Effects of Recurrent Acute Otitis Media on Cortical Speech-Sound Processing in 2-Year Old Children

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Objectives: To investigate at the age of 2 years the effects of childhood recurrent acute otitis media (RAOM) on central auditory processing by using cortical event-related potentials elicited by syllable stimuli.

Design: During a 1-year period, 22- to 26-month-old children fulfilling the criteria for tympanostomy tube insertion in Oulu University Hospital, Oulu, Finland, were recruited to the RAOM group (N = 20). The control group (N = 19) was matched by age, sex, and mother's educational level. In both groups, children were typically developing and had no family history of language disorder or developmental language problems. Finnish syllables /ke:/ and /pi:/ as standards and their variants with changes in frequency, intensity, vowel, consonant, and vowel duration as deviants were used to record P1, N2, and mismatch negativity (MMN) responses in the multifeature paradigm. The clinically healthy ears at the time of registration were a prerequisite for the participation.

Results: Children with RAOM and their controls showed the age-typical P1 and N2 responses with no differences in the amplitudes or latencies between the groups, which suggests unaffected basic encoding of sound features and sound representation formation. However, the groups showed different auditory discrimination profiles. In children with RAOM, frequency and vowel MMN amplitudes were increased. Furthermore, the MMN latency for the frequency change was shorter and the frequency MMN amplitude lateralized to the left hemisphere in the RAOM group instead of an adult-like right-hemispheric lateralization observed in the controls. The children with RAOM had a more anterior MMN amplitude scalp distribution for the intensity change than control children. In addition, the MMN amplitude elicited by consonant change was evenly distributed unlike in controls, who had a left-side preponderant lateralization. Taken together, these results suggest an elevated responsiveness for frequency, vowel, and intensity changes, and an immature pattern of discriminating small speech sound contrasts in children with RAOM.

Conclusions: The results suggest that childhood RAOM does not affect the central auditory pathway integrity or sound encoding. However, RAOM may lead to aberrant preattentive discrimination of sound features even when the peripheral auditory input is normal. These results are clinically significant because even transient problems with auditory processing may delay language development.

Key words: Auditory processing, Children, Event-related potentials, Mismatch negativity, Otitis media.

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INTRODUCTION

During early childhood, about 30% of children undergo recurrent ear infections (Sipilä et al. 1987; Teele et al. 1989). Recurrent acute otitis media (RAOM) is most common during the first years of life and the incidence is increasing, partially because of large groups of children in day care centers (Teele et al. 1989; Möttönen & Uhari 1992; Hogan et al. 1997). Acute otitis media (AOM) causes fluctuating conductive hearing loss with a nadir of 20 to 30 dB (Koivunen et al. 2000; Ravicz et al. 2004), even 1 month after AOM (van Buchem et al. 1981). Medical care of children with RAOM has improved and only a few of these children have permanent deficits in peripheral hearing later in life (Valtonen et al. 2005). At the same time, effects of fluctuant hearing loss on immature central auditory system and language development remain under discussion.

Possible linguistic delays of children with RAOM are suggested to be consequences of auditory deprivation as a result of repeated periods of hearing loss (Whitton & Polley 2011). After the first report about linguistic and auditory problems in children with otitis media (OM) by Holm and Kunze in 1969, there were a series of studies supporting delayed language development (e.g., Wallace et al. 1988; Friel-Patti & Finitzo 1990; Teele et al. 1990; Luotonen et al. 1998; Winskel 2006) and auditory processing difficulties, such as weaknesses in auditory discrimination (Mody et al. 1999; Petinou et al. 2001), auditory memory (Mody et al. 1999; Nittrouer & Burton 2005), speech in noise listening (Gravel & Wallace 1992; Hogan & Moore 2003; Zumach et al. 2009), and dichotic listening (Asbjørnsen et al. 2005) as shown by behavioral methods. However, controversial findings with no developmental delays were also published (Roberts et al. 1995; Paradise et al. 2000, 2003, 2005, 2007).

The current knowledge emphasizes the need for identifying risk factors of early auditory development. Accurate functioning of the auditory system is a prerequisite for the optimal acquisition and sharpening of language-specific phonological representations (Benasich et al. 2006; Tallal & Gaab 2006; Kuhl et al. 2008). Phonological development is the first gate toward language, and its critical period takes a stance before the end of the first year (Kuhl 2010). During the first year of life, sensations of the first language induce permanent physiological changes in the central auditory nervous system, as demonstrated by studies on discrimination of native and non-native phoneme contrasts in infants (Kuhl et al. 1992, 2006; Cheour et al. 1998; Jansson-Verkasalo et al. 2010). Moreover, early auditory perception correlates with later behavioral measures of language development (Guttorm et al. 2005; Benasich et al. 2006; Maurer et al. 2009; Jansson-Verkasalo et al. 2010; for a review, see Kujala 2007).

