

AUDITORY CORTICAL NARROWING TO NATIVE SPEECH: CHANGES ACROSS  
DEVELOPMENT AND IMPLICATIONS FOR READING DIFFICULTY

By

Chang Gu

Dissertation

Submitted to the Faculty of the  
Graduate School of Vanderbilt University  
in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Psychology

December, 2014

Nashville, Tennessee

Approved:

Bruce D. McCandliss Ph.D.

Megan M. Saylor Ph.D.

Geoffrey F. Woodman Ph.D.

Paul J. Yoder Ph.D.

## ACKNOWLEDGEMENTS

First, I would like to thank my advisor and friend, Dr. Bruce McCandliss, for all his help and support for the past five years. You gave me an academic home and provided the training I needed on my career pursuit. I am proud to be a member of the Educational Cognitive Neuroscience lab and to have the distinction of being a doctoral student graduating of ECN lab at Vanderbilt Peabody, Peabody School of Education and Human Development, and the Psychology & Human Development Department.

I would like to thank my committee advisor and friend, Dr. Paul Yoder. I have enjoyed our friendship and I am so grateful to have you on my committee. Your encouragement and faith in my abilities has helped me gain confidence as a graduate student.

I would like to thank my committee professors Dr. Megan Saylor and Dr. Geoff Woodman for their help and guidance. I truly appreciate all the supports from you throughout my graduate study. I would also like to thank all of the members in ECN lab, Vanderbilt Psychology faculty and staff, who have always been more than gracious, always willing to help, and I have enjoyed their valuable assistance throughout my career.

Finally, thank you to my wife whom I met at Vanderbilt and my parents for everything. I would not be the person I am today without you.

This work was conducted under the support of NIH/NIDCD grant R01 DC007694 to Dr. Bruce McCandliss (B.D.M).

## TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENTS.....	ii
LIST OF TABLES .....	v
LIST OF FIGURES.....	vi
Chapter	
I. INTRODUCTION .....	1
Research Goals .....	6
II. METHOD .....	9
Participants .....	9
Design .....	11
Procedure .....	13
Data Analysis .....	16
III. STUDY 1: CROSS-LANGUAGE INVESTIGATION ON AUDITORY CORTICAL NARROWING IN ADULTS.....	18
Methods .....	18
Results .....	19
Discussion .....	24
IV. STUDY 2: DEVELOPMENTAL CHANGES OF AUDITORY CORTICAL NARROWING IN TYPICAL SCHOOL-AGE INDIVIDUALS.....	26
Methods .....	27
Central Questions .....	30

Results .....	32
Discussion .....	45
V. STUDY 3: DIFFERENTIAL CORTICAL NARROWING AND READING DIFFICULTY IN SCHOOL-AGE INDIVIDUALS.....	49
Methods .....	50
Results .....	51
Discussion .....	55
VI. GENERAL DISCUSSION .....	57
Auditory cortical narrowing in adults .....	58
Auditory cortical narrowing in school-age individuals .....	59
Auditory cortical narrowing in poor readers .....	62
Conclusion .....	63
APPENDIX .....	65
REFERENCES .....	67

## LIST OF TABLES

Table	Page
1. Behavioral measures of the three groups .....	28
2. ERP Amplitude of MMN and P3a from the three groups.....	35
3. GFP of MMN and P3a from the three groups .....	39
4. Behavioral measures of the two reading groups.....	50

## LIST OF FIGURES

Figure	Page
1. ERP waveforms of MMN to a native phonetic contrast .....	2
2. Proposed development of MMN native language effect .....	4
3. Perceptual narrowing to native speech in adults .....	12
4. Diagram of passive auditory oddball paradigm.....	14
5. ERP waveform of MMN from adults.....	20
6. ERP amplitude of MMN from the two language groups.....	21
7. GFP curves of MMN from adults.....	22
8. GFP of MMN from the two language groups.....	23
9. Proposed age-related change of MMN .....	32
10. ERP waveform of MMN from school-age individuals.....	33
11. Age-related change in ERP amplitude of MMN and P3a.....	34
12. GFP curves of MMN from school-age individuals.....	37
13. Age-related change in GFP of MMN and P3a.....	38
14. Age moderation brain-behavior relationship.....	43
15. Positive relationship between cortical narrowing and reading.....	45
16. ERP waveform of MMN from the two reading groups.....	52
17. Reduced amplitude of MMN from poor readers.....	53
18. GFP curves of MMN from the two reading groups.....	54

## CHAPTER I

### INTRODUCTION

Auditory cortical processing of speech sounds is influenced by one's native language experiences (Chandrasekaran, Krishnan, & Gandour, 2007; Kuhl & Rivera-Gaxiola, 2008; Näätänen, 2001; Yang Zhang, Kuhl, Imada, Kotani, & Tohkura, 2005). Previous cross-linguistic studies have demonstrated that adult listeners are sensitive in discriminating subtle differences between phonemes in their ambient language, but insensitive to phonetic contrasts that are non-native (Best, McRoberts, & Goodell, 2001; Tsao, Liu, & Kuhl, 2006; Werker & Tees, 2005). This phenomenon, often described as the 'perceptual narrowing to native speech', has been attributed to one's cortical speech processing becoming specialized toward, or 'tuned to' the native language over the course of development (Werker & Tees, 2002; Werker & Tees, 2005). Recent electrophysiology research further demonstrated that, the brain specialization, referred to as the auditory cortical narrowing to native speech, stems from the development of one's pre-attentive auditory discriminative processing in brain being shaped by the language-specific experiences (Kirmse et al., 2008; Näätänen, 2001; Winkler et al., 1999).

The brain processing of pre-attentive auditory discrimination is indexed by the mismatch negativity ERP component (MMN) (Näätänen, Paavilainen, Rinne, & Alho, 2007) (Figure 1). The response strength or the 'size' of MMN is correlated with a listener's behavioral-level auditory discrimination of speech contrasts (Cheoura, Korpilahti, Martynova, & Langa, 2001; Näätänen, 2001). The MMN is defined as the difference waveform between the auditory ERP to a stream of sound stimulus with frequent recurrence (the standard) and the ERP to occasionally occurring

stimuli with deviating properties (the deviant). When subtracting the standard ERP from the deviant ERP, a negative deflection i.e., MMN can usually be observed at 100~250 milliseconds after the stimulus onset (Figure 1).

Cross-language MMN studies have demonstrated that, among adult listeners, MMN response that is elicited by a native language speech contrast is typically stronger than MMN elicited by a non-native contrast (Näätänen, et al., 2007). This native language effect of MMN has been observed in adult subjects across different language populations (Jacquemot, Pallier, LeBihan, Dehaene, & Dupoux, 2003; Kirmse, et al., 2008; Winkler, et al., 1999). Importantly, the MMN native language effect is suggested as a neural signature reflecting that an individual's cortical speech processing is shaped by the subject's native language experiences over development and becomes specialized or 'narrowed' to native speech sounds (Kuhl & Rivera-Gaxiola, 2008; Yang Zhang et al., 2009; Yang Zhang, et al., 2005).

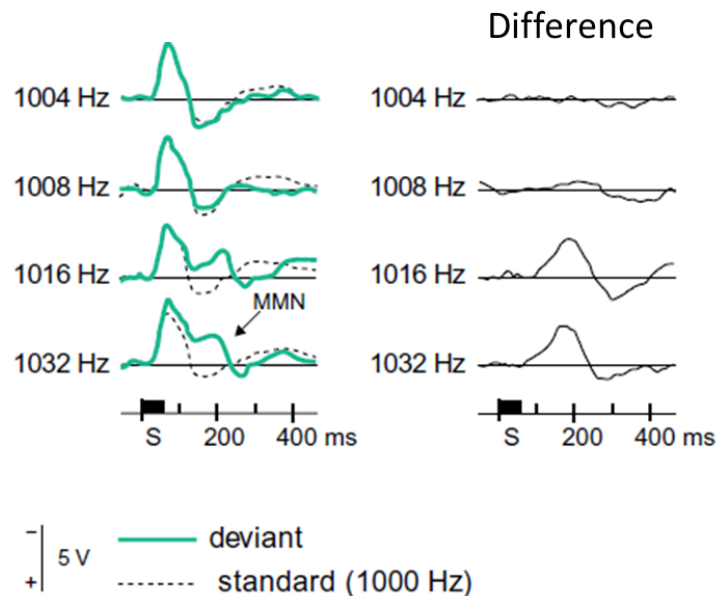


Figure 1. ERP waveform of MMN to sound contrasts. The left side of the figure displays the waveform of ERP response to the 'standard' 1000Hz sound stimulus and the waveforms of ERP response to the 'deviant' sound stimuli at different frequencies. The right side of the figure



displays the difference waveform (mismatch ERP) obtained by subtracting the standard stimulus ERP from that of the deviant stimulus for the different deviant stimuli. Mismatch Negativity (MMN) is elicited at 100~200 milliseconds (ms). Adapted from Naatanen et al., 2007.

The MMN native language effect and its close relationship to a listener's auditory cortical narrowing to native speech have been demonstrated by multiple ERP studies on adult subjects (Näätänen, 2001; Naatanen et al., 1997; Werker & Tees, 2005; Zevin, Datta, Maurer, Rosania, & McCandliss, 2010). Despite the extensive adult research, it remains unclear about how MMN develops under the influences of one's native language experiences in childhood and adolescence. In particular, the age-related change of MMN response to native and non-native speech sounds has not been systematically investigated among school-age individuals (Bishop, 2007; Cheoura, et al., 2001; Näätänen, et al., 2007). Until now, very few cross-sectional ERP studies have been conducted to map out the development of MMN native language effect on children and adolescents.

The current thesis investigates the development of MMN to native and non-native speech among school-age individuals from age 6 to age 17. Here, we propose a plausible development trajectory of the MMN native language effect after infancy: beyond the early emergence of MMN native language effect that has been well established in infants (for review, see Kuhl & Rivera-Gaxiola, 2008), we propose that MMN responses to native and to non-native phonetic contrasts continue to become increasingly differentiated across school-age individuals from childhood through late adolescence. This protracted development hypothesis for MMN native language effect signifies the continuous narrowing of one's auditory cortical systems for better processing native speech. Specifically, this hypothesis leads to two distinct predictions: (a) as language-specific experiences progressively sharpen a child's pre-attentive auditory discrimination, this

will result in a continuous increase in the MMN response to native phonetic contrasts, and (b) a continued lack of experiences with non-native language contrasts will serve to degrade cortical speech discrimination, thus resulting in a progressive decrease in MMN to non-native contrasts and the loss of sensitivity to non-native speech. Together, these two divergent development trends for MMN responses to native speech and MMN responses to non-native speech reflect an emergent underlying process, which can be described as a progressive narrowing of auditory cortical processing to native speech that continues beyond infancy, and progresses through both childhood and adolescence (Figure 2).

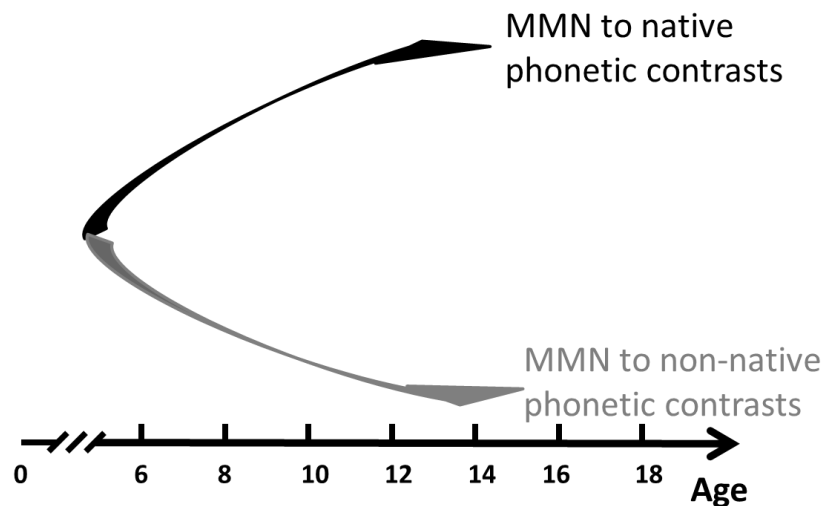


Figure 2. Proposed development of MMN native language effect. We predict that the response strength of MMN to native phonetic contrasts may increase and the response strength of MMN to non-native contrasts may decrease over development in school-age individuals from age 6 to age 17.

MMN not only offers a window for examining normative brain response of pre-attentive auditory discrimination from typically developing populations, it also provides a way to identify atypical patterns of cortical speech processing among individuals with dyslexia (Näätänen et al., 2012). The association between defective MMN and reading difficulties has been demonstrated

across different language populations (Bishop, 2007; Csépe, 2003; Heim & Keil, 2004; Leppänen & Lyytinen, 1997; Schulte-Körne & Bruder, 2010). Reduced response strength, delayed latency and abnormal hemisphere lateralization of MMN has been reported in children and adults with reading problems (Bishop, 2007; Cheour, Leppänen, & Kraus, 2000; Teija Kujala et al., 2000). Understanding the development of MMN and how it is influenced by the native language experiences among typical school-age individuals will lay a foundation for future dyslexia research.

It has been consistently demonstrated that the strength of MMN to native speech contrasts from dyslexic populations is significantly reduced relative to typical controls. Recently, an ongoing longitudinal electrophysiology study further demonstrated that, in addition to reduced MMN to native speech, school-age individuals with reading problems (6 to 15 years of age) tend to also have unusually large MMN to non-native phonetic contrasts, compared with their age-matched typical controls (Leppänen et al., 2012; Noordenbos, Segers, Serniclaes, Mitterer, & Verhoeven, 2012). The excessive MMN response to non-native speech sounds from dyslexic school-age individuals indicates their auditory discrimination is hypersensitive to speech elements that are not used in the ambient language, and further suggests that insufficient auditory cortical narrowing to native speech is one of the attributes of dyslexia (Bitz, Gust, Spitzer, & Kiefer, 2007).

In the current thesis, we propose that, lack of MMN native language effect can be one of the attributes of school-age individuals with reading difficulty. Specifically, in line with the protracted development hypothesis for MMN native language effect outlined above, we predict that typical school-age individuals (e.g. 6 to 17 years of age) will demonstrate progressively increasing MMN amplitudes for native phonetic contrasts and continuous decreasing MMN

amplitudes to non-native contrasts. However, we further hypothesize that this native language effect is not occurring to the same degree for school-age individuals with reading difficulty, and thus predict that, relative to typically developing children of the same age, they will demonstrate both weaker native MMN, and at the same time, larger non-native MMN. Such a pattern of findings would indicate that pre-attentive auditory discrimination is hyposensitive to native speech contrasts but hypersensitive to speech contrasts that are not used in their ambient language. Such proposed reduction in age-typical MMN native language effects in individuals with reading difficulties would provide additional support for theoretical accounts of reading difficulty that are linked to insufficient narrowing of auditory cortical processing to native speech sounds (Bitz, et al., 2007; Leppänen, et al., 2012; Noordenbos, et al., 2012).

### *Research Goals*

The current thesis aims to (a) examine the age-related change of MMN to native and non-native speech among typically developing school-age individuals and (b) examine whether reading difficulties in children are linked to developmental atypicalities in progressively emerging MMN native language effects. Investigating the developmental change of MMN native language effect will help us better understand how one's pre-attentive auditory discriminative processing, as reflected in MMN brain responses, become tuned to one's native language over development and how narrowing of cortical speech processing to native speech is related to reading development (Leppänen, et al., 2012; Noordenbos, et al., 2012).

