time of ERP measures with Bayley scales (Table 2 and 3) and the results of regression analyses (Tables 4 and 5) suggest this lower speed of processing did not negatively influence behavioral development in BF infants.

For all groups, P_i150 latency decreased between 3 and 6 months, while P_i350 latency decreased in BF infants but slightly increased (SF) or was unchanged (MF) for formula-fed infants. Shorter latencies are consistent with the general positive relationships in early development between increasing age, advanced myelination and synaptic efficacy (Vaughan & Kurtzberg, 1992). The P_i350 results suggest an earlier trend for BF infants in the maturation of processes involving more extended evaluation of language stimuli.

Having more group effects at 3 months than 6 months runs counter to the expectation that dietary influences would become more evident as a function of time. Instead, these results suggest that with longer exposure there is a general equivalence across diets of influences on the measures of physiological and behavioral development used in this investigation.

Significant correlations between response amplitudes and developmental scales at both ages were present nearly exclusively in BF infants, and were focused on early components (P_i150, N_i250). Significant associations between latency measures of the various response components and behavioral scores showed group-specific differences in age and component–behavioral scale relationships. In addition, the pattern of relationships between ERP measures and behavioral test scores (see Table 3) suggest the following: (1) at both 3 and 6 months the greater number of significant correlations of behavioral measures with ERP latency than amplitude suggest an emphasis on factors related to connectivity rather than efficiency of synaptic organization. This interpretation is supported by reports indicating an earlier time course for myelination than for synaptogenesis and pruning in brain areas important for language processing (Paterson, Heim, Friedman, Choudhury, & Benasich, 2006; Thompson & Nelson, 2001); and (2) during this time period behavioral developmental relationships with brain processes involved in perception and early processing of language-related stimuli are most prominent.

Regression analyses complemented and elaborated on these brain response-behavioral relationships. In these analyses two linear models related to ERP response measures were used: one based on response amplitude and considered to reflect synaptic organization among neural response elements, and the other based on response latency reflecting factors influencing speed of processing. At 3 months, response amplitude and latency factors were more predictive of Bayley Mental scores for BF than formula-fed infants. At this time, Bayley Motor scores were predicted by response amplitude for BF and MF infants and by response latency for SF infants. At 6 months the linear response amplitude model was a weak predictor of Bayley Mental and Motor scores for all groups, but for formula-fed infants response latencies were significantly related to Bayley Mental (MF and SF) and Motor (SF) scores. In these analyses there were diet-related patterns of predictive relationships between specific ERP variables and behavioral measures. For example, at 3 months both Bayley Mental and Motor performance were predicted by response amplitudes of early components for BF infants (P_i150, N_i250) and later components for (P_i350) for MF infants. These relationships were no longer present at 6 months.

For response latency, predictive relationships with behavioral measures at both 3 and 6 months for all groups were largely limited to early components (P_i150, N_i250). These relationships were usually negative, with shorter latencies associated with higher developmental scores. However, longer N_i250 latencies predicted better Bayley Mental scores for BF infants at 3 months and SF in-

fants at 6 months. Taken together, the regression analyses indicate diet- and gender-related variations in relationships among brain response variables and measures of behavioral development during the first 6 months of life. These early differences may signal diet-associated influences that modulate developmental trajectories in brain–behavior relationships.

Because of the putative estrogenic effects of soy isoflavones and their relatively high concentrations in infants fed soy formula, determining whether this diet would affect females and males differently was of particular interest. Significant group-specific gender effects for P_i150 and P_i350 amplitudes at 3 months were not found. Maximal effects of soy isoflavones might be expected at 6 months when infants are consuming the greatest amount of soy per body size than any time in their lives and isoflavone concentrations in the brain would the highest, but such effects were not present at this time either.

In summary, the influence of early diet on cortical syllable processing was investigated at 3 and 6 months in infants who were either breastfed or fed milk formula or soy formula. Behavioral development was normal for all three groups and diet group differences within the normal range were marginal, transient, and suggest some behavioral advantage for breastfed infants early in development. Although effects on behavioral measures related to gender were inconsistent across time, improvement in developmental scores was generally greater in females than males across the study period. Significant group differences were found in ERP amplitude and latency measures, but effect sizes were small. Latency effects in breastfed infants were associated with better neuropsychological performance at 6 months, suggesting more advanced neural maturation in these infants at this time. It is important to note the remarkable degree of similarity between the formula-fed groups in both the nature and developmental variations of study measures. Furthermore, despite concerns regarding potential estrogenic effects of soy formula isoflavones on developmental processes, our results do not indicate important differences between milk-based and soy-based formula on either behavioral development or brain activity related to the processing of speech stimuli during this early period of development.

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NOTE

1. To avoid repetition in the text, the degrees of freedom associated with gender-related regression analyses are as follows: BF males (3,16), females (3,16); MF males (3,25), females (3,18); SF males (3,14), females (3,17).

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