In small children, it is complicated to study the functioning of auditory system with behavioral methods because cognitive skills and fluctuation of attention interfere with performance on tasks. Noninvasive brain research techniques were shown to be eligible for studying objectively neural processing from early infancy and even during the fetal period (Sambeth et al. 2006,

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2008; Huotilainen et al. 2005). These methods provide information on the underlying neural mechanisms of speech, language, and academic skills. Event-related potentials (ERPs), time-locked to stimuli with an excellent temporal resolution, provide a promising tool for examining auditory perception at different levels of central auditory system. These small changes in electrical activation of brain, elicited by external stimuli, are extracted from the EEG with their latencies and amplitudes reflecting the processing speed and accuracy (Kujala & Näätänen 2010).

Obligatory ERPs, such as the positive P1 and negative N2, represent cortical sensory processing of physical stimulus features received by the senses. Typically, the children's auditory P1 is elicited at about 100 msec and N2 at about 200 msec after the stimulus onset (Korpilahti & Lang 1994). The complex developmental effects on the morphology, amplitudes, and latencies of these responses in children are well documented (Čeponienė et al. 1998, 2002; Ponton et al. 2000; Choudhury & Benasich 2011). Generated by thalamic and cortical sources and preceding other more endogenous cortical components, the auditory P1 primarily reflects the integrity of central auditory pathway and basic encoding of sound properties (Sharma et al. 1997; Ponton et al. 2000). Children's auditory N2 is generated mainly by cortical sources and reflects sound representation formation—a crucial function for language development (Choudhury & Benasich 2011). However, the link between early auditory responses and language development is ambiguous. Some studies have shown atypical auditory P1 response in children with developmental language problems (Gilley et al. 2006) or auditory P1 to correlate with language development (Mikkola et al. 2007). However, normal auditory P1 amplitudes and latencies in children with language disorder have been reported (Korpilahti & Lang 1994; Kabel et al. 2009). Wagner et al. (2013) also suggested that there were no differences between the obligatory auditory ERPs elicited by non-native and native language syllable stimuli. In addition, attention may have an effect on auditory obligatory responses (Sanders et al. 2006; Karns & Knight 2009).

When a discriminable deviation occurs in some repetitive aspect of stimulation, the mismatch negativity (MMN) is elicited at 150 to 250 msec after the change (Näätänen et al. 1978; for recent reviews, see Kujala et al. 2007; Garrido et al. 2009; Kujala & Näätänen 2010; Näätänen et al. 2011). The auditory MMN reflects preattentive sound discrimination and sensory memory (Kujala 2007), and it has subcomponents that reflect speech memory traces (Pulvermüller & Shtyrov 2006) and their early development (Cheour et al. 1998). The MMN is usually recorded while the participant ignores the stimuli, which eliminates the effects of overlapping ERPs reflecting other cognitive functions. Elicited also when a participant is not attending the auditory stimuli, the MMN is an attractive tool to study auditory processing in children and infants. It can be detected even in fetuses and newborn babies, and its developmental trajectories during childhood are fairly well known (for a review, see Kujala & Näätänen 2010).

The so-called multifeature MMN paradigm ("Optimum-1"; Näätänen et al. 2004) was shown to be beneficial for studying auditory discrimination profiles of adults (Näätänen et al. 2004; Kujala et al. 2006; Pakarinen et al. 2009), school-age children (Lovio et al. 2010; Kujala et al. 2010), and toddlers (Putkinen et al. 2012; Niemitalo-Haapola et al. 2013). The great advantage of the multifeature paradigm, especially in measuring auditory profiles of children and clinical groups, is a short examination time with information on the MMNs for multiple variables during the same recording. Several kinds of deviants are included in the sound stream where the standard and deviants alternate. In deviants, one sound feature (e.g., frequency, vowel, intensity) of the standard stimulus is changed while the other features remain the same and strengthen the memory representation of the standard stimulus. Unlike the oddball paradigm, the stimulus variability of the multifeature paradigm more closely resembles speech. Furthermore, the multifeature paradigm might be more sensitive than the oddball paradigm for detecting deficits of auditory processing in clinical groups (Kujala et al. 2006).