Three electrophysiology studies are included in the current thesis. In Study 1 (Chapter 3), a cross-language MMN investigation was conducted on a group of English-speaking and a group

of Mandarin-speaking adults. An English-specific phonetic contrast and a Mandarin-specific phonetic contrast were presented as the MMN stimuli to both language groups. The response strength of MMN to the native contrast and MMN to the non-native contrast was examined across these two groups to (a) validate the MMN native language effect within the particular experimental procedure to be used throughout this thesis is linked to an interaction between experimental stimuli and language experience differences across the groups, and (b) validate the the association between MMN native language effects and psychophysical evidence of perceptual narrowing to native speech in adults. Findings from Study 1 lay the foundation of the following Study 2 (Chapter 4) on the age-related change of MMN native language effect among typical school-age individuals and Study 3 (Chapter 5) on the relationship between deficient MMN native language effect and reading difficulty.

In Study 2, cross-sectional comparisons were conducted on a large cohort of typically developing school-age individuals from age 6 to age 17, with the goal of mapping out age-related changes of MMN to native and non-native speech and assessing our theory that auditory cortical narrowing continues through late childhood and adolescence years. The English and the Mandarin MMN stimulus contrasts in Study 1 were presented as a native and a non-native phonetic stimulus to this cohort of English-speaking school-age individuals. The response strength of MMN from three age groups (age 6 to 9, age 10 to 13, and age 14 to 17) was compared to examine age-related changes of MMN to native and non-native speech over development. In addition to the cross-sectional comparison for the development of MMN native language effect, Study 2 further investigated the brain-behavioral relationship between auditory cortical narrowing and reading development in the school-age individuals. Multiple regression of the behavioral scores for reading fluency on the ERP response strength of MMN to native and non-native contrasts

provides a critical test of the hypothesis that auditory cortical narrowing to native speech is linked to fluent reading among typically developing school-age individuals.

In Study 3, the MMN native language effect was further investigated within a group of school-age individuals with low reading fluency, following the same experimental procedure from Study 2. The goal of Study 3 is to further investigate the hypothesis that insufficient narrowing of auditory cortical processing to native speech is demonstrated in individuals with reading difficulty. Specifically, we predict that individuals with low reading fluency will demonstrate reductions in MMN native language effects. Furthermore, the proposed hypothesis that cortical narrowing for native speech is diminished for poor readers makes two diverse predictions: relative to age-matched control typical readers, poor readers will exhibit both reduced MMN responses to native phonetic contrasts, yet enhanced MMN responses to non-native phonetic contrasts.

The goal of the current thesis is to advance our understanding of auditory cortical narrowing to native speech over the course of development and its potential relationship with reading difficulty among school-age individuals. Results from Study 1 (Chapter 3), Study 2 (Chapter 4) and Study 3 (Chapter 5) will shed light on how the development of auditory cortical processing can be substantially tuned by one's native language experiences and how deficiency of cortical narrowing to native speech is linked to reading problems.

## CHAPTER II

### METHOD

The experimental design and procedure described in this section are applied to Study 1, Study 2 and Study 3 in the next three chapters. Native and non-native phonetic contrasts are presented as the MMN sound stimuli in passive auditory oddball EEG paradigm (Bishop, 2007; Näätänen, 2001; Näätänen, et al., 2007). The response strength of MMN to the native phonetic contrast stimulus and the response strength of MMN to non-native contrast are statistically compared to assess the native language effect of MMN in adults, typical school-age individuals and individuals with reading difficulty.

#### *Participants*

In Study 1 (Chapter 3), 16 native English-speaking adults and 16 Mandarin-speaking adults were recruited in a cross-language ERP study. Details of the auditory EEG experiment will be described in the ‘Procedure’ section in the current Chapter 2. The EEG data from the Mandarin-speaking group were recorded at National Key Laboratory of Cognitive Neuroscience and Learning at Beijing Normal University, China, and data from the English-speaking adults were recorded at Psychology and Human Development at Vanderbilt University, United States in 2011 and 2012. All of the 32 adult participants were healthy, right-handed college students with no reported hearing or neurological problems. The participants were given written informed consent for the study.

For Study 2 (Chapter 4) and Study 3 (Chapter 5), we collected both EEG data and behavioral data from a cohort of 156 school-age children and adolescents from age 6 to age 17 in Nashville, Tennessee. This cohort of school-age individuals are native English speakers without exposure to Mandarin. The participants were recruited by telephone contact from a birth-record database. None of the 156 subjects were diagnosed with hearing or neurological problems. Among the 156 school-age individuals, 12 subjects did not finish the experiment and 4 subjects had low quality EEG data (see ‘Procedure’ section in the current chapter for details). Data from these 16 subjects were excluded. The rest of the 140 school-age individuals were included in Study 2 and Study. Importantly, the 140 subjects had diverse reading fluency: 24 exhibited age-standardized scores of Test of Word Reading Efficiency (TOWRE) below the 25th percentile. These 24 participants fell below the Study 2 reading inclusion criteria of >25th percentile performance in reading, and thus were not included from investigating the development of auditory cortical narrowing among typically developing individuals with fluent reading ability.

The rest of the 116 participants who had above the 25th percentile age-standardized TOWRE scores were considered typically developing readers. Their EEG and behavioral data are analyzed and presented in Study 2. Age-related developmental changes in the MMN native language effect was examined across three age groups: age 6-9 (n=47), age 10-13 (n=42) and age 14-17 (n=27). Cross-sectional comparisons on the MMN to native contrast and to non-native contrast between the three age groups were conducted to evaluate the extent to which development of pre-attentive auditory discrimination is progressively shaped by native language experiences beyond infancy and early childhood.

In Study 3, we investigate the hypothesis that insufficient auditory cortical narrowing to native language may contribute to reading difficulty. The MMN data from the 24 poor readers



describe above were systematically matched with 24 typical readers (i.e. TOWRE scores above the 25th percentile.) Direct comparisons between the response strength of MMN to native and non-native contrasts across both the poor reading group and the control group provided a specific test of our hypothesis that insufficient auditory critical narrowing to native speech is associated with reading difficulty.

### *Design*

Naturally produced English syllable pair /vi/ and /wi/ (abbreviated as /v-w/) and Mandarin syllable pair /tei/ and /te<sup>hi</sup>/ (abbreviated /j-q/) are chosen as the phonetic contrast stimuli of MMN for Study 1, Study 2 and Study 3. The sound spectrogram of the stimuli is presented in Supplement Figure 2 (Appendix). Mandarin and English are two languages having fundamentally different phonetic systems (Kuhl & Rivera-Gaxiola, 2008; Tsao, et al., 2006). The contrast /v-w/ is not used in Mandarin nor /j-q/ is used in English, and therefore each syllable pair forms a language-specific phonetic contrast.

We first carried out a pilot psychoacoustic ABX phoneme discrimination study (Dupoux, Pallier, Sebastian, & Mehler, 1997), to demonstrate the behavior-level perceptual narrowing to native speech in adults across the two language populations. The MMN contrast stimuli /v-w/ and /j-q/ used in the auditory oddball paradigm were presented to English-speaking adults (n=12) and Mandarin-speaking adults (n=12), with eight trials per contrast condition. The English group showed high discriminative sensitivity to the English contrast /v-w/ but low sensitivity to the Mandarin contrast /j-q/, whereas the Mandarin group showed the reverse pattern of phoneme discrimination accuracy for the contrast /v-w/ and /j-q/ (Figure 3).

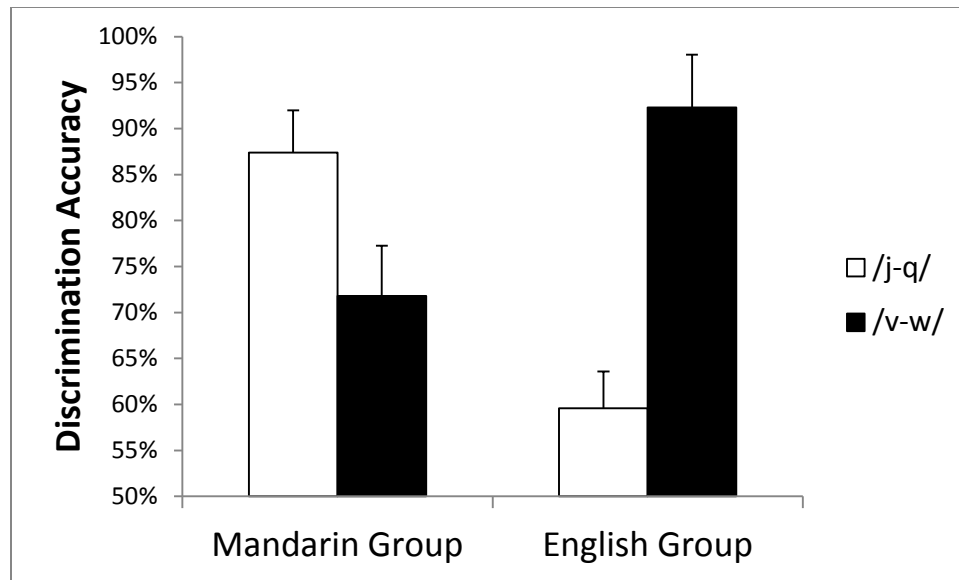


Figure 3. Perceptual narrowing to native speech in adults. Behavioral performance of ABX phoneme discrimination from English speakers and Mandarin speakers is displayed. Both groups showed higher discrimination accuracy to the native contrast than the non-native contrast.

For Study 1 on the Mandarin-speaking and English-speaking adults, the language-specific contrasts /v-w/ and /j-q/ are presented as standard and deviant pairs to elicit the ERP response of MMN to native speech and non-native speech contrasts. Within a contrast pair, each syllable served as the standard stimulus in one block and as the deviant in the other (two blocks per contrast). Therefore, each subject listens to 2 blocks of English condition (/v/ as the standard for one block, /w/ as the standard for the other) and 2 blocks of Mandarin condition (/j/ for the standard in one block, /q/ for the other), with a short 5-minute break between blocks. Auditory ERP response to the deviant stimulus and it to the standard stimulus preceding the deviant are computed by collapsing across the two blocks for /v-w/ and the two blocks for /j-q/ respectively (Näätänen, et al., 2007; Zevin, et al., 2010). Accordingly, for each of the phonetic contrast pairs i.e. /j-q/ and /v-w/, the deviant ERP and standard ERP are elicited by the same number of the two sound stimuli within the pair. The MMN to /v-w/ and the MMN to /j-q/ are computed by

subtracting the deviant ERP and standard ERP to control the ERP difference introduced by acoustic distinction of the two sounds within one contrast (May & Tiitinen, 2010; Näätänen, et al., 2007; Zevin, et al., 2010).

For Study 2 and Study 3 on the English-speaking school-age individuals, the same English contrast /v-w/ (referred to as native condition in Chapter 3 and 4) and the Mandarin contrast /j-q/ (referred to as non-native condition in Chapter 3 and 4) were delivered through identical auditory oddball paradigm as in Study 1 (two blocks with reverse standard and deviant for each phonetic contrast pair). In addition to /v-w/ and /j-q/, another phonetic contrast pair, /b-t/, was also presented as MMN stimulus in the last two blocks of EEG reading in Study 2 and Study 3. The /b-t/ contrast (referred to as the ‘acoustic condition’ in Chapter 3 and 4) has more pronounced acoustic differences than the contrast /v-w/ and /j-q/, because the consonant /b/ and /t/ differ in both voice onset time and place of articulation (Bishop, Hardiman, & Barry, 2010, 2011; Maurer, Bucher, Brem, & Brandeis, 2003). Therefore, we expect that robust MMN can be elicited by /b-t/ across individuals from the three age groups.

### *Procedure*

Identical auditory EEG recording procedure was applied to Study 1, Study 2 and Study 3. The EEG experiment was conducted in an acoustically shielded chamber. Participants were instructed to ignore the sounds while watching a selected animation movie. The movie was presented in mute mode on a portable DVD player positioned approximately 1 meter in front of the seat. For the adult participants in Study 1, the silent movie was presented with subtitles at the bottom of the screen. For the school-age individuals in Study 2 and Study 3, the movie was self-

explanatory with no subtitles. Sound stimuli were presented over a single free-field speaker positioned approximately 1 meter from the subjects, placed toward the center of the room, above the DVD player.

The auditory EEG was recorded through ‘passive auditory oddball’ paradigm (Bishop, 2007; Näätänen, et al., 2007; Näätänen, Pakarinen, Rinne, & Takegata, 2004). For Study 1, there were two blocks of MMN recording using the Mandarin /j-q/ contrast stimulus and two blocks of the English /v-w/ contrast stimulus. The order of the four blocks was counterbalanced across participants, so that half the participants heard the two blocks of Mandarin /j-q/ condition followed by the two blocks of English /v-w/ condition, and the other half heard the blocks in the reverse order. For Study 2 and Study 3, there were two blocks of MMN recording using the /v-w/ contrast (native condition), two blocks of the /j-q/ contrast (non-native condition) and two blocks of the /b-t/ contrast (acoustic condition), with the /b-t/ being the last two blocks of EEG recording. For each of the blocks (four blocks for Study 1, six blocks for Study 2 and Study 3), 723 syllable stimuli with stimulus onset asynchrony (SOA) of 650 milliseconds were presented to a subject in order to elicit the MMN ERP response (Figure 4). The “standard” sound stimulus was presented with the probability of 87.5% of the time, and the “deviant” stimulus was presented with 12.5%. There are at least 4 standards between the two consecutive deviants. All stimuli were delivered at 75 dB from a single loudspeaker placed at a distance of one meter from the subject.

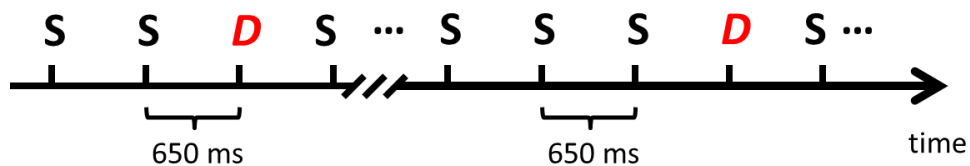


Figure 4. Diagram of passive auditory oddball paradigm. ‘S’ denotes that the ‘standard’ sound stimulus is presented and ‘D’ denotes that the deviant sound stimulus is presented. The stimulus onset asynchrony (SOA) in the oddball paradigm is 650 milliseconds (ms).

EEG data recording and off-line preprocessing followed the procedure of ‘EEG recording and preprocessing’ in Zevin, et al., 2010. The continuous EEG was recorded using a Hydrocel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR) referenced to Cz. Data were sampled at 500 Hz/channel with filters set at 0.1-200 Hz and calibrated technical zero baselines. Electrode impedances were below 50 k $\Omega$ . The off-line continuous EEG data from channels with excessive artifacts were spline-interpolated (no more than 15 channels per subject), and eye blinks were corrected using the standard ICA module in EEGLAB (Delorme & Makeig, 2004). To obtain the ERP for deviant and the standard stimulus, data were then digitally filtered band-pass from 0.3~30 Hz (24dB/oct, zero phase), re-referenced to the average reference, segmented as epochs relative to stimulus onset (-100~500 milliseconds for Study 1, -100~600 milliseconds for Study 2 and Study 3), and baseline corrected (100 milliseconds pre-stimulus interval) in EEGLAB. Trials with artifacts exceeding  $\pm 75\mu\text{V}$  in any channel were rejected. 4 of the 144 school-age participants who completed the experiment had more than half of the single-trial EEG segments being rejected when the  $\pm 75\mu\text{V}$  segment rejection was applied. The EEG data from these four subjects were considered having low quality and were not included in the following data analyses. The deviant-minus-standard difference waves i.e. the mismatch ERPs were calculated for each of the rest 140 participants for each condition in Study 2 and Study 3.

