Brain Electrophysiology Reveals Intact Processing of Speech Sounds in Deformational Plagiocephaly

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Background: The prevalence of deformational plagiocephaly has risen dramatically in recent years, now affecting 15 percent or more of infants. Prior research using developmental scales suggests that these children may be at elevated risk for developmental delays. However, the low positive predictive value of such instruments in identifying long-term impairment, coupled with their poor reliability in infants, warrants the development of methods to more precisely measure brain function in craniofacial patients. Event-related potentials offer a direct measure of cortical activity that is highly applicable to young populations and has been implemented in other disorders to predict long-term cognitive functioning. The current study used event-related potentials to contrast neural correlates of auditory perception in infants with deformational plagiocephaly and typically developing children.

Methods: Event-related potentials were recorded while 16 infants with deformational plagiocephaly and 18 nonaffected controls passively listened to speech sounds. Given prior research suggesting their association with subsequent functioning, analyses focused on the P150 and N450 event-related potential components.

Results: Deformational plagiocephaly patients and normal controls showed comparable cortical responses to speech sounds at both auditory event-related potential components.

Conclusions: Children with deformational plagiocephaly demonstrate neural responses to language that are consistent with normative expectations and comparable to those of typical children. These results indicate that head shape deformity secondary to supine sleep is not associated with impairments in auditory processing. The applicability of the current methods in early infancy suggests that electrophysiologic brain recordings represent a promising method of monitoring brain development in children with cranial disorders. (*Plast. Reconstr. Surg.* 133: 835e, 2014.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Risk, II.

Deformational plagiocephaly is a common head shape disorder that is characterized by unilateral occipital flattening and asymmetric frontal bossing. The condition, also known as positional plagiocephaly, plagiocephaly without synostosis, or flat head syndrome, develops because of mechanical forces acting on the skull in utero or early in life.[1,2] Multiple-gestation pregnancies, prematurity, and forceps-assisted delivery have been identified as risk factors.[3–5] Skull deformity secondary to uterine constraint may improve within the first few weeks of life, whereas flattening from supine postnatal positioning (with or without associated torticollis)

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tends to progressively worsen if no alterations in sleeping habits or corrective therapy are implemented.[6,7] The characteristic cranial asymmetry of deformational plagiocephaly remains an important consideration for craniofacial specialists, as similar head shapes result from unicoronal craniosynostosis (anterior plagiocephaly) and lambdoid craniosynostosis (posterior plagiocephaly).

The incidence of deformational plagiocephaly has risen significantly since the American Academy of Pediatrics issued recommendations for infant supine sleep in 1992.[8] Implementation of the Back to Sleep campaign has been highly successful, leading to a decreased frequency of prone sleeping and reduced rates of sudden infant death syndrome.[9] However, this positive trend has been accompanied by a notable rise in cases of deformational plagiocephaly, presumably caused by reduced variability in sleep posture and more consistent pressure on specific cranial regions during rest.[10] Once considered a rare condition, occipital flattening is now estimated to affect upward of 15 percent of infants.[9]

The increased prevalence of this skull deformity has raised public concern regarding the potential impacts on brain development. At present, the developmental implications of deformational plagiocephaly are poorly understood. Miller and Clarren[10] reported that children with persistent plagiocephaly use more school-associated special help programs relative to their healthy siblings. Standardized developmental assessment with the Bayley Scales of Infant Development has shown that patients with deformational plagiocephaly obtain below-average scores on the examination's cognitive and motor indices.[11–15] Although the Bayley Scales of Infant Development instrument is useful in defining performance at a single point in early life, lower scores in infancy demonstrate limited predictive value in estimating long-term cognitive function.[16–19]