In studies concerning the effects of OM, neurophysiological methods have not been widely used (for a review, see Whitton & Polley 2011). Auditory brainstem responses in children with a history of OM show signs of immaturity in neural integrity but no actual auditory neuropathy (e.g., Wallace et al.,1988; Gravel et al. 2006; Maruthy & Mannarukrishnaiah 2008). To date, the only study using the cortical auditory ERPs in investigating effects of OM was that by Maruthy and Mannarukrishnaiah (2008). They found that at 3 years of age, children with a history of OM had abnormally long auditory brainstem response latencies elicited by nonspeech click stimuli, whereas the latencies of cortical obligatory responses for the same clicks were decreased. The authors suggested that this may reflect possible compensatory changes at the higher level of central auditory system due to a longer conduction time at the level of brainstem. However, at 4 years of age no significant differences were found between these children and controls, which indicates that the changes observed may be reversible.

The purpose of the present study was to evaluate whether the childhood RAOM leads to atypical cortical neural encoding and preattentive discrimination of speech at the age of 2 years. The multifeature paradigm was used for recording P1 and N2 responses elicited by standard stimuli and MMNs elicited by frequency, intensity, vowel, consonant, and vowel duration changes in syllables. To our knowledge, this is the first study to use cognitive ERPs with linguistic stimuli to investigate the central auditory processes of children with RAOM.

PARTICIPANTS AND METHODS

Participants

On a 1-year scale in 2009–2010, all 24- ± 2-month-aged children whose history of ear disease was evaluated to be severe enough to meet the criteria (3 AOM per 6 months or 4 AOM per 1 year preceding period before EEG recording) for tympanostomy tube insertion in Oulu University Hospital's Ear, Nose, and Throat Clinic were recruited for the study. The total number of these children was 24. On the average, children came to the ERP recording 33 days (range 20 to 56 days) after the insertion of tympanostomy tubes. The study was approved by the Ethical Committee of the Northern Ostrobothnia Hospital District. An informed written consent was acquired from the parents of children and a supplement of 15 € was offered for travelling costs.

Inclusion criteria for both children with RAOM and controls were a normal gestation and full-term birth, with normal birth weight, monolingual Finnish-speaking family, and no family history of any speech, language, or developmental impairments or severe neuropsychiatric problems like schizophrenia. All children had to have a normal cognitive and motor development,

and no congenital hearing or visual abnormalities as assessed by parental questionnaires and at the family and healthcare clinics, where Finnish children are followed-up regularly during their first years of life. To exclude children with major language deficit like specific language impairment, the standardized Finnish version of the Reynell Developmental Language Scales III, the Comprehension scale (Edwards et al. 1997; Kortesmaa et al. 2001) was applied. The inclusion criteria for the EEG recording were clinically healthy ears proved by an otolaryngologist and the presence of transient evoked otoacoustic emissions (TEOAEs; nonlinear click sequence 1.5 to 4.5 kHz, 73 dB SPL, pass/refer result; MADSEN AccuScreen® pro, GN Otometrics, Taastrup, Denmark). TEOAEs of 4 children from the RAOM group and 6 children from the control group were not gained at the time of examination because of lack of children's cooperation, but all the children had passed a TEOAE screening at a postnatal period in Oulu University Hospital.

One child with RAOM had to be excluded because of a family history of dyslexia. Another child was excluded because the results of the Reynell Developmental Language Scales did not meet the criteria for normal speech comprehension, and an additional examination carried out by an experienced speech-language pathologist showed signs of severe language disorder and cognitive impairment. Families of 2 children did not arrive at the appointed time. Thus, the total number of children in RAOM group was 20 (Table 1).

Twenty-two children with a history of maximum two AOMs from volunteer families were recruited with a public advertisement and they served as a control group. Two control children had to be excluded from the analysis because of a large amount of alpha activity in the EEG and 1 child because of AOM diagnosed at the time of the recording. The remaining 19 children matched the research group with age (RAOM group mean 24 months, range 22 to 26 months, control group mean 24 months, range 22 to 26 months), sex (RAOM group 8 girls and 12 boys, control group 8 girls and 11 boys), and mother's education after 9 years of elementary school (RAOM group mean 6.2 years, range 0 to 10 years, and control group mean 8.1 years, range 3 to 14 years). The educational information of 1 mother in the RAOM group was not available. No significant differences between the groups were observed with two-tailed independent samples *t* test.

Stimuli and Procedure

The multifeature paradigm (see Näätänen et al. 2004) with five types of deviants was used to investigate P1, N2, and MMN responses. Stimuli were Finnish semisynthetic consonant–vowel syllables (Alku et al. 1999). The standard stimuli were /ke:/ or /pi:/ with the fundamental frequency (F_0) of 101 Hz and duration of 170 msec. Changes in deviants were frequency (F_0 ± 8%, lower 93 Hz/higher 109 Hz), intensity (± 7 dB), consonant (from /ke:/ to /pe:/ and from /pi:/ to /ki:/), vowel (from /ke:/ to /ki:/ and from /pi:/ to /pe:/), and vowel duration (from syllable length of 170 to 120 msec). Stimuli were presented quasirandomly so that every other stimulus was a standard ($p = 0.5$) and every other was one of the deviants or a novel environmental sound ($p = 0.08$ for each). The occurrence of the same deviant or a novel sound in succession was prohibited. Stimulus onset asynchrony was 670 msec. Stimuli were presented in the epochs lasting for about 6 min via loudspeakers (Genelec® 6010A, Genelec Ltd., Iisalmi, Finland) with the sound pressure level of 75 dB. Children heard three to four stimulus sequences, each starting with 10 standards and including 540 stimuli.