### *Data Analysis*

For Study 1, Study 2 and Study 3, an individual's MMN response strength i.e. 'size' of MMN was quantified by two measures: (a) the ERP peak amplitude on landmark electrode Cz (Bishop, 2007; Cheour, et al., 2000; May & Tiitinen, 2010; Näätänen, 2001; Näätänen, et al., 2007) and (b) the peak value of global field power (GFP) (Brunet, Murray, & Michel, 2011; Skrandies, 1990).

To investigate the MMN native language effect on Mandarin-speaking and English-speaking adults in Study 1, the ERP peak amplitude of MMN to the English-specific speech contrast /v-w/ and the amplitude of MMN to the Mandarin-specific contrast /j-q/ were measured as the negative maximum between 100 ~ 250 milliseconds on Cz for each adult, after averaging across 10 consecutive time frames (20 milliseconds) of the standard-deviant mismatch ERP data. For Study 2 and Study 3 on English-speaking school-age individuals, an individual's ERP peak amplitudes of MMN to the acoustic contrast /b-t/, native contrast /v-w/ and non-native contrast /j-q/ were measured as the negative maximum between 50 ~ 200 milliseconds on Cz after averaging across 10 consecutive time frames of the mismatch ERP data (Bishop, et al., 2011; Cheour, et al., 2000; Kraus et al., 1996).

In addition to the ERP peak amplitude as a measure of the 'size' of MMN, Global Field Power (GFP) that does not require pre-selecting a landmark EEG electrode was calculated for the mismatch ERP under each condition, in order to measure an individual's whole-brain response strength of MMN (Brunet, et al., 2011; Murray, Brunet, & Michel, 2008). GFP of a standard-deviant mismatch ERP at each moment in time was calculated for instantaneous response strength across all 128 channels. Here, we adopt the idea of GFP being the power increase that exceeds the

average value of GFP across time frames of the -100 to 0 milliseconds pre-stimulus baseline period. Accordingly, we divided each instantaneous GFP after the stimulus onset by the mean GFP during the baseline period for each individual MMN. By doing so, the general difference of inter-subject EEG amplitude, for example due to differences of skull conductivity, was adjusted (Brunet, et al., 2011; Murray, et al., 2008). Finally, after averaging across 10 consecutive time frames, GFP peak value (in 100~250 milliseconds for Study 1, in 50~200 milliseconds for Study 2 and Study 3), which reflects the maximum of the whole-brain response strength of MMN to a phonetic contrast from an individual, was compared between subject groups and stimulus conditions.

It has been documented that the latency of certain auditory ERP components such as N1 and P2 can change over the course of development (Bishop, 2007; Cheour, et al., 2000). The choice of time windows to measure the response strength of MMN at individual level, i.e. 100~250 milliseconds for Study 1 and 50~200 milliseconds for Study 2 and Study 3, is based on visual inspection of grand-averaged MMN waveforms on landmark electrodes including Cz, Fcz and Fz. The approach of utilizing visual inspection to determine the time window of MMN for following statistical analysis has been frequently used across previous studies on children and adults (Bishop, 2007; Bishop, Hardiman, Uwer, & Von Suchodoletz, 2007; Bishop, et al., 2011; Cheour, et al., 2000).

## CHAPTER III

### STUDY 1: CROSS-LANGUAGE INVESTIGATION ON AUDITORY CORTICAL NARROWING IN ADULTS

The primary goal of Study 1 is to verify that, the desired MMN native language effect which indexes auditory cortical narrowing to native speech is presented in adult listeners (Näätänen, 2001; Naatanen, et al., 1997; Winkler, et al., 1999). Thus, we conducted a symmetric cross-language MMN experiment to investigate to what extent the response strength of MMN to a native phonetic contrast is different from it to a non-native contrasts (Winkler, et al., 1999). Findings from Study1 will allow us to confirm whether adult individuals' cortical speech processing is fundamentally influenced by language-specific experiences (Näätänen, 2001; Naatanen, et al., 1997; Zevin, et al., 2010; Yang Zhang, et al., 2005). Study 1 would lay the foundation for Study 2 on the age-related changes of the MMN native language among school-age individuals.

#### *Methods*

16 native English-speaking adults and 16 Mandarin-speaking adults participated in the cross-language ERP study. Details of the participants and EEG data collection were described in Chapter 2.

An individual's MMN response strength i.e. 'size' of MMN was quantified by two measures: (a) the ERP peak amplitude on landmark electrode Cz and (b) the peak value of global



field power (GFP) (Brunet, et al., 2011; Skrandies, 1990). Study 2 and Study 3 also use these two measures for the MMN response strength. To examine the MMN native language effect, paired t-comparison between the native and the non-native condition was conducted within each group to evaluate the response strength difference of MMN to the native and the non-native phonetic contrast.

### *Results*

Waveform of MMN. The symmetric cross-language design allowed us to verify that to what extent adults' MMN response that indexes the pre-attentive auditory discrimination is influenced by native language experiences. The standard-deviant mismatch ERP was calculated for the native and the non-native condition on both language groups. The grand-averaged waveforms of MMN on electrode Cz are displayed in Figure 5. The ERP topography of MMN is displayed in Supplementary Figure 1 (Appendix). Robust MMN (peaked at ~200 milliseconds) was found under the native condition across both groups. In contrast, the MMN to the non-native contrast was greatly reduced from both groups.

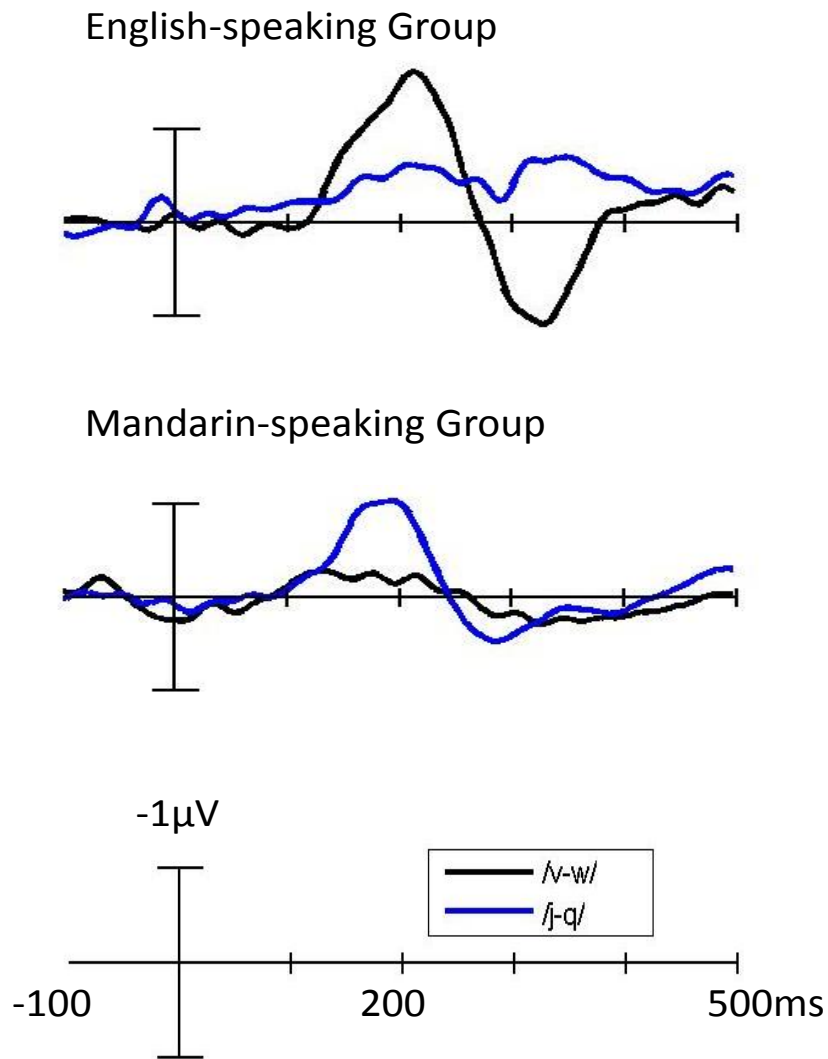


Figure 5. ERP waveform of MMN from adults. Both Mandarin-speaking adults and English-speaking adults showed robust MMN to the native phonetic contrast and reduced MMN to the non-native contrast on electrode Cz at 100~250 milliseconds (ms).

Amplitude of MMN. The ERP peak amplitudes of MMN were measured as the negative maximum between 100 ~ 250 milliseconds on Cz after averaging across 10 consecutive time frames (20 milliseconds) from each individual. A group (Mandarin, English) x contrast (/j-q/, /v-w/) 2-way repeated measure ANOVA was conducted on the MMN ERP amplitude to examine the main effects and interaction between these variables. A significant crossover interaction was

found ( $F(1, 31) = 17.3, p < 0.0001$ , Figure 6). Within-group pairwise t-comparisons revealed that the ERP amplitude of MMN to the native contrast is significantly larger than that to the nonnative stimulus across both language groups (Mandarin Group:  $t(15) = 5.12, p < 0.001$ , English Group:  $t(15) = 3.01, p < 0.01$ ).

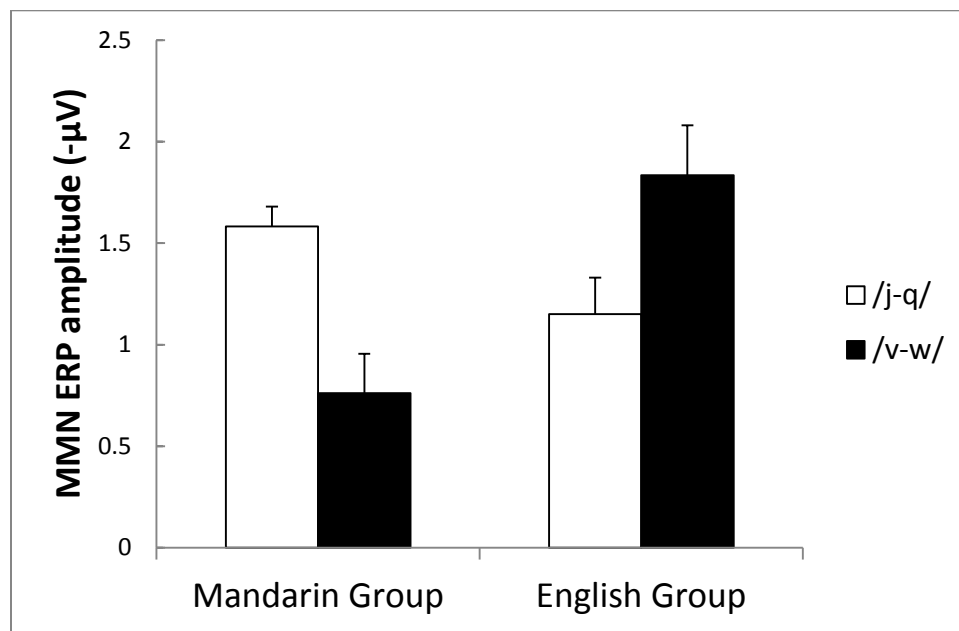


Figure 6. ERP amplitude of MMN from the two language groups. Significant crossover interaction between group and condition was found. Both groups of adults showed significantly larger MMN to the native contrast than the non-native contrast.

GFP of MMN. The Global Field Power (GFP) of mismatch ERPs to /v-w/ and /j-q/, which captures the whole-brain response strength of MMN, was displayed in Figure 7. After averaging across 10 consecutive time frames, the GFP peak value from 100 to 250 milliseconds, which characterizes the maximum of the whole-brain response strength of MMN, was measured from individual subjects for comparison. The GFP of MMN showed a crossover interaction between

the language group and phonetic contrast similar to the ERP amplitude of MMN ( $F(1,31) = 27.6$ ,  $p < 0.0001$ , Figure 8.). The within-group paired t-tests between the two contrasts also revealed significant larger GFP of MMN to the native contrasts across both groups (Mandarin group  $t(15) = 3.26$ ,  $p < 0.01$ , English group,  $t(15) = 5.74$ ,  $p < 0.001$ ).

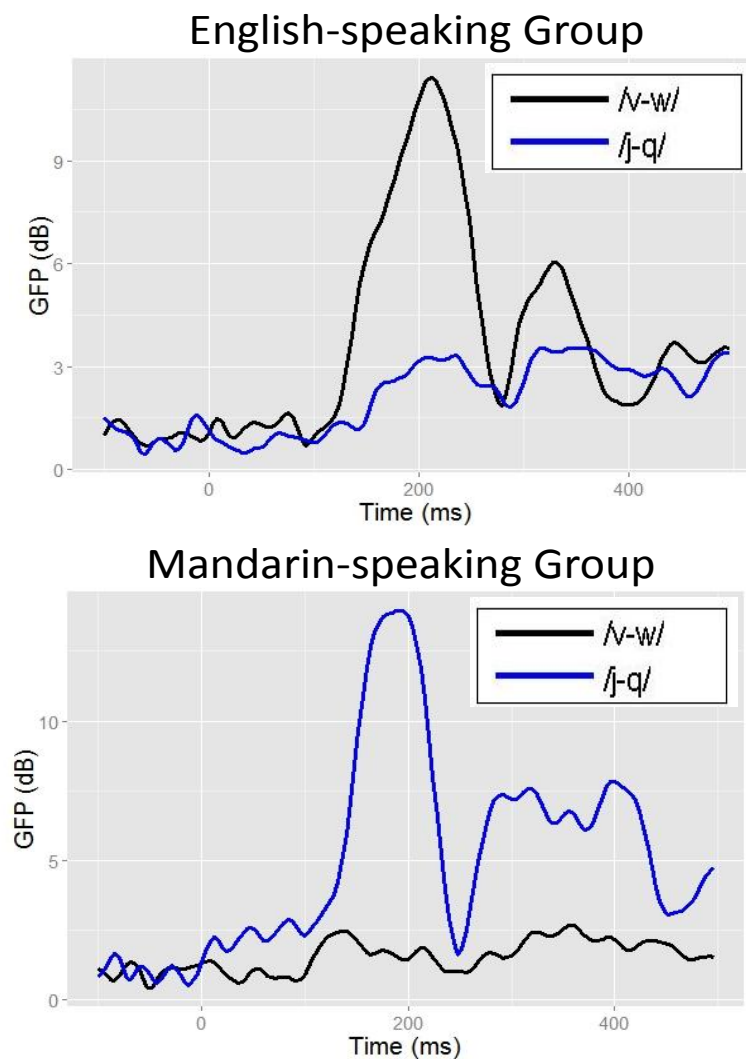


Figure 7. GFP curves of MMN from adults. Both Mandarin-speaking adults and English-speaking adults showed large GFP of MMN to the native phonetic contrast and small GFP of MMN to the non-native contrast.