Noninvasive neuroimaging methods offer the potential to more precisely investigate neural processing, thereby detecting cognitive atypicalities and predicting developmental outcomes. One such technique, the recording of event-related potentials, can be safely obtained from infants and has shown predictive value in long-term language outcomes.[20–24] These electrical events within the brain are extracted from continuous electroencephalographic recordings and measure changes in cortical voltage activity evoked by external stimuli. The temporal resolution of event-related potentials is high, measured on the order of milliseconds, enabling the examination of complex patterns of neural functioning with a focus on individual stages of processing. These advantages, and the relative ease of data collection in infants, make event-related potentials an ideal tool for studying early deviations from typical development.[25]

One prior investigation applied event-related potentials to evaluate early development in infants affected by head shape disorders. Balan et al.[26] examined auditory event-related potentials in infants (mean age 11 months) with plagiocephalic skull deformity (secondary to deformational plagiocephaly, unicoronal synostosis, or lambdoid synostosis) and compared their results to typical cranial development.[26] The investigation focused on a series of event-related potential components that characterize school-age auditory processing (the P150-N250-N450 complex) and the precursors of these components that are evident within the first year of life.[27] Using tone stimuli, the authors examined the maximum amplitude and latency of the P150 and N250 in affected versus nonaffected infants. Results showed attenuated amplitudes at both event-related potential components when a group comparison was made between all forms of plagiocephalic head shape and typical cranial development. In infants with plagiocephaly secondary to sleep positioning, decreased amplitudes were described in several participants, but the study's analytic design did not permit a statistical comparison of this subgroup to the control population. To date, this single study using direct brain recordings demonstrates atypical auditory processing in cases of skull deformity but leaves ambiguity regarding the capabilities of infants with deformational plagiocephaly.

The current study sought to apply direct brain recordings to refine these suggestive results. First, we specifically focused on children with deformational plagiocephaly, without the inclusion of synostotic cases of plagiocephalic head shape. This approach allowed for the examination of neurodevelopment specific to sleep-associated occipital flattening, the most common form of plagiocephaly and the most germane in terms of public health ramifications. Second, given evidence of lower scores on Bayley language indices in infants with skull deformity,[12–14] the current study applied electrophysiologic methods to specifically focus on neural responses to native speech sounds. Event-related potential components associated with native phoneme perception have been demonstrated to predict long-term outcomes; Molfese and Molfese[20–22] used English phonemes to predict rates of dyslexia in children at 3, 5, and 8 years of age, and Guttorm et al.[23,24]

Table 1. Participant Characteristics

	No. of Patients	Male Sex	Age (mo)	
			Mean ± SD	Range
Typically developing	18	10	7.50 ± 2.7	3–12
Plagiocephaly	16	9	7.25 ± 2.5	4–12

showed that event-related potential correlates of phoneme perception in newborns are associated with receptive language and verbal memory skills at 6 years of age. Through the examination of event-related potentials to native phonemes in patients with deformational plagiocephaly, the present study aimed to determine whether affected infants displayed atypicalities that could help to predict developmental deficits and facilitate earlier intervention.

The study evaluated two potential hypotheses regarding the role of plagiocephaly in cognitive development. First, given the observation by Balan et al.[26] of attenuated neural responses in infants with plagiocephalic head shape, we examined whether infants with plagiocephaly secondary to supine sleep demonstrate abnormal auditory processing. Second, given that the previous study's findings confounded conditions of varying etiopathologic causes, we evaluated whether language processing specific to deformational plagiocephaly was intact (i.e., statistically equivalent to typically developing infants).

PATIENTS AND METHODS

Two groups participated in this study: 16 infants with deformational plagiocephaly and 18 typically developing infants without head shape deformity (Table 1). Cases of deformational plagiocephaly were diagnosed at the Yale Craniofacial Center. Exclusionary criteria were known preexisting neurologic disorders, a history of prenatal or perinatal complications (including traumatic head injury or hemorrhage), and a history of hearing problems. All procedures were conducted with written consent from the participants' legal guardians and with approval of the Human Investigations Committee at the Yale University School of Medicine.