The EEG recordings were carried out in an electrically shielded and sound-attenuated booth with a reverberation time of 0.3 seconds and a background noise level of 43 dB. Children sat in a chair or in their parent's lap. To ignore the sounds the children watched voiceless cartoons and picture books, or played with silent toys. The loudspeakers were situated in front of the child at a distance of 1.3 m and in a 40 degree angle from the child's head. The child was camera monitored from the next room and the quality of EEG signal was observed by the experienced EEG technician.

ERP Recording and Analyses

EEG was recorded using ActiCAP 002 and Brain Vision BrainAmp system and software (Brain Products GmbH, Gilching, Germany) with 32 Ag–AgCl electrodes placed according to the international 10 to 20 system. The FCz electrode served as a common reference during the recording (sampling rate 5000 Hz, bandpass filter 0.16 to 1000 Hz). Ocular artefacts were detected by bipolar montage of electrodes placed above the outer cantus of the right eye and below the outer cantus of the left eye. Impedances were kept below 20 kohm and were checked after the movements of the child and between stimulus blocks.

The EEG was analyzed off-line with Brain Vision Analyzer 2.0 (Brain Products GmbH). To avoid aliasing and signals not originated from the brain (Luck 2005), off-line filtering of 0.5 to 45 Hz, 24 dB/oct was used. The data were down sampled to 250 Hz and rereferenced to the average of the mastoids. Seven EEG channels (Fp1, Fp2, PO9, PO10, O1, Oz, and O2) were disabled because of artefacts. Independent component analysis ocular correction was applied, and all the epochs containing voltage exceeding ± 150 μV were defined as artefacts and excluded from further analysis. Next, the data were filtered with band pass of 1 to 20 Hz, 48 dB/oct. The averaging was done for segmented and baseline corrected epochs (600 msec length, including the time window −100 to 0 msec prestimulus for baseline calculation) by combining ERPs for the standard stimuli /ke:/ and /pi:/, and in a same way clustering the ERPs for the frequency, intensity, vowel, consonant, and vowel duration deviants separately. The responses for novel stimuli were not included in this analysis, and will be reported in another publication. The first 10 standard stimuli in each recorded sequence and the standard stimuli right after the novel stimuli were not included in the average. A two-tailed independent samples *t* test indicated no significant differences between the groups in the means of accepted trials elicited by the standard and deviant stimuli (Table 2).

Because the MMN is known to be largest at fronto-central electrodes (Kujala et al. 2007), the channels selected for the further analysis were F3, Fz, F4, C3, Cz, and C4. A two-tailed *t* test was used to determine whether the amplitudes differed from zero. The obligatory responses and the MMNs for intensity, consonant, vowel, and vowel duration were determined at the Cz electrode. The MMN elicited by the frequency deviant was clearly right-hemispheric lateralized in the control group, and did not reach significance at Cz. Therefore, the frequency

TABLE 1. History of ear infections in children with recurrent acute otitis media

Child	Sex	First AOM Diagnosed (mos)	Number of Diagnosed AOM Episodes Before TTI	
			UNILAT	BILAT
1	M	2	2	2
2	M	1	8	1
3	M	5	7	5
4	F	9	0	4
5	M	3	4	2
6	M	5	7	0
7	F	11	8	1
8	F	8	3	1
9	M	4	4	2
10	M	10	2	3
11	F	1	5	1
12	M	7	3	4
13	F	14	0	3
14	M	15	0	3
15	F	14	2	3
16	M	17	1	2
17	M	14	1	4
18	F	19	0	4
19	M	18	1	3
20	F	18	4	1

AOM, acute otitis media; BILAT, bilateral acute otitis media; F, female, M, male; TTI, tympanostomy tube insertion, UNILAT, unilateral acute otitis media.

MMN was determined at the C4 electrode. The obligatory P1 and N2 were detected from the grand average waveform elicited by the standard stimuli and the difference waveforms (deviant minus standard) were used to identify the MMN. The peak latencies were determined from the most positive (P1) or negative (N2 and MMN) peaks in the response-specific time window reported in children (Lovio et al. 2010), and the peak amplitude values were calculated from the ± 24 msec (±6 data points) window centered around the peak (see Table 2).