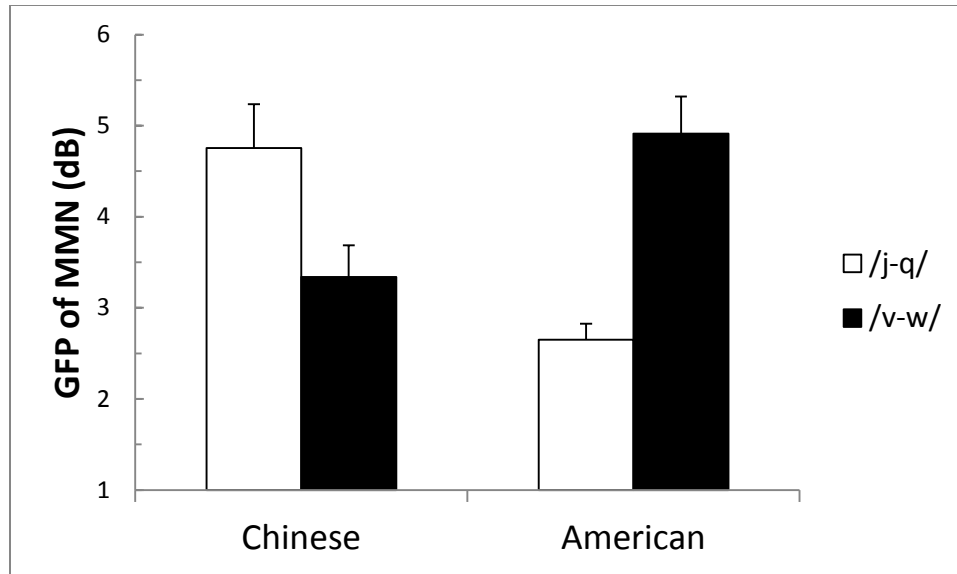


Figure 8. GFP of MMN from the two language groups. Similar the pattern of ERP amplitude of MMN, both groups showed significantly larger GFP of MMN to the native contrast than to the non-native contrast.

In Study 1, we found that the response strength of MMN (measured by ERP peak amplitude and GFP) varies as the function of an individual’s native language: both language groups showed enhanced MMN response to the native contrast than to the non-native phonetic contrast. The crossover interaction (Figure 6 and Figure 8) verified the MMN native language effect in adults and indicates that an adult’s pre-attentive auditory discriminative processing is ‘tuned’ to native speech (Kirmse et al., 2008; Winkler et al., 1999).

P3a. In addition to MMN component i.e. the negative deflection at 50 to 200 milliseconds, the mismatch ERP to native contrasts also presented a positive deflection at 250 to 400 milliseconds following MMN (Figure 5, Supplementary Figure 1). This positive ERP component is referred to as auditory P3a component (Escera, Alho, Winkler, & Näätänen, 1998; Escera & Corral, 2007; Tsang, Jia, Huang, & Chen, 2011; L. Zhang, Xi, Wu, Shu, & Li, 2012). It has been suggested that the P3a indexes the second state of auditory cortical processing, the involuntary

orienting to deviant sounds. Theoretically, when the brain encounters a sound change, the central auditory systems automatically (a) detect the deviance and (b) orientate to the sound deviance. These two stages of cortical processing of sounds, referred to as pre-attentive auditory discrimination and involuntary orienting, are indexed by the MMN and the P3a respectively (Escera, et al., 1998; Escera & Corral, 2007; Horváth, Winkler, & Bendixen, 2008; Tsang, et al., 2011). The waveforms of the mismatch ERP from Study 1 revealed that, in both the Mandarin speaking and the English speaking adults, the native phonetic contrast not only elicited robust MMN but also elicited the following P3a. Comparing to the non-native condition, the enhanced MMN and P3a responses under the native condition across both groups indicate that, adults' auditory cortical processing is tuned to their native speech.

### *Discussion*

Study 1 verified the MMN native language effect under our experimental procedure and demonstrated the auditory cortical narrowing to native speech in Mandarin-speaking adults and English-speaking adults. It. Using a symmetric cross-language design, we isolated the native language effect on MMN and P3a from both language populations (Winkler, et al., 1999). We found that the MMN to the native phonetic contrast is significantly larger than the MMN to the non-native contrast across both subject groups. This result indicates that an adult's brain processing of auditory discrimination is profoundly shaped by the native language experiences. The enhancement of MMN response strength under the native condition is consistent with previous studies, in which the MMN has been demonstrated as a neural correlate of the perceptual narrowing to native speech (Kirmse, et al., 2008; Näätänen, 2001; Naatanen, et al., 1997;

Näätänen, et al., 2007; Winkler, et al., 1999). In addition to MMN, we also uncovered the native language effect on P3a. That is, similar to MMN, the presence of P3a, which indexes the cortical stage of involuntary orienting in auditory speech processing, was also specific to the native speech condition in both language groups.

To sum, the native language effect on MMN and P3a revealed in Study 1 supports our hypothesis that an adult individual's cortical speech processing is specialized or tuned to native language (Näätänen, 2001; Näätänen, et al., 2007). It sets the stage for Study 2 on the development of MMN native language effect and continuous narrowing of cortical speech processing among school-age children and adolescents.

## CHAPTER IV

### STUDY 2: DEVELOPMENTAL CHANGES OF AUDITORY CORTICAL NARROWING IN TYPICAL SCHOOL-AGE INDIVIDUALS

Study 1 has demonstrated native language effect on MMN and P3a in adults that indexes their auditory cortical narrowing to the native speech. Study 2 aims at investigating the development of the native language effect on cortical speech processing from late childhood through adolescence years (Bishop, 2007; Čeponienė, Rinne, & Näätänen, 2002; Cheour, et al., 2000; Cheoura, et al., 2001). Specifically, we investigated the age-related change in the response strength of MMN and P3a among typical school-age individuals from age 6 to age 17. We propose that, the auditory cortical narrowing to native speech continues after infancy, such that the response strength of MMN indexing auditory discrimination and P3a indexing involuntary orienting to a native phonetic contrast continuously increases, while the strength of MMN and P3a to a non-native phonetic contrast continuously decreases in late childhood through adolescence years. To investigate the development of native language effect, a cross-sectional study was conducted on a large cohort of typically developing individuals from age 6 to age 17, with the goal of mapping out the developmental trajectory of MMN and P3a to native and non-native phonetic contrasts. This normative development of auditory cortical processing for native and non-native speech will serve a reference for the Study 3 on the association between insufficient auditory cortical narrowing and reading difficulty.



## *Methods*

All methods were the same as Study 1, except as follows.

Participants. 156 school-age children and adolescents were recruited and 144 of these participants completed the EEG experiment. This cohort of subjects consisted of healthy individuals from age 6 to 17 in Nashville, TN. They are native English speakers without exposure to Mandarin. Participants were recruited from Vanderbilt children database. None of the participants were diagnosed with hearing or neurology problems. 12 subjects did not complete the experiment and 4 subjects had low quality EEG data (see chapter 2 for details). Data from these 16 subjects were excluded from the analysis.

The 140 individuals included had diverse reading fluency: 24 of them had age-standardized scores of Test of Word Reading Efficiency (TOWRE) below the 25<sup>th</sup> percentile. We considered these 24 individuals being ‘poor readers’ and excluded their data in Study 2. Their EEG and behavioral data were examined in Study 3, which investigates our hypothesis that deficient auditory critical narrowing to native speech is one of the attributes of reading difficulty. The rest 116 participants who had above the 25<sup>th</sup> percentile age-standardized TOWRE scores were considered being ‘typical individuals’ with normal reading fluency. Their data are presented in the current Chapter 4. In order to examine the age-related change in the native language effect on MMN and P3a, the 116 subjects were divided into three age groups for Study 2, namely Age 6-9 group (n= 47), Age 10-13 group (n=42) and Age 14-17 group (n=27). Cross-sectional comparisons on response strength of MMN and P3a between the three age groups were conducted to evaluate age-related changes in auditory discrimination and attentional orienting to native and non-native phonetic contrasts among typical English-speaking school-age individuals.

Procedure. Study 2 consists of a behavioral assessment session (0.5 hrs) and an auditory EEG recording session (1.5 hrs). In the behavioral session, standardized assessments including Matrix Reasoning from Wechsler Abbreviated Scale of Intelligence (WASI), Test of Word Reading Efficiency (TOWRE), Elision and Memory for Digits from Comprehensive Test of Phonological Processing (CTOPP) were given to each participant. The scores of these standardized assessments provide behavioral measures of an individual’s non-verbal IQ, reading fluency, phoneme omitting and auditory working memory (Table 1). In particular, the age-standardized score of TOWRE, which captures an individual’s reading fluency, was used to (a) differentiate poor readers and typical readers and (b) conduct regression for the brain-behavior relationship between the response strength of MMN and P3a and reading fluency.

Table 1. Behavioral measures of the three age groups

	Age 6-9 (n= 47)		Age 10-13 (n=42)		Age 14-17 (n=27)	
	M	SD	M	SD	M	SD
Age	8.45	1.07	11.83	1.17	16.13	1.29
<i>Behavioral Measures</i>						
TOWRE	114.49	9.89	105.60	12.25	102.22	7.19
Elision	12.49	2.52	10.81	2.22	10.19	2.68
Matrix Reasoning	116.43	12.37	104.00	14.59	104.93	13.35
Memory for Digits	11.17	2.54	11.02	3.03	12.07	3.17

The EEG recording was under the same experimental procedure of Study 1. Details are described in Chapter 2 and Chapter 3. In brief, the English consonant contrast /v-w/ (native condition), the Mandarin contrast /j-q/ (non-native condition) and contrast /b-t/ (acoustic condition) were delivered through passive auditory oddball paradigm with two blocks for each MMN stimulus contrast. The acoustic contrast /b-t/ has more pronounced acoustic differences than contrast /v-w/ and /j-q/, and thus robust MMN and P3a responses are expected across all three age groups in /b-t/ condition.

Data Analysis. In Study 2, the response strength of MMN and P3a to the acoustic contrast /b-t/, native contrast /v-w/ and non-native contrast /j-q/ was measured from the subjects in Age 6-9 group, Age 10-13 group and Age 14-17 group. Similar to Study 1, an individual's response strength of MMN was measured by (a) ERP peak amplitude on landmark electrode Cz and (b) GFP peak value in the time window of 50~200 milliseconds, after averaging across 10 consecutive time frames. For P3a component, an individual's response strength of it was measured by the ERP peak amplitude on Cz and the peak value of GFP at the time window of 200~400 milliseconds, after the running average on 10 time frames. The calculation of GFP for MMN and P3a follows the procedure in Chapter 2. Comparing to the measure of ERP peak amplitude on electrode Cz, the GFP measure can capture a subject's ERP response strength at the whole-brain level irrespective of scalp topographic distribution of the brain activation. Previous literature suggests a potential systematic topographic change of MMN (the posterior to anterior shift of MMN negative pole) from younger to older school-age children (Bishop, 2007; Cheour, et al., 2000; Cheoura, et al., 2001; Näätänen, et al., 2007). With this regard, comparing the MMN peak amplitude at a fixed electrode Cz between different age groups may lead to biased results. However, using the measure of GFP to quantify the whole-brain response strength of MMN

would avoid the possible systematic bias (Brunet, et al., 2011; Murray, et al., 2008; Skrandies, 1990).

### *Central Questions*

Question 1. How does the response strength of MMN and P3a to the three types of stimulus contrasts change with development among this cohort of school-age individuals with typical reading? Investigating this question will advance our understanding on age-related changes of the native language effect on MMN and P3a and further justifies our hypothesis that the narrowing of cortical speech processing to native language continues far beyond infancy (Kuhl & Rivera-Gaxiola, 2008; Werker & Tees, 2002; Werker & Tees, 2005). We predict that cross-sectional comparisons between the three age groups will reveal an increase of brain response strength in MMN and P3a to the acoustic /b-t/ and native /v-w/ contrasts but a decrease in the ‘size’ of MMN and P3a to the non-native /j-q/ over development (Figure 9). This divergent trend is due to the fact that /b-t/ and /v-w/ are used as phonetic contrasts in English. If this developmental trend of MMN and P3a can be observed, it would indicate that school-age individuals’ cortical speech processing continuously becomes more specialized toward or ‘tuned’ to native speech with development, and supports our hypothesis that auditory cortical narrowing to native speech continues in late childhood and adolescence.

Question 2. What is the relationship between one’s MMN and P3a response strength and reading fluency among school-age individuals? We hypothesize that, an individuals’ reading development is associated with the degree of auditory cortical specialization or ‘narrowing’ to native phonemes (Bishop, 2007; Cheour, et al., 2000; Kraus, Koch, McGee, Nicol, &

Cunningham, 1999; Kraus, et al., 1996). To investigate this brain-behavioral relationship, we conduct regression of TOWRE scores on the strength of MMN and P3a on the entire cohort of 116 individuals to understand to what extent individual differences in cortical speech processing can account for the variability in reading fluency. Specifically, we propose that, the regression will reveal that the response strength of MMN and P3a to the native contrast /v-w/ is positively correlated with age-standardized scores of TOWRE, but the strength of MMN and P3a to the non-native /j-q/ is negatively correlated with the TOWRE scores for reading fluency.

Question 3. Whether the relationship between one's MMN and P3a response and scores of TOWRE is consistent across different age ranges, or the brain-behavioral relationship is different between individuals at different age level? We hypothesize that, perhaps at the early stage of learning to read, young readers heavily rely on the grapheme-to-phoneme conversion for phonological decoding of a word, whereas old readers may develop other strategies later in life for word decoding and become less dependent on phonological decoding. Along this reasoning, we suspect that the reading fluency is possibly more influenced by and thus more correlated with auditory cortical processing of speech (discrimination and orienting) among elementary school students at age 6 to 11 than mid and high school students at age 12 to 17. To evaluate this hypothesis, we examine the developmental change in brain-behavior relationship between MMN, P3a and the reading fluency by using multiple regression that includes age-level moderator variable (young: age 6 to 11, old: age 12 to 17) and the interaction between MMN P3a and the age-level.

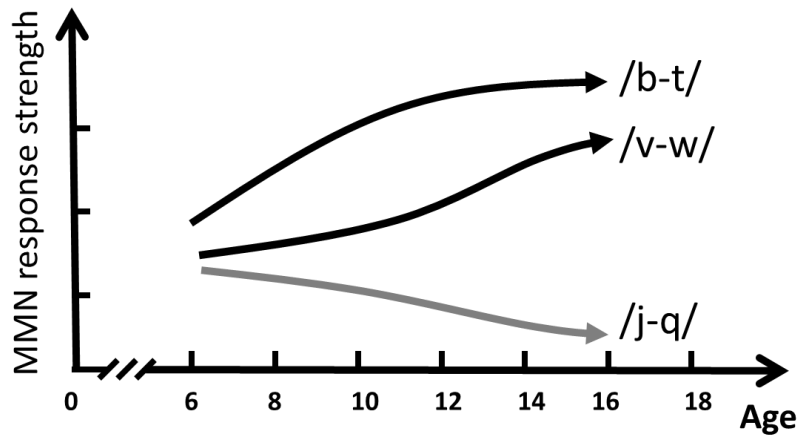


Figure 9. Proposed age-related change of MMN. We predict that the response strength of MMN to the acoustic /b-t/ and native /v-w/ contrasts should increase and the strength of MMN to the non-native /j-q/ contrast should decrease over development, because contrast /b-t/ and /v-w/ are used in English and contrast /j-q/ is not used in English.