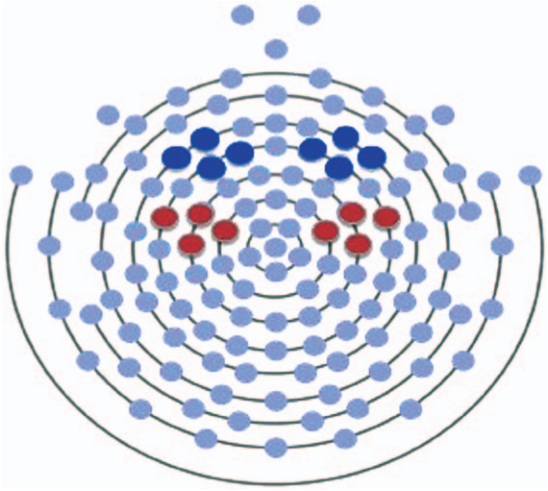

Fig. 1. Electrode layout showing frontal scalp regions (*blue*) and central scalp regions (*red*).

Experimental Design

The experimental paradigm consisted of auditory presentations of the English retroflex phoneme /da/. Each trial lasted 250 msec, followed by 610 msec of silence before the start of the next trial. Two loudspeakers were positioned 90 cm from the participant, presenting stimuli at 80 dB.

Data Collection, Processing, and Analyses

A 128-lead Geodesic Sensor Net Hydrocel (Electrical Geodesics, Inc., Eugene, Ore.) was fitted on the infant's head according to the manufacturer's specifications, and electrical impedances were kept below 40 kΩ during data acquisition. Electroencephalographic data were recorded continuously at a frequency of 250 Hz using Net Station 4.5 (Electrical Geodesics). The central electrode Cz served as the reference point for all other electrodes during recording. During the experiment, each participant was seated in his or her parent's lap or an infant highchair. Infants passively viewed bubbles during the phoneme repetitions.

Electroencephalographic data were processed using Net Station 4.5 software. To reduce sporadic fluctuations in the data, frequencies lower than 0.1 Hz or higher than 30 Hz were filtered out. Data were segmented into an epoch from 100 msec before stimulus to 700 msec after stimulus. Regions of interest were created using four electrodes over the left frontal (19, 23, 24, and 27), right frontal (3, 4, 123, and 124), left central (29, 30, 35, and 36), and right central scalp (104, 105, 110, and 111) (Fig. 1). These electrodes were chosen to mirror the frontal and central scalp regions previously examined by Balan et al.[26]

An initial positive inflection (P150) was identified, followed by a smaller negative deflection (N450). The N250 component was not applicable for examination, as it may be less prominent than the P150 and N450 components at 6 months of age.[27] Maximum P150 amplitude and latency were extracted between 100 and 300 msec after

stimulus. Maximum N450 amplitude and latency were extracted between 400 and 550 msec after stimulus.

Analyses of amplitudes and latencies for each event-related potential component were completed with separate univariate repeated measures analysis of variance at front and central scalp locations using group as a between-subjects factor and hemisphere as a within-subjects factor.

Based on data from Balan et al.,[26] we assumed a difference of approximately 4.0 μV between controls and patients, corresponding to a Cohen *d* of 1.0. Using these values, we calculated that our sample would yield a power of 98 percent to detect an effect of this size.

When significant differences were not observed between groups, the equivalence of amplitude and latency means between controls and cases was examined with a two one-sided *t* test, a bioequivalence testing method used to establish equivalence of means.[28] Based on case and control differences previously identified by Balan et al.,[26] the two one-sided *t* test acceptance criterion, theta, was designated as 3 μV for amplitude; theta was designated as 15 msec for latency.

RESULTS

P150 Component

The maximum amplitude and latency of the P150 component, previously examined by Balan et al.,[26] were compared between the two groups across all four scalp regions. There were no significant effects of group by hemisphere or group for the P150 amplitude or P150 latency (all *F* ratios ranged from 0.00 to 1.97; $p = 0.17$ to $p = 0.99$ for all). Two one-sided *t*-test revealed equivalence of means for the P150 amplitude at the left frontal, right frontal, left central, and right central regions ($p < 0.05$ for all) (Fig. 2). P150 latency showed neither difference nor equivalence over the four scalp regions.

