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## A longitudinal study of auditory evoked field and language development in young children

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#### ABSTRACT

The relationship between language development in early childhood and the maturation of brain functions related to the human voice remains unclear. Because the development of the auditory system likely correlates with language development in young children, we investigated the relationship between the auditory evoked field (AEF) and language development using non-invasive child-customized magnetoencephalography (MEG) in a longitudinal design.

Twenty typically developing children were recruited (aged 36–75 months old at the first measurement). These children were re-investigated 11–25 months after the first measurement. The AEF component P1m was examined to investigate the developmental changes in each participant's neural brain response to vocal stimuli. In addition, we examined the relationships between brain responses and language performance. P1m peak amplitude in response to vocal stimuli significantly increased in both hemispheres in the second measurement compared to the first measurement. However, no differences were observed in P1m latency. Notably, our results reveal that children with greater increases in P1m amplitude in the left hemisphere performed better on linguistic tests. Thus, our results indicate that P1m evoked by vocal stimuli is a neurophysiological marker for language development in young children. Additionally, MEG is a technique that can be used to investigate the maturation of the auditory cortex based on auditory evoked fields in young children. This study is the first to demonstrate a significant relationship between the development of the auditory processing system and the development of language abilities in young children.

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#### Introduction

Language acquisition in early childhood is one of the most fundamental human traits. Dramatic developmental changes occur in the brains of young children in concert with this ability (Sakai, 2005). Our previous magnetoencephalography (MEG) study reported that the auditory evoked brain response (i.e., P50m) to vocal stimuli in the left hemisphere was significantly correlated with language conceptual inference ability in normal 2- to 5-year-old children (Yoshimura et al., 2012) and 3- to 7-year-old children (Yoshimura et al., 2013). Although the relationships between longitudinal changes in the brain response to

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vocal stimuli and language development remain unknown, Choudhury and Benasich (2011) examined auditory responses to tone stimuli using electroencephalography (EEG) in longitudinal samples of typically developing children and children at higher risk for language disorders between 6 and 48 months of age. Their results demonstrated that infants with larger responses and shorter peak latencies from 6 to 9 months old had better language and cognitive skills at 3 and 4 years old. Moreover, other studies have reported that brain responses to auditory stimuli in infancy and childhood are associated with subsequent language-related skills (Espy et al., 2004) or language impairments such as dyslexia (Leppänen et al., 2010, 2012). However, to date, there has been no study that has followed this change in the brain response evoked by vocal stimuli using a longitudinal design or that has investigated its relationship to language development in young, typically developing children without family risk factors for language-related impairment (e.g., dyslexia).







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The purpose of this study was to investigate the relationship between longitudinal changes in the auditory evoked response (P1m) to vocal stimuli and language development in early childhood in typically developing children using MEG. A previous study demonstrated that the maturational patterns in auditory processing differ depending on the type of stimulus (e.g., speech or non-speech stimuli) (Pang and Taylor, 2000). In the present study, we focused on human voice-evoked responses. Understanding the normal maturation pattern of AEFs evoked by the human voice may aid in the development of neurophysiological techniques for evaluating the central auditory maturation that coincides with language development in young children.

P1(m) is a prominent component in 1- to 10-year-old children (Gilley et al., 2005; Oram Cardy et al., 2004; Ponton et al., 2002; Sharma et al., 1997) and provides insight into the development of auditory processing. P1m is thought to be a suitable metric for measuring changes in auditory input for speech-like signals (Chait et al., 2004; Hertrich et al., 2000). A recent study indicated that P1m is sensitive to the place-of-articulation features of speech and their co-articulatory processes (Tavabi et al., 2007). In previous MEG studies, this component has been alternatively labeled M50 (Oram Cardy et al., 2004) or P100m (Orekhova et al., 2012, 2013). In our previous study, this component was labeled P50m (Yoshimura et al., 2012). Some EEG studies have also labeled this component P1 (Gilley et al., 2005; Ponton et al., 2002). According to Orekhova et al. (2012), the P1m component at approximately 100 ms after stimulation is the most prominent component of the auditory evoked magnetic field response in children, and the equivalent current dipoles (ECD) of P1m have a predominantly anterosuperior direction. This component can be reliably identified in the majority of children because of its large amplitude (Oram Cardy et al., 2004). This component, which we analyzed in our previous study, was identical to the results of previous MEG studies (Oram Cardy et al., 2004; Orekhova et al., 2012; Pihko et al., 2007). To avoid confusion, we call this component P1m in the present study.