### *Results*

#### Question 1: Development of MMN and P3a response strength

Waveforms of mismatch ERP from the three age groups under the condition of /b-t/, /v-w/ and /j-q/ are displayed in Figure 10. Robust MMN at 100~200 milliseconds and P3a at 200~350 milliseconds was elicited by the /b-t/ contrast across the groups. Figure 11 displays age-related changes in the ERP peak amplitude of MMN and P3a. The mean and the standard error (SE) of ERP amplitude are presented in Table 2. To investigate the first central question, Group (age 6-9, 10-13 and 14-17) x Condition (/b-t/, /v-w/ and /j-q/) 2-way repeated measure ANOVA was conducted on the ERP peak amplitude of MMN and P3a respectively. Significant main effect of the condition was found in both MMN and P3a ERP amplitude (MMN,  $F(2, 226) = 12.18$ ,  $p < 0.0001$ ; P3a,  $F(2, 226) = 6.13$ ,  $p < 0.01$ ). No significant interaction between group and condition was found on ERP amplitude (MMN,  $F(2, 226) = 1.32$ ,  $p = 0.27$ ; P3a,  $F(2, 226) = 0.56$ ,  $p = 0.57$ ).

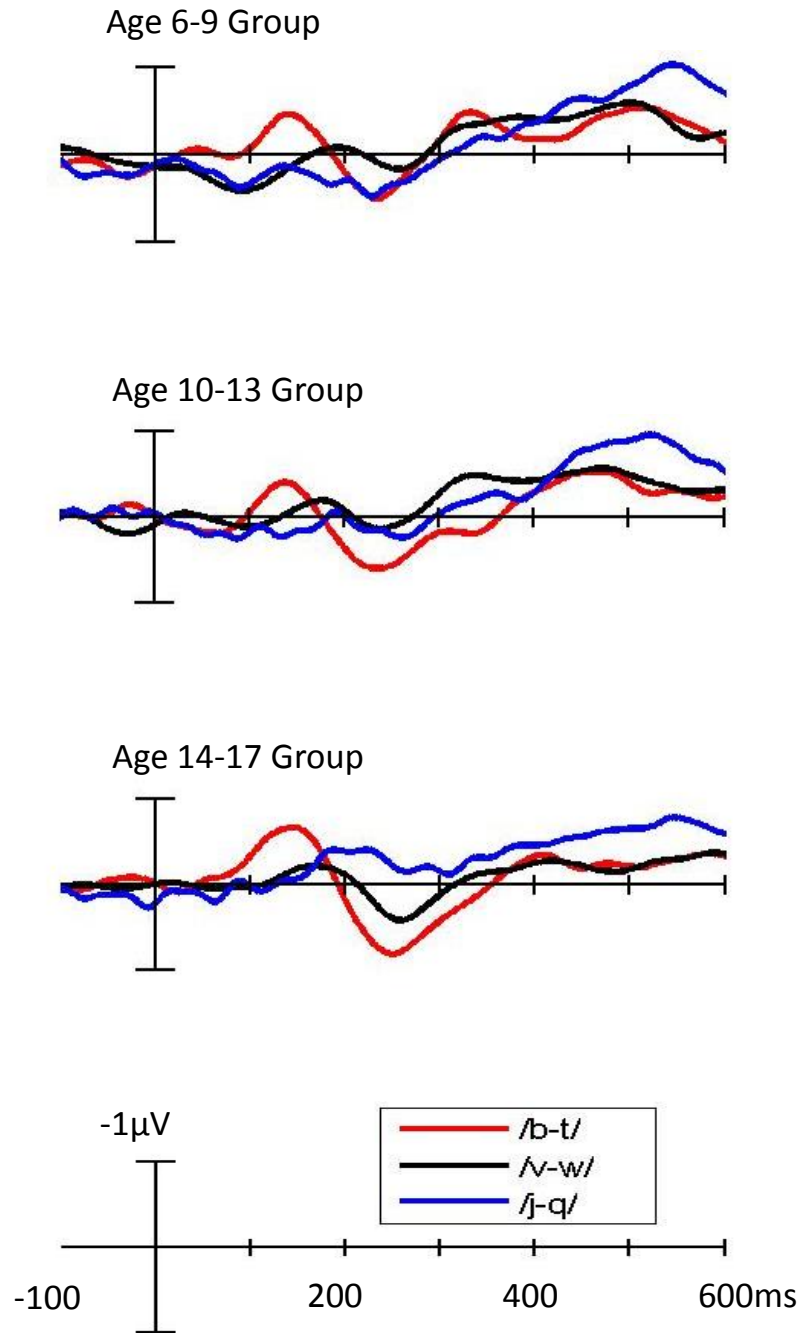


Figure 10. ERP waveform of MMN from school-age individuals. The standard-deviant mismatch ERP to /b-t/, /v-w/ and /j-q/ on electrode Cz is displayed for the three age groups. Robust MMN is elicited by /b-t/ at 100~200 milliseconds (ms) following by P3a at 200~350 milliseconds in the three age groups.

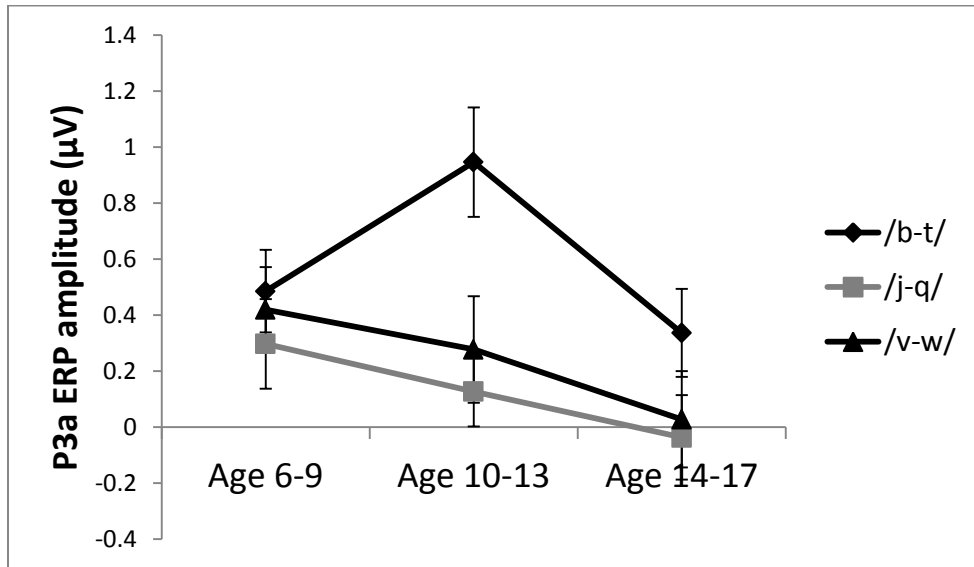
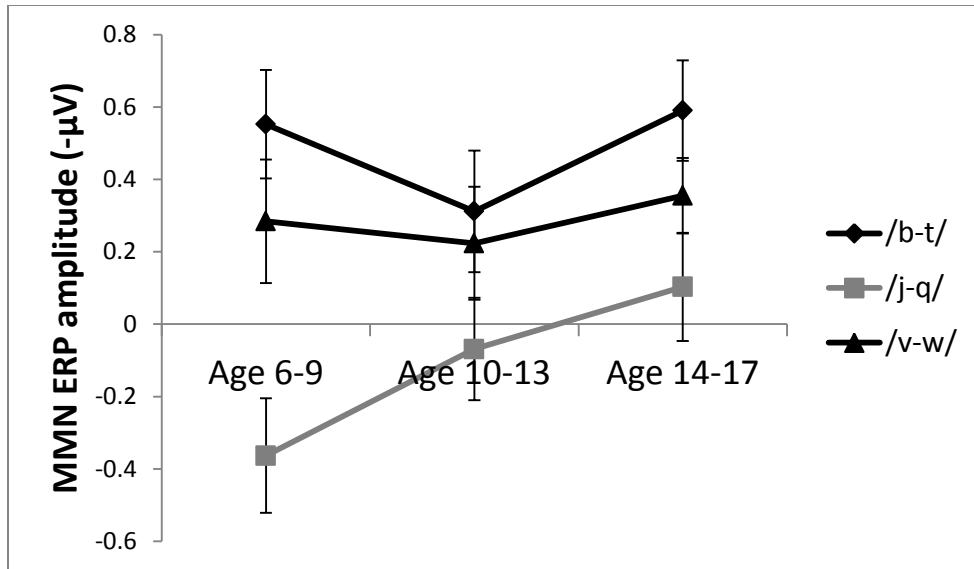


Figure 11. Age-related change in ERP amplitude of MMN and P3a. The ERP peak amplitudes of MMN (upper panel) and P3a (lower panel) to contrast /b-t/, /v-w/ and /j-q/ are displayed for the three age groups. Error bars denote one standard error around the mean.



Table 2. ERP Amplitude ( $\mu\text{V}$ ) of MMN and P3a from the three groups

Age	Age 6-9 (n=47)		Age 10-13 (n=42)		Age 14-17 (n=27)	
	M	SD	M	SD	M	SD
Age	8.45	1.07	11.83	1.17	16.13	1.29
<i>ERP Amplitude</i>	M	SE	M	SE	M	SE
MMN to /b-t/	-0.55	0.15	-0.31	0.17	-0.59	0.14
MMN to /v-w/	-0.28	0.16	-0.22	0.14	-0.36	0.15
MMN to /j-q/	0.36	0.17	0.07	0.16	-0.10	0.10
P3a to /b-t/	0.49	0.15	0.95	0.20	0.34	0.16
P3a to /v-w/	0.42	0.16	0.28	0.13	0.03	0.15
P3a to /j-q/	0.30	0.15	0.13	0.19	-0.04	0.17

The GFP curves of mismatch ERP to the contrast /b-t/, /v-w/ and /j-q/ from the three age groups are displayed in Figure 12. The GFP increase for MMN was found at 100~200 milliseconds and the GFP increase for P3a was found at 200~400 milliseconds, which indicates an age-related difference in whole-brain ERP response strength (Figure 13). Children from age 6 to 9 group showed little GFP differences in response to the acoustic /b-t/, native /v-w/ and non-native /j-q/. In contrast, individuals in age group 14 to 17 showed stronger MMN and P3a to the contrasts /b-t/ and /v-w/ comparing to the response to /j-q/. The mean and the standard error (SE) of the GFP of MMN and P3a are presented in Table 3. Group x Condition 2-way repeated measure ANOVA on the GFP of MMN and on the GFP of P3a revealed significant interaction between the condition and group for both MMN ( $F(2,226) = 4.28, p < 0.05$ ) and P3a ( $F(2, 226) = 5.74, p < 0.01$ ). As displayed in Figure 13, over the course of development, the whole-brain response strength of MMN and P3a tends to increase for speech contrasts used in one's ambient

language (/b-t/ and /v-w/) but tend to decrease for speech contrasts that is non-native (/j-q/) to the subject. This age-related change in the GFP of MMN and P3a supports our hypothesis that auditory cortical narrowing to native speech continues in late childhood and adolescence, such that school-age individual's cortical speech processing (auditory discrimination and involuntary orienting) becomes specialized to native language with development.

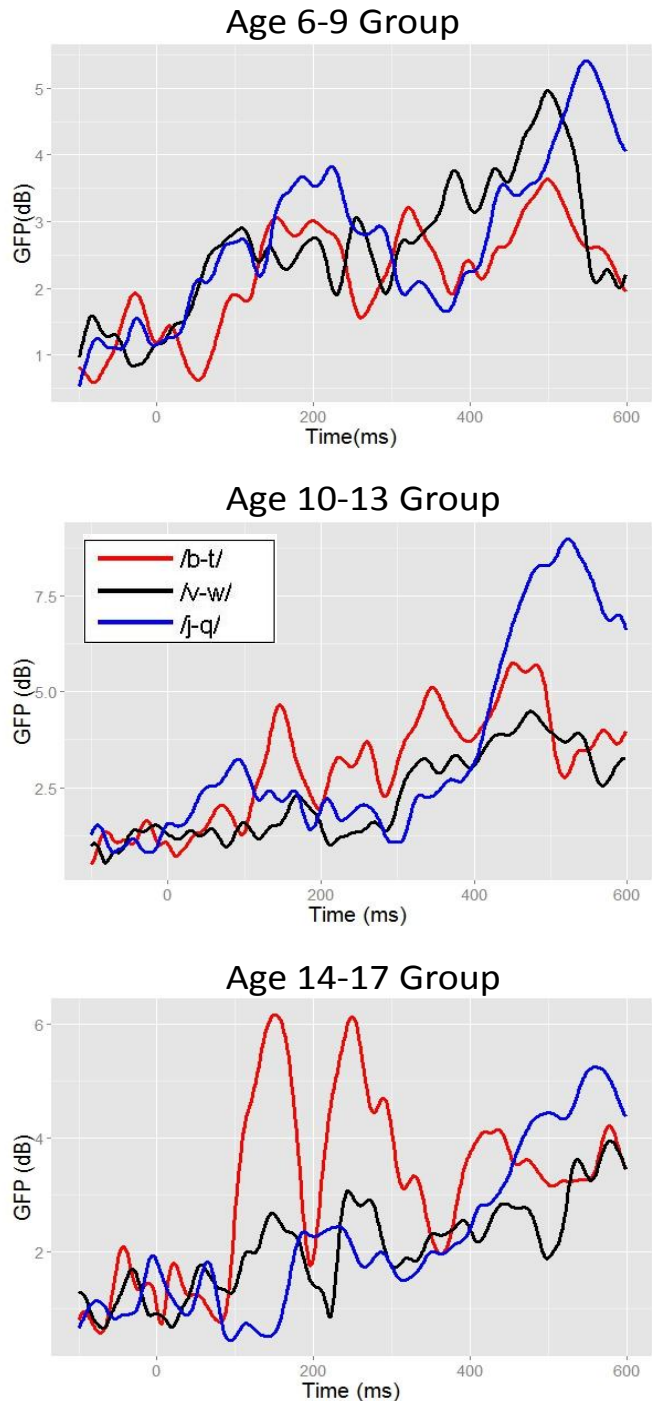


Figure 12. GFP curves of MMN from school-age individuals. The GFP of the mismatch ERP to /b-t/, /v-w/ and /j-q/ is displayed for the three age groups. GFP increase that is associated with MMN and P3a can be observed at 100~200 milliseconds (ms) and at 200~300 milliseconds under the /b-t/ and /v-w/ conditions on the age 14-17 group.