N450 Component

The maximum amplitude and latency of the N450 component were also compared between plagiocephaly patients and nonaffected controls. There were no significant effects of group by hemisphere or group for the N450 amplitude or N450 latency (*F* ratios, 0.13 to 2.16 for all; $p = 0.15$ to $p = 0.72$ for all). Two one-sided *t* test revealed equivalence of means for the N450 amplitude over the left central region ($p < 0.05$). N450 latency showed neither difference nor equivalence over the four scalp regions.

Figure 3 depicts an example waveform illustrating comparable amplitudes between groups for P150 and N450 components over the left frontal electrode cluster.

DISCUSSION

Controversy exists regarding the neurologic implications of deformational plagiocephaly. Previously, Panchal et al.[11] used the Bayley Scales of Infant Development to examine infants with

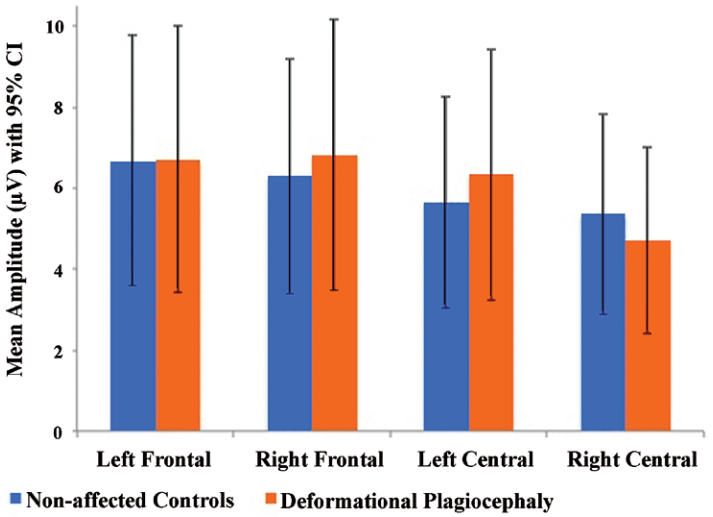

Fig. 2. Mean P150 amplitudes (with 95 percent confidence interval) from infants with plagiocephaly and nonaffected peers over several different scalp regions. The cortical responses to language are equivalent between the two groups.

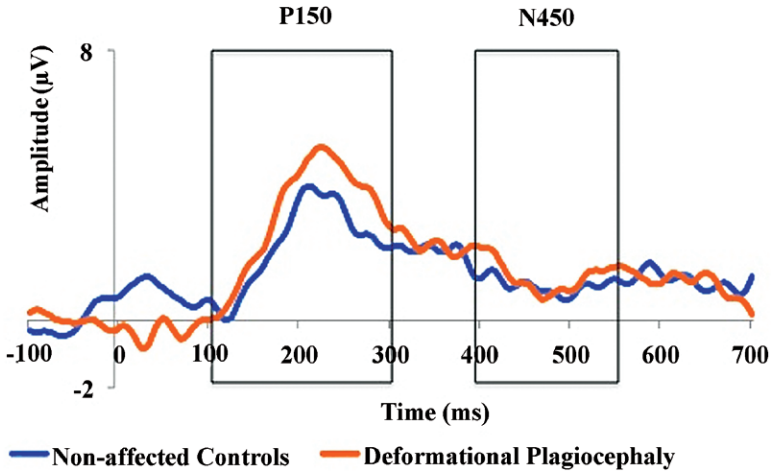

Fig. 3. Aggregate event-related potential waveforms from plagiocephalic and control infants over the left frontal scalp illustrating the P150 and N450 components.

head shape deformity secondary to either deformational plagiocephaly or craniosynostosis and reported mild delays in cognitive and psychomotor development. Collett et al.[12] followed individuals with deformational plagiocephaly up to 36 months, finding lower Bayley Scales of Infant Development scores in cognition, language, parent-reported adaptive behavior, and motor development. Although these studies raise concern for delay in early childhood, conclusions regarding long-term outcomes necessitate more sensitive and precise evaluations of neurodevelopment. Electrophysiologic assessments offer direct insight into neural perception. In other disorders of infancy, such measures of brain function have detected differences in contexts where behavioral methods were unsuccessful.[29] The precision of these direct recordings may provide a more reliable method of evaluation in young patients.