We hypothesize that changes in P1m amplitude/latency are correlated with language development in early childhood. The aim of this study was to investigate the brain response to human vocal stimuli measured using a longitudinal design in 3- to 7-year-old typically developing children and to investigate the relationship between language development and the changes in brain response.

#### Methods

#### Participants

Twenty children (3 females and 17 males) participated and were 36-75 months old at the first measurement. All children participated in additional measurements at 11- to 25-month intervals for 3 years. All participants were native Japanese and had no previous developmental, learning, or behavioral problems according to information obtained from their caregivers by questionnaire. All participants confirmed (through an interview with their caregivers) that they had no diagnosed hearing problems (mass screening at age 3) and that there were no hearing problems in their daily lives. Left- or right-hand dominance was determined based on the participants' preferences when handling objects, and all children were right-handed. All children participated in cognitive tasks and MEG measurements separately over 2 days. On the first day, the participants performed cognitive tests and were introduced to the environment used for the MEG measurements. The actual MEG measurements were performed on the second day. The caregivers consented to their child's participation in the study with full knowledge of the experimental nature of the research. Written informed consent was obtained from the caregivers prior to participation in this study. The Ethics Committee of Kanazawa University Hospital approved the methods and procedures, all of which were performed in accordance with the Declaration of Helsinki. The demographic data for all participants are presented in Table 1.

#### Table 1

Demographic characteristics of all participants.

	First measurement	Second measurement	t	Р
Number of subjects Gender (male/female) Chronological age (months) Head size (cm) K-ABC	20 17/3 51.0 (±9.7) 50.7 (±1.8)	69.0 (±8.9) 51.6 (±1.8)	22.20 5.37	<.0001 <.0001
Mental processing scale Achievement scale Language conceptual inference task (riddles)	98.2 (±7.8) 99.7 (±17.1) 96.6 (±17.2)	99.5 (±11.5) 100.1 (±12.7) 97.2 (±12.9)	0.13 0.11 -0.19	n.s. n.s. n.s.

K-ABC, Kaufman Assessment Battery for Children.

The values are the mean (and standard deviation) for chronological age, head size and standardized scores for the mental processing scale, achievement scale and language conceptual inference task in the K-ABC. n.s., not significant.

#### Cognitive and language performance measurements

The children were assessed using the Japanese adaptation of the Kaufman Assessment Battery for Children (K-ABC) (Kaufman and Kaufman, 1983), which is typically used to assess the cognitive skills of 30- to 155-month-old children. To confirm the standardized scores of the mental processing and achievement scales in children, subtests from this battery that are appropriate for the ages of the children were used. In this study, the potential correlation between one of the components of the AEF (i.e., P1m amplitude and latency) and performance on a single language-related task (i.e., a subtest of K-ABC 'riddles') in a previous study (Yoshimura et al., 2012) was assessed. In the riddle task, children must respond to the examiner's question, such as "Which fruit has a rounded shape with a depression at the top where the stem is attached? The color of the skin can be red, green, yellow, or a combination of these colors." In this case, the answer is "an apple." The riddle task consists of 32 questions, and the questions are presented in ascending order of difficulty. The linguistic level is defined by the child's degree of achievement. The K-ABC 'riddle' subtest reflects conceptual language inference abilities (Kaufman and Kaufman, 1983).

#### Magnetoencephalography recordings

The conditions in the first and second MEG recordings were completely identical to those detailed in our previous study (Yoshimura et al., 2012). MEG data were recorded using a 151-channel SQUID (Superconducting Quantum Interference Device), whole-head coaxial gradiometer MEG system for children (PQ 1151R; Yokogawa/KIT, Kanazawa, Japan) in a magnetically shielded room (Daido Steel, Nagoya, Japan) installed at the MEG Center of Yokogawa Electric Corporation (Kanazawa, Japan). The custom child-sized MEG system facilitates the measurement of brain responses in young children, which would otherwise be difficult using conventional adult-sized MEG systems. The child MEG system ensures that sensors are easily and effectively positioned for the child's brain and that head movements are constrained (Johnson et al., 2010). We determined the position of the head within the helmet by measuring the magnetic fields after passing currents through coils attached at 3 locations on the surface of the head, which served as fiduciary points relative to specific landmarks (the bilateral mastoid processes and nasion). Although we could not account for the effect of individual head shape on the accuracy of dipole estimation, to calculate ECD without magnetic resonance imaging anatomical data, a sphere (as a spherical model of the volume) conductor was fitted to the center of the helmet after confirming that each participant's head was located in the center of the MEG helmet by measuring the above-described three locations on the surface of the head (Yoshimura et al., 2012). An examiner remained in the room to encourage the children and to prevent movement throughout the analysis. Stimuli were presented while the

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