The latency of each ERP response was compared between the RAOM and the control group with a one-way analysis of variance (ANOVA) at the Cz, except for the MMN elicited by the frequency deviant, which was compared at the C4. The amplitudes and amplitude scalp distributions of P1 and N2

TABLE 2. The average means of accepted trials and the time windows for the event-related potential peak detection in the controls and in the children with recurrent acute otitis media

Measure	Accepted Trials per Participant		Time Window (msec)
	Controls	RAOM	
P1	728 (88)	685 (125)	80–200
N2			200–300
Frequency MMN	147 (17)	136 (24)	150–300
Intensity MMN	145 (17)	137 (25)	150–350
Vowel MMN	146 (18)	138 (24)	150–300
Consonant MMN	145 (17)	136 (26)	150–300
Vowel duration MMN	146 (18)	138 (24)	200–400

Standard deviations in the parentheses.
MMN, mismatch negativity; RAOM, recurrent acute otitis media.

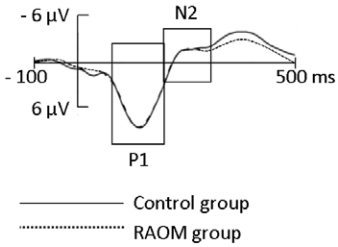

Fig. 1. The grand average waveforms elicited by standard stimuli at the Cz electrode in the controls and in the children with RAOM. There were no significant differences in the P1 or N2 amplitudes and latencies between the groups. RAOM indicates recurrent acute otitis media.

were compared with a repeated-measures three-way ANOVA including group (RAOM-control) as a between-subject factor, and fronto-central (F-C; F3-Fz-F4, C3-Cz-C4) and right–left (R-L; F3-C3, Fz-Cz, F4-C4) electrode location as within-subject factors. Furthermore, a repeated-measures four-way ANOVA including between-subject factor group, and within-subject factors deviant type, F-C, and R-L electrode location was used for MMN amplitudes and amplitude scalp distribution comparisons. When appropriate, the Huynh–Feldt correction was applied, and the sources of the significant effects were inspected with the Fisher's least significant difference (LSD) post hoc test. The partial eta squared (η_p^2) was checked for the effect-size estimation.

RESULTS

P1 and N2

The P1 and N2 responses (Fig. 1, Table 3) significantly differed from zero at the Cz ($p \leq 0.001$) in both groups. No significant amplitude, amplitude scalp distribution, or latency differences were found between the two groups.

Mismatch Negativity

All deviant stimuli elicited MMNs significantly differing from zero both in the children with RAOM and in the controls (Fig. 2, Table 4). A four-way repeated-measures ANOVA on MMN amplitudes and scalp distributions revealed a significant deviant main effect ($F(4,148) = 5.55$, $p = 0.0003$, $\eta_p^2 = 0.13$), which resulted from a stronger MMN for the vowel duration deviant than for other deviants in both groups ($p \leq 0.02$).

In addition, a significant Group × Deviant × F-C × R-L interaction ($F(8,296) = 2.46$, $p = 0.01$, $\eta_p^2 = 0.06$) was found. According to the post hoc tests, the MMN amplitude for the frequency

TABLE 3. The mean amplitudes and latencies of obligatory event-related potentials at the Cz electrode elicited by the standard stimuli in the controls and in the children with recurrent acute otitis media

	Amplitude (µV)		Latency (msec)	
	Controls	RAOM	Controls	RAOM
P1	8.8 (3.1)***	8.6 (3.7)***	137 (11)	139 (13)
N2	–2.2 (2.4)***	–2.0 (3.4)***	252 (24)	247 (23)

The amplitudes significantly differing from zero are marked with asterisks:
****p ≤ 0.001, standard deviations in the parentheses.*
RAOM, recurrent acute otitis media.