In the current study, we examined neural responses to speech in infants with plagiocephaly to evaluate the possible compromise of language functioning. Averaged responses from both patients and control subjects demonstrated prominent P150 and N450 deflections, consistent with the auditory waveform components typically evident in 6-month-old subjects.[27] In contrast to prior research,[26] infants with deformational plagiocephaly did not differ from controls with respect to the maximum P150 amplitude and latency. No significant P150 abnormalities were observed over either the frontal or central scalp that might suggest depressed cortical sound processing.

We also examined amplitudes and latencies of the N450 component in affected and nonaffected infants. Molfese[20] Previously measured N250 and N450 components in neonates and found that atypical responses correlated with poorer long-term verbal outcomes. Our results showed no evidence of abnormal N450 signals in infants with plagiocephaly.

In all, these responses indicate normative patterns of auditory processing in infants with deformational plagiocephaly. This study marks the first electrophysiologic examination to demonstrate that deformational plagiocephaly is not likely associated with significant impairments in language function.

Notably, our results differ from those of Balan et al.,[26] who previously reported decreased P150 and N250 amplitudes in a similar population and sample size. These contrasting observations may have resulted from differences in experimental stimuli, with our study using phonemes, rather than tones, to directly examine language processing.

In addition, the group statistical comparisons of Balan et al.[26] incorporated various forms of plagiocephalic head shape, including unicoronal and lambdoid craniosynostosis. Craniosynostosis and deformational plagiocephaly arise from markedly different pathophysiologic mechanisms and may share little in the form of neurodevelopmental implications. Even following surgical treatment, nonsyndromic craniosynostosis has been linked to an increased risk of mild long-term cognitive impairments and learning disabilities.[30–33] Including such patients in the evaluation of infants with deformational plagiocephaly may thus falsely skew results toward abnormalcy. As

such, we chose to exclude synostotic causes of plagiocephaly to more accurately examine the neurodevelopmental patterns of positional head shape deformity alone.

SUMMARY

We present data demonstrating normative patterns of language processing in infants with deformational plagiocephaly. These results indicate that nonsynostotic flattening of the occipital skull, now commonly associated with supine sleep, may not correlate with brain injury. Such information holds important ramifications for parents and physicians in light of the widespread implementation of the Back to Sleep campaign (now known as the Safe to Sleep campaign). Deformational plagiocephaly may represent a solely cosmetic condition, with plastic changes in the brain parenchyma allowing for the toleration of gradually acquired deformation.

It is important to consider that the scope of this investigation was limited to language systems, and other areas of brain functioning may be at risk in infants with deformational plagiocephaly. In this regard, the functional implications of our study are primarily relevant to auditory processing. Further electrophysiologic studies into other cognitive domains are needed to evaluate the array of developmental risks that these children may face. Long-term studies of affected infants are especially important, as only through school age intelligence and achievement testing can the cognitive implications of deformational plagiocephaly be conclusively determined.

The functional effects of corrective treatment with physical and helmet therapy also warrant clarification. To investigate these interventions, patients from this study are being followed longitudinally through their therapy protocols and assessed after treatment.

Given the rise in prevalence of infant head shape deformity and the limited utility of behavioral assessments in this age group, continued study into the processes of cognitive development is needed. Electrophysiologic measures may play a valuable role in understanding the neurologic networks of infant patients and helping to define proper recommendations for parents and physicians.

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