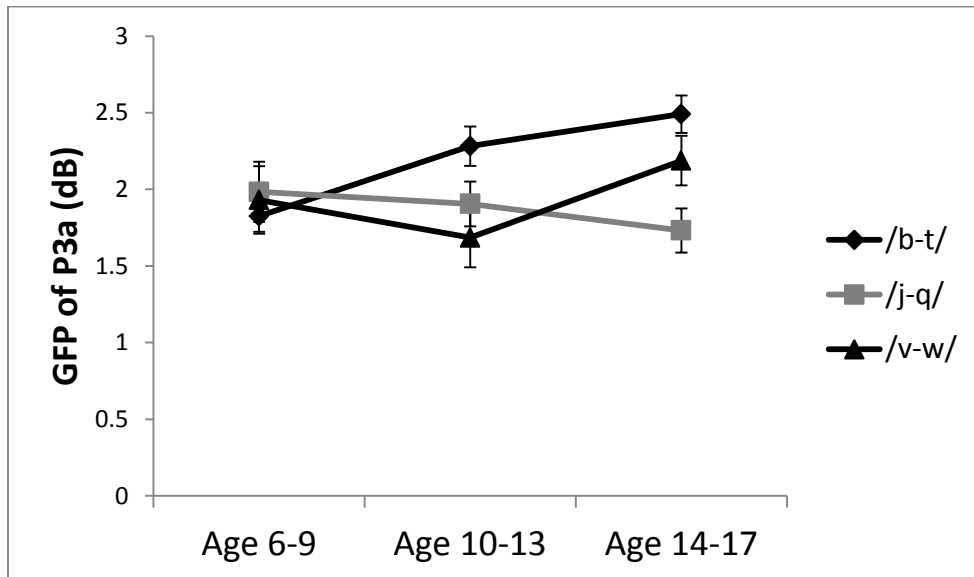
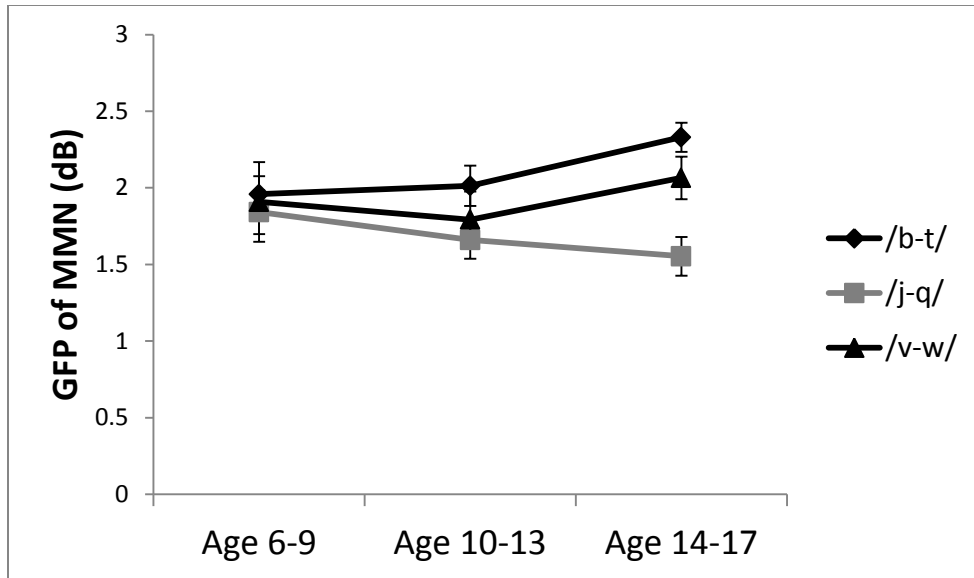


Figure 13. Age-related change in GFP of MMN and P3a. The GFP of MMN (upper panel) and P3a (lower panel) is displayed for the three age groups. Error bars denote one standard error around the mean. Increasing developmental trend of GFP to /b-t/ and /v-w/ contrasts and decreasing trend of GFP to /j-q/ was found for both MMN and P3a.

Table 3. GFP (dB) of MMN and P3a from the three age groups

Age	Age 6-9 (n= 47)		Age 10-13 (n=42)		Age 14-17 (n=27)	
	M	SD	M	SD	M	SD
	8.45	1.07	11.83	1.17	16.13	1.29
<i>GFP value</i>	M	SE	M	SE	M	SE
MMN to /b-t/	1.96	0.12	2.01	0.14	2.33	0.26
MMN to /v-w/	1.91	0.13	1.79	0.12	2.06	0.18
MMN to /j-q/	1.84	0.10	1.66	0.13	1.55	0.14
P3a to /b-t/	1.82	0.10	2.28	0.20	2.49	0.22
P3a to /v-w/	1.93	0.13	1.68	0.15	2.19	0.19
P3a to /j-q/	1.98	0.12	1.91	0.14	1.73	0.16

Question 2: Brain-behavior relationship for reading fluency

To study the relationship between one's auditory cortical processing of speech and reading fluency, we conducted multiple regression of TOWRE scores on the ERP amplitude of MMN and multiple regression of TOWRE scores on the ERP amplitude of P3a on the entire cohort of typical individuals (n=116). Each of the two regressions has one dependent variable (Y) being the age-standardized scores of TOWRE that measures an individual's reading fluency. For the regression on MMN, independent variables include the ERP peak amplitude of MMN to /b-t/ ( $X_1$ ), to /v-w/ ( $X_2$ ) and to /j-q/ ( $X_3$ ). For the regression on P3a, independent variables include the ERP peak amplitude of P3a to /b-t/ ( $X_1$ ), to /v-w/ ( $X_2$ ), and to /j-q/ ( $X_3$ ).

The multiple regression of TOWRE on MMN revealed (a) significant positive relationship between the amplitude of MMN to the native contrast /v-w/ and the age-standardized TOWRE scores ( $b = 2.56$ ,  $t = 2.19$ ,  $p < 0.05$ ) and (b) marginal significant negative relationship ( $b = -1.83$ ,  $t = -1.76$ ,  $p = 0.08$ ) between the amplitude of MMN to non-native /j-q/ and the reading fluency (adjusted  $R^2 = 0.045$ ,  $p < 0.05$ ). The regression on P3a revealed significant positive relationship between the ERP amplitude of P3a to /v-w/ and the age-standardized TOWRE scores ( $b = 2.63$ ,  $t = 2.30$ ,  $p < 0.05$ ; adjusted  $R^2 = 0.075$ ,  $p < 0.01$ ).

In addition to the ERP peak amplitude for measuring the strength of auditory brain response, GFP measures of MMN and P3a were also examined by two separate multiple regressions for the brain-behavior relationship. For the multiple regression of TOWRE scores on the GFP of MMN, independent variables include the GFP peak value of MMN to /b-t/ ( $X_1$ ), to /v-w/ ( $X_2$ ) and to /j-q/ ( $X_3$ ). For the regression on the GFP of P3a, independent variables include the GFP value of P3a to /b-t/ ( $X_1$ ), to /v-w/ ( $X_2$ ), and to /j-q/ ( $X_3$ ). Both of the multiple regressions do not reveal that significant proportion of variance in the age-standardized scores of TOWRE can be accounted for by the GFP measures (MMN: adjusted  $R^2 = 0.03$ ; P3a: adjusted  $R^2 = -0.01$ ). This result indicates a lack of relationship between an individual's GFP brain response strength of auditory speech processing and reading fluency.

### Question 3: Age moderation on the brain-behavioral relationship

In the third central question, we reasoned that the relationship between auditory cortical processing of speech and reading fluency may present differently between individuals at younger ages and individuals at older ages (Bishop, 2007; Bishop, et al., 2007; Bishop, et al., 2011).

Specifically, we predicted that, because phonological skills are so critical for children to learn to read, cortical speech processing involving auditory discrimination and orienting to phonetic contrasts can be fundamental for reading development at early stage of learning to read. With this regard, the correlations between the response strength of MMN as well as P3a and scores of TOWRE are perhaps stronger in young individuals such as elementary school students compared to old individuals such as middle school and high school students.

To investigate the potential different brain-behavioral relationship between young and old individuals, we defined an age moderator variable and included interactions of the age moderator and the ERP measures to explain reading fluency in a multiple regression. In particular, we defined a binary age moderator *age-level* by splitting the cohort of 116 individuals into two age groups: Old (12-17 years of age with mean of 14.7, dummy coding 0 as reference level, n= 48,) and Young (6-11 years of age with mean of 9.2, dummy coding 1, n= 68). We then examined the interactions between the age-level and the response strength of MMN and P3a in the regression of reading fluency. That is, for the multiple regression of age-standardized TOWRE scores (Y) on MMN, independent variables include the ERP peak amplitude of MMN to /b-t/ ( $X_1$ ), to /v-w/ ( $X_2$ ) and to /j-q/ ( $X_3$ ), the categorical moderator variable age-level ( $X_4$ ) and the interaction product terms of  $X_1 * X_4$ ,  $X_2 * X_4$ , and  $X_3 * X_4$ . Similarly, for the multiple regression of TOWRE scores on P3a ERP amplitude, independent variables include the ERP peak amplitude of P3a to /b-t/ ( $X_1$ ), to /v-w/ ( $X_2$ ) and to /j-q/ ( $X_3$ ), the age-level ( $X_4$ ) and the terms of  $X_1 * X_4$ ,  $X_2 * X_4$ , and  $X_3 * X_4$ .

The regression of TOWRE on MMN revealed a significant proportion of variance in the reading fluency measure can be explained by the ERP amplitude of MMN to /b-t/, /v-w/ and /j-q/ and the corresponding interaction with the age-level (adjusted  $R^2=0.14$ ,  $p<0.01$ ). A significant positive interaction of MMN to native /v-w/ and the age-level was found ( $b = 5.29$ ,  $t = 2.47$ ,  $p<$

0.05). This interaction revealed a stronger positive relationship between one's auditory discrimination of native contrast /v-w/ and reading fluency among individuals at age 6 to 11, compared with individuals at age 12 to 17 (Figure 14). The multiple regression of TOWRE scores on P3a ERP amplitude, however, did not find significant interaction between ERP measures and the age-level moderator.



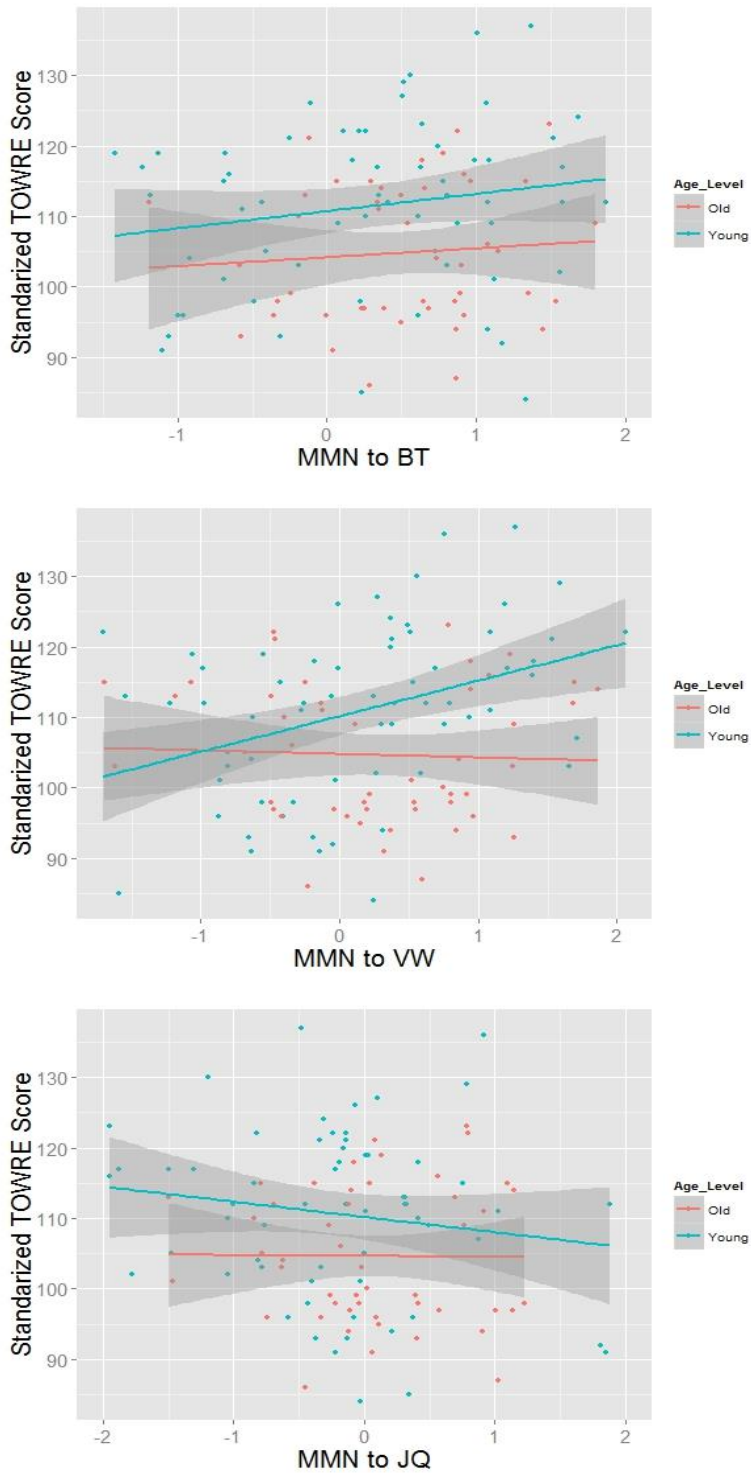


Figure 14. Age moderation on brain-behavior relationship. The correlation between amplitudes of MMN to /v-w/ and scores of TOWRE is moderated by the age-level moderator. More positive correlation was presented in the young group (age 6 to 11) comparing to the old group (age 12 to 17).

In addition to the ERP peak amplitude, similar regression analyses were also conducted on the GFP value of MMN and the GFP of P3a to investigate the relationship between whole-brain response strength and reading fluency among young and old individuals. One regression of age-standardized scores of TOWRE (Y) was conducted on independent variables including the GFP of MMN to /b-t/ ( $X_1$ ), /v-w/ ( $X_2$ ) and /j-q/ ( $X_3$ ), the age-level ( $X_4$ ) and the interaction of  $X_1 * X_4$ ,  $X_2 * X_4$ , and  $X_3 * X_4$  and the other regression of TOWRE was conducted on the GFP of P3a to /b-t/ ( $X_1$ ), /v-w/ ( $X_2$ ) and /j-q/ ( $X_3$ ), the age-level ( $X_4$ ) and the interaction of  $X_1 * X_4$ ,  $X_2 * X_4$ , and  $X_3 * X_4$ . Neither of the two multiple regressions on the whole-brain response strength found significant interaction between GFP of MMN or P3a and the age level.

#### Degree of cortical narrowing and reading

In both Study 1 and Study 2, we proposed that an individual's auditory cortical processing becomes specialized or 'tuned' to native speech over the course of development, and this cortical narrowing can benefit one's perception of native speech and be fundamental for reading development. Reading difficulties have been attributed to deficient narrowing to native speech at behavioral level and at brain level in previous ERP research on typical population and dyslexic populations (Bruder et al., 2011a; Noordenbos, Segers, Serniclaes, Mitterer, & Verhoeven, 2012; Schulte-Körne & Bruder, 2010).

Here, to further investigate to what extent an individual's reading fluency is linked to auditory cortical narrowing to native speech, the GFP difference between the native condition /v-w/ and the non-native condition /j-q/ (GFP to the /v-w/ minus GFP to /j-q/) in MMN and the GFP difference between /v-w/ and /j-q/ in P3a were computed as two measures for the degree of one's

auditory cortical narrowing to native speech. Regression of age-standardized scores of TOWRE (Y) on the native versus non-native GFP difference in MMN ( $X_1$ ) and the GFP difference in P3a ( $X_2$ ) revealed that the GFP strength difference between the native and non-native contrasts in MMN (but not in P3a) is significantly correlated with one's reading fluency ( $b = 3.67$ ,  $t = 2.98$ ,  $p < 0.01$ , Figure 15).