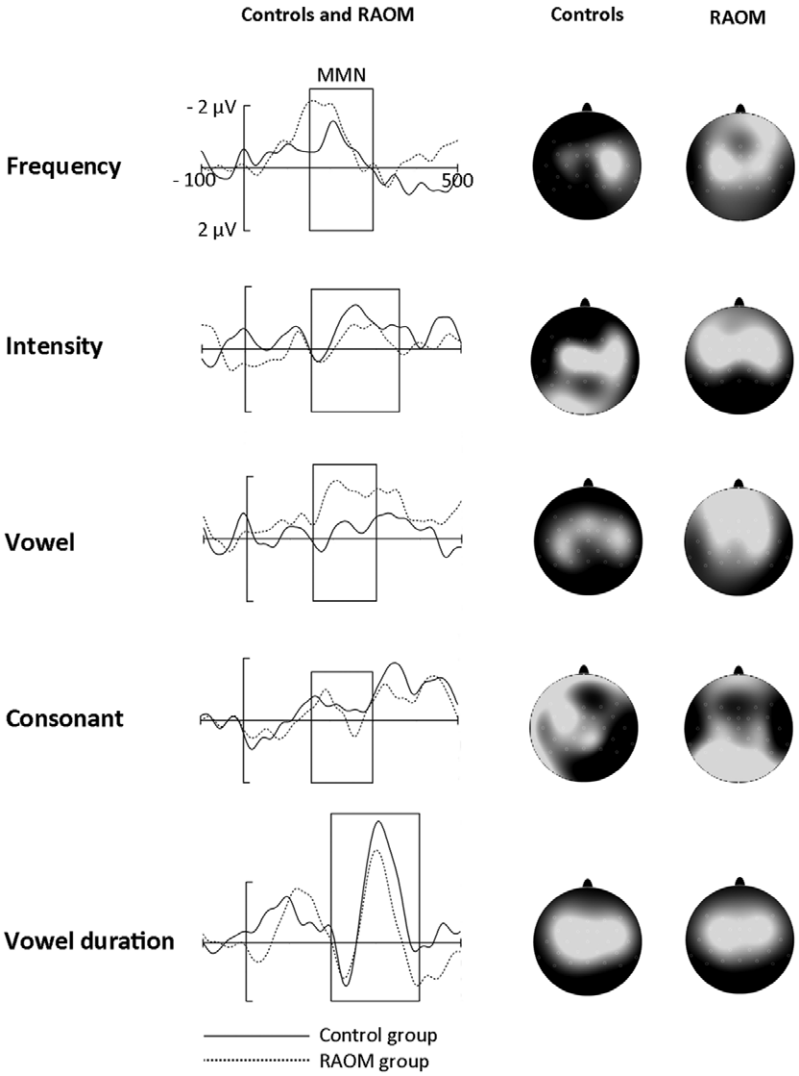

Fig. 2. MMN responses with amplitude scalp distribution for five deviant stimuli. Grand average difference waveforms (ERPs elicited by standard stimuli subtracted from ERPs elicited by deviant stimuli) and the time windows for MMNs are presented at the Cz electrode except the frequency at C4. MMN amplitude scalp distributions are presented from 26 electrodes, bright areas indicating negativity. ERP indicates event-related potential; MMN, mismatch negativity; RAOM, recurrent acute otitis media.

deviant was larger in the RAOM than control group at C3 and Cz electrodes ($p \leq 0.04$). The MMN amplitude for the vowel deviant was also larger in the children with RAOM than in controls at all electrodes in the analysis ($p \leq 0.05$) except at C3. The scalp distribution of the frequency MMN amplitude was lateralized to the left side in the RAOM group, and was strongest at C3 electrode ($p < 0.03$). In contrast, the control group showed a more prominent frequency MMN at the right-side C4 electrode than C3 ($p = 0.05$). The MMN for the intensity change was evenly distributed between the frontal and central electrodes in the RAOM group while it was strongest at the central electrodes in the control group ($p < 0.01$). Also, the consonant MMN was evenly distributed in the children with RAOM but was more prominent at the left-side electrodes in the controls ($p = 0.01$–0.07).

TABLE 4. The mean amplitudes and latencies of the mismatch negativities in the controls and in the children with recurrent acute otitis media

		Amplitude (µV)		Latency (msec)	
Deviant		Controls	RAOM	Controls	RAOM
Frequency	C4	–1.9 (2.6)**	–2.1 (2.6)**	235 (41)	211 (30)
Intensity	Cz	–2.4 (2.3)***	–2.0 (2.1)***	253 (41)	255 (39)
Vowel	Cz	–1.3 (2.6)*	–3.0 (2.0)***	233 (30)	226 (38)
Consonant	Cz	–1.7 (1.5)***	–2.1 (3.1)**	242 (39)	227 (40)
Vowel duration	Cz	–4.2 (2.8)***	–3.2 (2.4)***	189 (21)	180 (16)

The amplitudes significantly differing from zero are marked with asterisks:
****p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05.*
RAOM, recurrent acute otitis media.
Standard deviations in the parentheses.

Furthermore, the frequency MMN latency was shorter in the RAOM than in the control group ($F(1,38) = 4.25$, $p = 0.05$, $\eta_p^2 = 0.10$; 1-way ANOVA). There were no other MMN latency differences between the groups.

DISCUSSION

With the linguistic multifeature paradigm, we assessed cortical auditory processing of 2-year-old children with RAOM. We

found robust auditory P1 and N2 responses for /ke:/ and /pi:/ syllables. These responses were typical for children at this age (Ponton et al. 2000; Čeponienė et al. 2002; Kushnerenko et al. 2002), and there were no amplitude, amplitude scalp distribution, or latency differences between the RAOM and the control groups. This finding is in line with the study by Maruthy and Mannarukrishnaiah (2008), which showed equal sound-encoding efficacy and an equal or even faster cortical conduction rate for nonspeech click stimuli in children with the history of OM compared with the healthy controls. Together, these results suggest unaffected basic encoding and sound representation formation of both nonspeech and speech-like stimuli in children with RAOM.

In addition to recording obligatory auditory ERPs, we determined preattentive auditory discrimination ability with the MMN response (see Kujala & Näätänen 2010). Consistent with a previous study using similar stimuli as our study (Lovio et al. 2010) the MMN amplitudes were significantly stronger for the vowel duration deviant than for other deviants. In our study, this pattern was found both in the children with RAOM and controls. The enhanced vowel duration MMN amplitudes may result from the acoustical saliency and the semantically distinctive role of quantity in Finnish language.

The MMN amplitudes were significantly stronger both for the frequency and vowel changes in the children with RAOM than controls. Eapen et al. (2008) studied the effect of removing one of the three frequency bands from sentences on speech-perception performance on 5- to 7-year-old children with a history of OM and tympanostomy tube placement. These children had significantly poorer speech-reception threshold than their age-matched peers when middle frequencies (1575 to 2425 Hz) from sentences were omitted but did not differ from controls when high (3000 to 5000 Hz) or low (798 to 1212 Hz) frequencies were manipulated. This suggests that children with OM history weighted more the middle-frequency band to comprehend sentences than their controls. Furthermore, Eapen et al. suggested that the development of frequency perception may be affected by childhood OM. Consistent with this, our neurophysiological results in the children with RAOM showed larger MMN amplitudes to the frequency changes than was found in the controls. The enhanced MMN amplitude is linked to hypersensitive reactivity, that is, elevated responsiveness to the sound feature (Lepistö et al. 2005), and supports the theory that children with OM history may compensate for degraded auditory signal at the level of central auditory system. Furthermore, the second formants of the Finnish vowels /e/ and /i/ we used are in the region of 2 kHz, which Eapen et al. (2008) found to be weighted in children with OM. Thus, the increased vowel MMN amplitude in the children with RAOM gives further support for the frequency weighting theory. Children with RAOM possibly neurally use the frequency content of speech differently than their healthy peers, for example, process more efficiently prosodic features of speech to find word boundaries.

In addition to the MMN amplitudes, we found differences in the MMN amplitude scalp distribution between the groups, which refers to partially distinct neural sources of processing. Besides the magnitude and speed, the place of processing is an important factor reflecting the efficacy of neural functions (Tervaniemi & Hugdahl 2003). The most prominent group difference in the MMN amplitude scalp distribution was found for the nonphonetic frequency change. It was left-hemispheric lateralized in children with RAOM, whereas in the control group it was right-hemispheric dominant as usually reported in healthy adults (Kujala et al. 2007). The left hemisphere dominates the processing of phonetic contrasts and is thought to be specialized for the language-specific content of sounds (Tervaniemi et al. 2000; for a review see Tervaniemi & Hugdahl 2003). The shift of the frequency MMN to the left-hemisphere regions in children with RAOM might suggest that their auditory system gives more linguistic weight to the frequency changes of speech than that of their controls. This finding may also relate to compensation mechanisms connected with the attenuated auditory signals during RAOM, and further support the frequency weighting theory (Eapen et al. 2008).

For the intensity changes, children with RAOM had a broader and more anterior MMN scalp distribution than the controls. This possibly reflects attention shifting toward the stimuli because the unattended auditory stimuli predominantly activate the auditory cortex, and broader brain activation is observed when the stimuli are attentively listened to (Degerman et al. 2006). Attention shifting toward the changes may indicate hypersensitivity and distractibility of auditory perception. Otitis media may be one of the possible background mechanisms behind the hyperacusis, a clinical condition appearing as symptoms of hypersensitivity to sounds with normal-hearing levels (Anari et al. 1999). For example, compared with their peers, adolescents with repeated ear infection history are behaviorally more sensitive to the loudness of sound stimuli (Olsen Widen & Erlandsson 2004). Furthermore, there is a strong clinical and parental experience that children with ear infections may show signs of hypersensitivity to sounds.

We also found a broad MMN amplitude scalp distribution for the consonant deviant in the children with RAOM while it was left-hemispheric lateralized in the controls. The lateralization refers to a better-organized neural system (Tervaniemi & Hugdahl 2003) for consonant discrimination in the controls compared with the children with RAOM. This finding is consistent with behavioral studies showing worse consonant categorization abilities in children with OM than in their age-matched peers (Petinou et al. 2001), even years after the infections had resolved (Mody et al. 1999; Zumach et al. 2011). The consonant discrimination is a pivotal part of language development, and deficits in it can predict disordered language development (Kraus et al. 1996; Benasich et al. 2006).