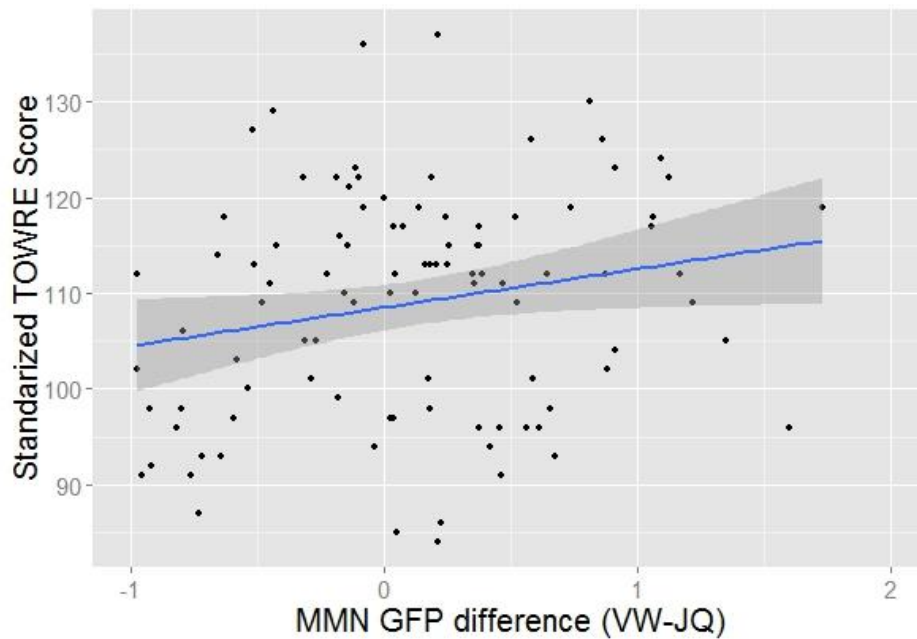


Figure 15. Positive relationship between cortical narrowing and reading. The GFP difference of MMN between /v-w/ and /j-q/ which measures the degree of an individual's cortical narrowing to native speech is positively correlated with the score of TOWRE that measures the subject's reading fluency.

### *Discussion*

In the current Chapter 3, the development of native language effect on cortical speech processing was investigated on a large cohort of typically developing individuals from age 6 to age 17. The age-related changes of MMN and P3a to native and non-native phonetic contrasts

were mapped out among the school-age subjects, which advances our understanding on the cortical narrowing to native speech over development (Bishop, 2007; Bishop, et al., 2007; Bishop, et al., 2011; Cheour, et al., 2000; Cheoura, et al., 2001). The results of the cross-sectional comparisons on MMN and P3a response strength in Study 2 support our hypothesis that the narrowing of one's auditory cortical processing to native speech continues in late childhood through adolescence, far beyond infancy.

Although the ANOVA on ERP peak amplitudes of MMN and P3a only found main effect on the condition, ANOVA on GFP for whole-brain response strength found significant interaction between the condition and the age group for both MMN and P3a. Consistent with our hypothesis that cortical narrowing to native speech continues far beyond infancy, the school-age individuals at elder age showed more pronounced native language effect on cortical speech processing compared with those at younger age. Specifically, individuals at age 14 to 17 showed stronger whole-brain GFP response of MMN and P3a to the native contrast /v-w/ than the non-native contrast /j-q/, whereas individuals at age 6 to 9 presented little difference in the GFP of MMN and P3a between the native and non-native conditions.

The significant interaction between age group and stimulus condition in both GFP of MMN and P3a suggests that, different from those at age 6 to 9, individuals at age 14 to 17 seem to be more sensitive and more likely to orientate to a native phonetic contrast but less sensitive to non-native phonetic elements (Čeponienė et al., 2003; Escera, et al., 1998; Escera & Corral, 2007). This age-related change in the native language effect of MMN and P3a suggests that, an individual's auditory cortical processing becomes more specialized or 'tuned' to native speech with development and the cortical narrowing to native language continues in childhood through

adolescence years (Tsang, et al., 2011; Wetzel, Widmann, Berti, & Schröger, 2006; Xi, Zhang, Shu, Zhang, & Li, 2010; Zhang, et al., 2012; Zhang et al., 2012).

In addition to the cross-sectional comparisons, an individual's brain response strength (ERP peak amplitude and GFP value) of MMN and P3a to native and non-native phonetic contrasts was also linked to the behavioral measure of reading fluency in this cohort of 116 typical individuals. Significant positive brain-behavioral correlation was found between the age-standardized scores of TOWRE and ERP peak amplitudes of MMN to the native contrast /v-w/. Marginally significant negative relationship was also found between the TOWRE scores and ERP amplitude of MMN to the non-native /j-q/. The positive relationship between reading fluency and MMN to the *native* contrast along with the negative relationship between reading fluency and MMN to the *non-native* contrast supports our hypothesis (central question 2) that auditory cortical narrowing to native speech is associated with an school-age individual's reading development (Bishop, 2007; Leppänen, & Kraus, 2000; Noordenbos, et al., 2012).

For central question 3, we hypothesized that the brain-behavioral relationship between the response strength of MMN and reading fluency can potentially be different between individuals at different age levels. We reasoned that, when children begin learning to read in elementary school, they perhaps heavily rely upon auditory speech processing such as phoneme discrimination in order to decode written words and develop fluent reading. In contrast, for elder individuals such as middle school and high school students, auditory speech processing might become less fundamental to fluent reading, because instead of solely relying on grapheme-to-phoneme conversion for phonological decoding of words, elder readers may already develop alternative strategies later in life to read efficiently.

To examine the potential different brain-behavior relationships among individuals at different age levels, we examined the interaction effect between an age moderator i.e. age-level and response strength of MMN in explaining individual differences in TOWRE scores for reading fluency. We found that the effect of ERP amplitude of MMN to the native contrast /v-w/ (X) on the dependent variable TOWRE scores (Y) depends on the third age-level moderator variable. The significant positive coefficient of the interaction between the ERP amplitude of MMN to /v-w/ and the age-level (i.e. the product term of the two variables in the multiple regression) indicates that, the reading fluency is statistically more positively associated with the size of MMN to native speech among children from age 6 to age 11, compared with this brain-behavioral relationship among individuals at age 12 to 17.

Finally, the extent to which the degree of one's auditory cortical narrowing to native speech is linked to reading fluency was examined in the regression of TOWRE scores on the GFP difference between MMN to the native contrast /v-w/ and MMN to the non-native contrast /j-q/. Significant positive relationship between the difference GFP of MMN and TOWRE is consistent with our hypothesis that an individual's reading fluency is perhaps associated with the degree to which one's pre-attentive auditory discrimination is specialized or 'tuned' to native speech.

## CHAPTER V

### STUDY 3: DEFICIENT CORTICAL NARROWING AND READING DIFFICULTY IN SCHOOL-AGE INDIVIDUALS

Study 2 revealed that the response strength of MMN to the native phonetic contrast is correlated with reading fluency and auditory cortical narrowing to native speech is fundamental to fluent reading among school-age individuals. In the current chapter, we further investigate our theory that reading difficulty can perhaps arise from deficient auditory cortical narrowing to native speech (Bruder et al., 2011b; Leppänen et al., 2012; Noordenbos, et al., 2012; Schulte-Körne & Bruder, 2010). For Study 3, we identified 24 individuals with age-standardized TOWRE score below the 25<sup>th</sup> percentile (defined as ‘poor reading group’) and 24 age-matched control individuals with TOWRE scores above the 25<sup>th</sup> percentile (defined as ‘typical reading group’). We set out to compare the response strength of MMN between the two reading groups to examine the association between defective cortical speech processing and reading difficulty.

In Study 3, we hypothesize that the native language effect of MMN is perhaps reduced in the poor reading group. In particular, we predict that the 24 poor readers with low reading fluency may possibly show abnormally small MMN to the native contrast /v-w/ and but excessively large MMN to the non-native contrast /j-q/, when compared with the age-matched typical controls with fluent reading. If a lack of MMN native language effect could be observed in the poor reading group, it would (a) support our hypothesis that unlike typically developing individuals with fluent reading, a poor reader’s auditory cortical processing is not well tuned to native speech and (b) further support the notion that insufficient cortical narrowing to native speech can be one of the

attributes of developmental dyslexia (Bruder, et al., 2011a, 2011b; Leppänen, et al., 2012; Noordenbos, et al., 2012; Schulte-Körne & Bruder, 2010).

### *Methods*

All methods were the same as Study 2 in Chapter 4, except as follows.

In Study 3, the response strength of MMN and P3a from the 24 participants whose age-standardized TOWRE scores were below the 25<sup>th</sup> percentile, i.e. the poor reading group, were compared to the data from the 24 age-matched controls with normal reading fluency i.e. the typical reading group with age-standardized TOWRE scores above the 25<sup>th</sup> percentile. In addition to the match on age, the controls were also matched to the poor readers with non-verbal IQ that was measured by Matrix Reasoning in CTOPP (described in Chapter 2). The details of the two reading groups are displayed in Table 4.

Table 4. Behavioral measures of the two reading groups

Measure	Poor Reading Group (n=24)		Typical Reading Group (n=24)	
	M	SD	M	SD
Age	12.08	3.92	12.10	3.83
Test of Word Reading Efficiency (TOWRE)	84.38	5.89	107.29	9.91
Elision	8.17	2.51	9.88	2.98
Matrix Reasoning	94.71	16.55	101.42	11.93
Memory for Digits	9.33	3.13	10.67	3.50



Similar EEG data analyses in Study 1 and 2 were conducted for Study 3 on the 24 poor readers and their age-matched controls. Both the running-average ERP peak amplitude on Cz and the GFP peak value were used to measure an individual's response strength of MMN at 50~200 milliseconds as well as P3a at 200~400 milliseconds to the acoustic contrast /b-t/, native contrast /v-w/ and non-native contrast /j-q/ from each group. Group by Condition 2-way repeated measure ANOVA was conducted to statistically evaluate the differences of response strength of MMN and P3a between the two reading groups.

### *Results*

Waveforms of the mismatch ERP to /b-t/, /v-w/ and /j-q/ on Cz from the poor reading group and the typical reading group are displayed in Figure 16. Robust MMN to the acoustic contrast /b-t/ and the native contrast /v-w/ was elicited in the typical reading group at 100~200 milliseconds. In contrast, the poor reading group showed a lack of MMN response to /v-w/ and reduced MMN to /v-w/ at 100~200 milliseconds. For the non-native /j-q/ contrast, different from the typical reading group showing a positive durative mismatch ERP response at 200~300 milliseconds, the poor reading group showed a negative mismatch response i.e. MMN to /j-q/ at 150~300 milliseconds instead.

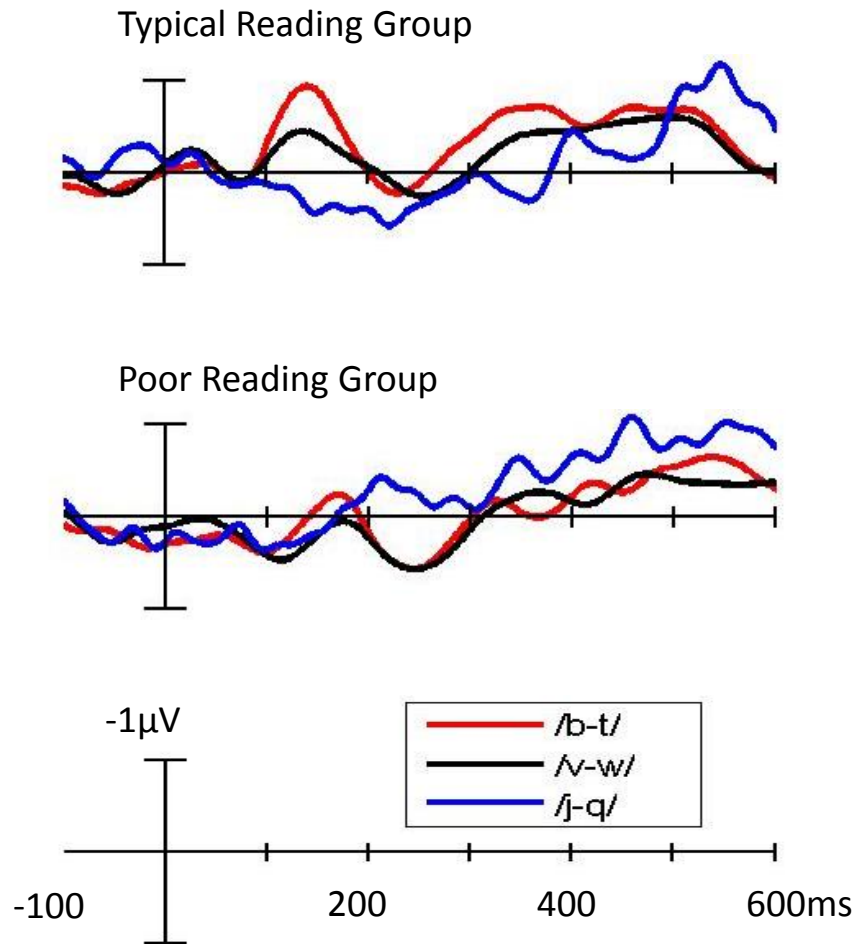


Figure 16. ERP waveform of MMN from the two reading groups. Typical readers showed MMN to contrasts /b-t/ and /v-w/ at 100~200 milliseconds (ms). Poor readers showed reduced MMN to /b-t/ and /v-w/ at 100~200 milliseconds but excessive MMN to /j-q/ at 200~300 milliseconds comparing to the typical readers.

Figure 17 displays the ERP amplitude of MMN and P3a from the two reading groups. Group by Condition 2-way repeated measure ANOVA on the MMN ERP peak amplitude revealed a significant interaction between the condition and the reading group ( $F(2, 95) = 5.85$ ,  $p < 0.01$ ). Post-hoc paired t-tests between the two groups revealed that, the poor readers had significantly weaker MMN to the acoustic contrast /b-t/ ( $p < 0.01$ ) and the native contrast /v-w/ ( $p < 0.05$ ) compared to the typical readers. On the contrary, for the non-native /j-q/ condition, the

poor readers instead showed larger MMN (marginal significant,  $p=0.08$ ) than the typical controls.

The 2-way ANOVA on P3a ERP amplitude did not find significant main effects or interaction.