Also the timing of preattentive auditory discrimination was altered in children with RAOM. We found a shorter MMN latency for the frequency change but not for the other changes in the RAOM than control group. The faster processing of the frequency changes only is consistent with our result of enhanced frequency processing, as reflected by the MMN amplitude and topography.

Taken together, our MMN results support the theory that the auditory system of children with a fluctuant hearing loss uses the frequency content of speech more efficiently than that of their controls (Eapen et al., 2008). They may also be more sensitive to the intensity of sound. In addition, they show signs of immaturity of neural organization for discrimination of small phonetic contrasts, as reflected by the MMNs for consonant changes.

Issues that might have to some extent affected the results of our study need to be discussed. First, it is well-known that OM causes fluctuant hearing loss, which further is linked to auditory

perceptual problems and difficulties in language acquisition (Zumach et al. 2011; Whitton & Polley 2011 for a review). To be able to assess the impact of OM on neurocognitive development, hearing level should be assessed at the time of OM. This was not, however, possible in our study. To get as homogenous group as possible, we decided to select a group of children whose history of middle ear infections was severe enough to fill the medical criteria of tympanostomy tube insertion in the Oulu University hospital area. From the mass of children with OM episodes, this clinical group was most probably undergoing a fluctuant hearing loss in infancy.

The second issue relates to the recruitment criterion. All the children in the RAOM group had tympanostomy tubes inserted unlike controls. The perforation of tympanic membrane may attenuate the peripheral transmission and the frequency content of sounds (Voss et al. 2001; see also Zhang et al. 2012) but there is a lack of studies comparing accurately the hearing of children with tympanostomy tubes versus children with intact tympanic membrane. Our results support the idea that the effect of inserted tubes was not reflected at the cortical level, because no differences in the early cortical sound encoding between the groups were observed. However, there is an urgent necessity for further research in this area.

Third, at the age of 2 years, the absolute exclusion of children with, for example, congenital auditory processing or attention-deficit disorders is challenging, even though we used the inclusion criteria with no family history and no professional or parental concerns of children's development. Children with OM may also exhibit language delay as a result of fluctuating hearing loss. Therefore, excluding children with signs of developmental language delay may accidentally result in excluding children with language delays caused by the RAOM. Yet, as severe language disorders, like specific language impairment, are known to modulate the MMN (for a review, see Kujala 2007), children suspected to have such disorders had to be excluded to avoid the contamination of the results. However, for this reason only 1 child had to be excluded, and we assume that this exclusion did not have a major impact on our findings.

This study included a homogenous age group of children to diminish intersubject variability, which is typical for children's ERPs. The variability might result from issues such as skull thickness, neural source orientations, variation of vigilance, artifacts, and individual differences in the neural development (Luck 2005). The intersubject variability in our study is consistent between the groups and with previous studies (e.g., Lovio et al. 2010), and there were no outliers in the groups. Thus, the differences between the groups found in this study may be considered reliable.

Our study is the first to report the effects of RAOM on the higher-level cortical speech sound processing. Precise auditory discrimination in early childhood helps to create exact memory representations that further avails to discriminate speech sound features also in degraded listening conditions (Kuhl et al. 1992, 2006). Because experiences affect development in a cumulative manner, even transient effects on sensory processes are significant (Whitton & Polley 2011). It would be important to increase the awareness of parents on the effects of fluctuating hearing loss with its consequences on speech perception, as well as compensatory strategies preventing the influence of degraded auditory input. These results also underline the importance of the identification of children who need intervention before linguistic problems are overt, in the medical care. The early intervention may prevent later deficits, for example, in reading and writing, which are very sensitive even to mild phonological problems (e.g., Leppänen et al. 2002; Bishop & Clarkson 2003; Maurer et al. 2009). In addition to clinical implications, our results point to the importance to take into account the history of ear infections when recruiting volunteers for the basic ERP research.

In conclusion, our results suggest that the early history of RAOM has no effect on sound-encoding accuracy and speed indexed by the auditory P1 and N2 responses for the standard syllable stimuli. However, preattentive auditory discrimination was atypical in the children with RAOM, as reflected by the enhanced MMN amplitudes for frequency and vowel changes, atypical MMN amplitude scalp distributions for the frequency, intensity, and consonant deviants, and a decreased MMN latency for the frequency deviant. In the future, expressive language and phonological development of these children should be analyzed to see whether the neural consequences of RAOM are overt at the behavioral level. Furthermore, it should be determined whether the changes observed are permanent or resolving after the auditory input is stabilized.

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