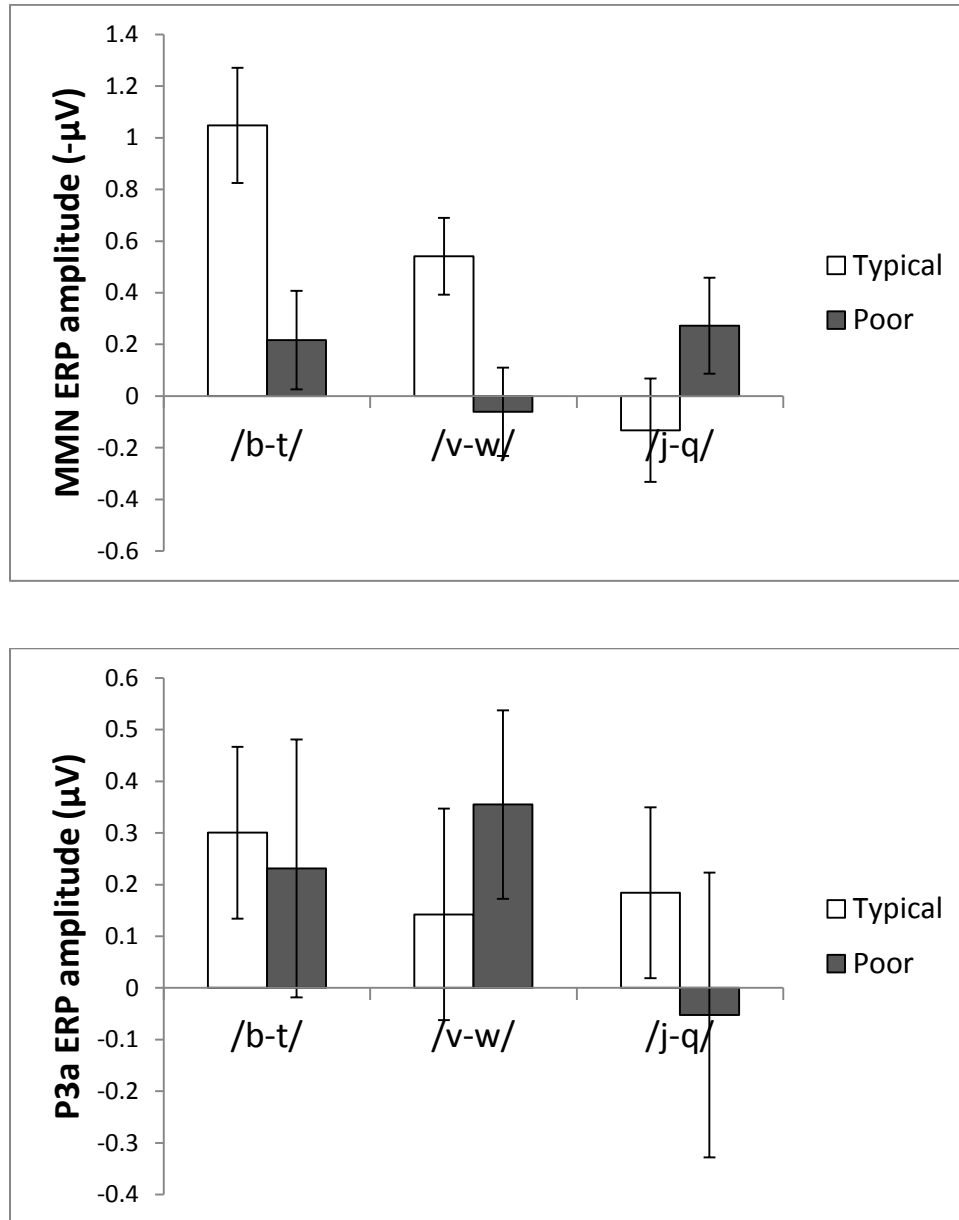


Figure 17. Reduced amplitude of MMN from the poor readers. The ERP peak amplitude of MMN (upper panel) and ERP amplitude of P3a (lower panel) are displayed for the two reading groups. Error bars denote one standard error around the mean. Significant interaction between the group and condition was found on MMN.

The GFP curves of the mismatch ERP from the poor reading group and from the typical reading group are displayed in Figure 18. Group by Condition 2-way ANOVA was also conducted on the GFP value of MMN and the GFP of P3a. No significant interaction or main effects was found on the GFP data.

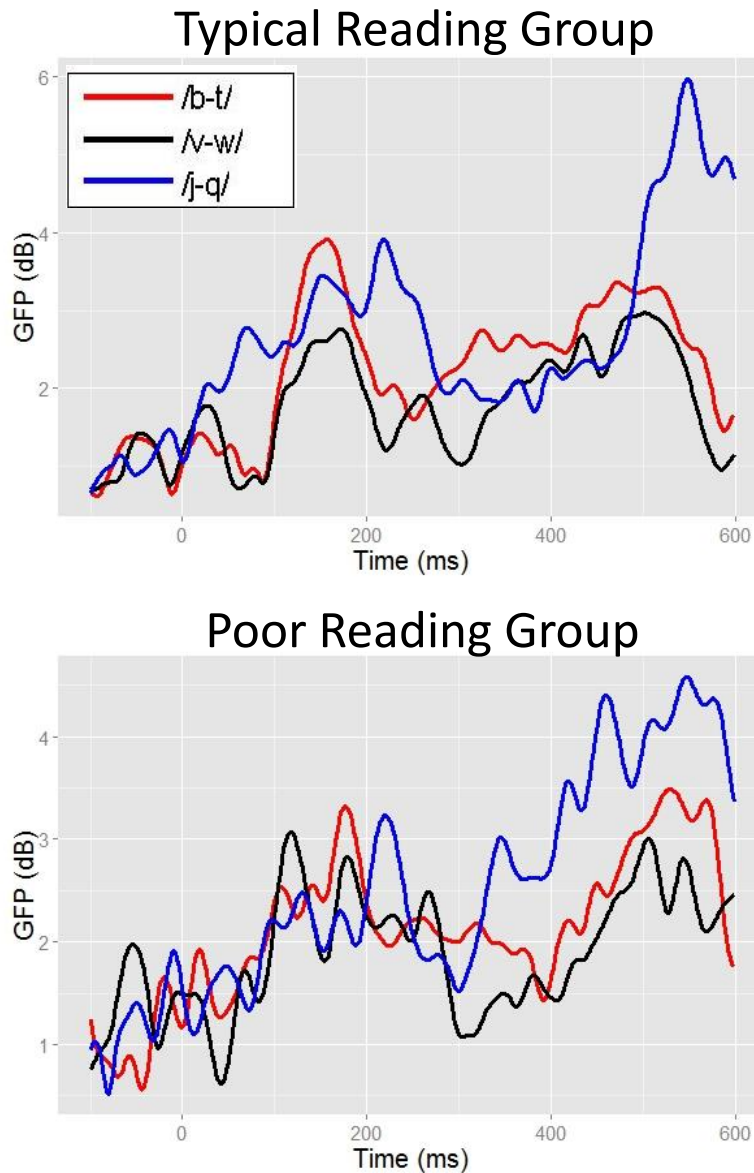


Figure 18. GFP curves of MMN from the two reading groups. GFP of mismatch ERP to /b-t/, /v-w/ and /j-q/ contrasts from the poor readers and the typical readers.

## *Discussion*

In the current Chapter 5, auditory cortical processing of native and non-native phonetic contrasts was compared between a group of individuals with low reading fluency and their age-matched controls with typical reading. Consistent with previous MMN studies, we found that the poor reading group had significantly weaker MMN to the native /v-w/ contrast, when compared to the typical reading group (Bishop, 2007; Lovio, Halttunen, Lyytinen, Näätänen, & Kujala, 2012; Lovio, Näätänen, & Kujala, 2010; Pakarinen et al., 2009; Schulte-Körne & Bruder, 2010). The lack of MMN to native contrast is consistent with our hypothesis that reading difficulty can result from defective auditory discrimination of native speech sounds.

Similar group difference in ERP amplitude was also found in MMN to the acoustic /b-t/ contrast: the poor reading group showed greatly reduced of MMN compared with the typical group. The contrast stimulus /b-t/ has largely pronounced acoustic distinction and it elicits robust MMN across the three age groups in Study 2 and the typical reading group in Study 3. The greatly reduced MMN to /b-t/ from the poor reading group seems to point out that perhaps there is low-level defectiveness in pre-attentive auditory discrimination of sounds among individuals with reading difficulty. The results of reduced MMN to /b-t/ together with a lack of MMN to /v-w/ seem to support the ‘basic auditory dysfunction’ theory of dyslexia, stating that dysfunctions of low-level auditory processing can impair the cortical processing of acoustic features such as sound frequency, duration and amplitude, and such basic auditory dysfunctions can degrade one’s ability in perceiving phonetic structures of speech and further results in reading difficulties (Bishop, 2007; Bruder, et al., 2011a; Kujala, Lovio, Lepistö, Laasonen & Näätänen, 2006; Kujala, et al., 2000; Näätänen, et al., 2012; Pakarinen, et al., 2009; Schulte-Körne & Bruder, 2010).

The poor reader's excessive MMN to non-native contrasts in Study 3 seem to indicate that, basic auditory dysfunction is *not* the only factor that contributes to low reading fluency (Bishop, 2007; Bruder, et al., 2011a, 2011b). That is, if the basic auditory dysfunction such as low sensitivity to sound duration were the only cause for poor reading, a reduction of MMN to non-native contrast /j-q/ would be observed in the poor reading group, because the acoustic attribute that differentiates /j/ and /q/ is aspiration, an acoustic feature primarily involving sound duration. However, different from the prediction of basic auditory dysfunction theory, we found that, when listening to the non-native /j-q/ contrast, the poor reading group presented even stronger MMN than the typical reading group. This excessive MMN response to non-native speech indicates that this group of poor readers' auditory cortical discrimination is not universally insensitive. Instead, the result from the non-native condition suggests that individuals with poor reading may perhaps suffer from abnormal hypersensitivity to speech sounds that are not relevant to their native language (Bruder, et al., 2011a, 2011b; Leppänen, et al., 2012; Noordenbos, et al., 2012).

The finding of reduced MMN to /b-t/ and /v-w/ along with excessive MMN to /j-q/ in Study 3 demonstrated a lack of MMN native language effect in the 24 school-age individuals with low reading fluency. It indicates that, at least some individuals with reading difficulty seem to suffer from hyposensitivity of auditory discrimination to native phonemes but hypersensitivity of pre-attentive cortical discrimination to non-native phonemes. The lack of MMN native language effect from the poor reading group in Study 3 supports our hypothesis that deficient auditory cortical narrowing to native speech can be one of the attributes of individuals with reading difficulty.

## CHAPTER VI

### GENERAL DISCUSSION

In the current thesis, we studied the auditory cortical narrowing to native speech over development and to what extent it is related to reading difficulty among school-age individuals. Theoretically, we hypothesize that, with development, an individual's auditory cortical processing becomes specialized or 'tuned' to native speech, which facilitates an individual's brain process of speech sounds that are used in the ambient language.

The mismatch negative, .i.e. MMN to native and non-native phonetic contrasts is studied in the current thesis as the brain measure of auditory cortical processing of speech. In particular, we investigated how an individual's MMN response, which indexes the pre-attentive auditory discriminative processing of speech contrasts, can be influenced by the listener's native language experiences. We compared the response strength of MMN between the native and the non-native phonetic condition among adults (Study 1), typically developing school-age individuals (Study 2) and individuals with reading difficulty (Study 3). We found that, (a) both English-speaking and Mandarin-speaking adults show native language effect of MMN i.e. enhanced MMN to the native phonetic contrast but reduced MMN to the non-native phonetic contrast, (b) the auditory cortical narrowing to native speech extends through childhood and adolescence years, such that continuously the MMN to the native contrast increases while the MMN to the non-native contrast decreases among a cohort of typical school-age individuals from age 6 to 17, and (c) a lack of

MMN native language effect that indexes deficient cortical narrowing to native speech is found on school-age individuals with reading difficulty.

### *Auditory cortical narrowing in adults*

In Study 1, we verified the native language effect of MMN in a group of Mandarin-speaking adults and a group of English-speaking adults under our EEG experimental procedure. In a symmetric Mandarin-English cross-language design, we presented the Mandarin-specific phonetic contrast /j-q/ and the English-specific phonetic contrast /v-w/ to both language populations. We found that the response strength (ERP peak amplitude, Global Field Power) of MMN to the native phonetic contrast is significantly larger than MMN to the non-native contrast across both language groups. This result indicates that an adult's pre-attentive auditory discriminative processing is tuned by native language experiences.

Our finding of enhanced MMN response to native speech is consistent with previous ERP studies on adults, in which the MMN native language effect has been suggested as a neural correlate of behavioral-level perceptual narrowing to native language (Kirmse, et al., 2008; Näätänen, 2001; Naatanen, et al., 1997; Näätänen, et al., 2007; Winkler, et al., 1999). In addition to the native experience influences on the MMN component, in Study 1 we also uncovered the native language effect on the P3a ERP component. That is, similar to MMN, the P3a response that indexes the brain stage of involuntary orienting in cortical speech processing was also enhanced to the native phonetic contrast across both language groups.

Study 1 has demonstrated the native language effect on MMN and P3a in adult subjects and supported our fundamental hypothesis that an individual's auditory cortical processing is



substantially influenced by native language experiences. Study 1 also verifies our experimental procedure for MMN and lays the foundation for Study 2 on the development of auditory cortical narrowing among school-age individuals.

### *Auditory cortical narrowing in school-age individuals*

The native language influence on pre-attentive auditory discriminative processing has been studied in adults from different language populations (Čeponienė, Rinne & Näätänen, 2002; Kirmse, et al., 2008; Näätänen, 2001; Naatanen, et al., 1997; Winkler, et al., 1999). However, there have been few studies on the development of MMN to native and non-native speech beyond infancy (Bishop, 2007; Näätänen, et al., 2007). Further, despite of the wide speculation, it has not been well demonstrated that the tuning of MMN to native speech is functionally linked to reading fluency among school-age individuals. Therefore, mapping out the age-related changes of MMN and P3a to native and non-native phonetic contrasts would advance our understanding on the development of auditory cortical narrowing and its relationship with reading development.

In Study 2, we proposed that the native language effect on MMN as well as P3a in adults arises from a *continuous* cortical narrowing to native speech that extends through childhood and adolescence years. Thus, a large cohort of English-speaking school-age individuals from age 6 to age 17 were recruited. This cohort of subjects is divided into three age groups: age 6-9, age 10-13 and age 14-17. Their response strength of MMN and P3a were cross-sectional compared to map out age-related changes of native language effect on cortical speech processing.

Consistent with our theory that cortical narrowing to native speech continues beyond infancy, a significant interaction between age group and contrast stimulus condition was found in

the GFP of MMN and P3a. That is, elder individuals among this cohort of school-age individuals showed more pronounced native language effect on the whole-brain response strength of MMN and P3a, compared with younger individuals. The individuals in age 14-17 group showed stronger GFP of MMN and P3a to the native phonetic contrast /v-w/ than to the non-native contrast /j-q/. In contrast, those in age 6-9 group showed little GFP difference of MMN and P3a between the native and the non-native condition.

The cross-sectional comparison on the response strength of MMN and P3a suggests that, over the course of development, school-age individuals seem to become more sensitive in discriminating and orienting to native speech contrast but less sensitive to non-native phonetic elements (Cheour, et al., 2000; Cheoura, et al., 2001; Näätänen, et al., 2007). This age-related change in the native language effect of MMN and P3a supports our theory that auditory cortical narrowing to native speech continues in childhood through adolescence years, during which an individual's brain processing of speech develops to become specialized or 'tuned' to native language.

In Study 2, we also hypothesized that the auditory cortical narrowing is functionally linked to an individual's reading development. Thus, we investigated the brain-behavioral correlation between one's MMN and P3a response and reading fluency in this cohort of typical school-age individuals. We found that the score of Test of Word Reading Efficiency (TOWRE) is (a) positively correlated with the ERP amplitude of MMN to the native contrast and (b) negatively correlated with the amplitude of MMN to the non-native contrast. The opposite direction of brain-behavioral relationship indicates that individuals whose pre-attentive auditory discriminative processing is more tuned to native language tend to have better fluent reading. This finding

supports our hypothesis that auditory cortical narrowing to native speech is functionally linked to reading development among school-age individuals.

In Study 2, we further evaluated our hypothesis that the brain-behavioral relationship between MMN response strength and reading fluency may perhaps differ between individuals at different age levels. To examine the potential age-related differences in the brain-behavior relationship, we included the ‘age-level’ moderator variable in the regression and examined the interaction between age-level and MMN amplitude in explaining the variance of reading fluency in this cohort of school-age individuals. We found that the relationship between the ERP amplitudes of MMN to the native contrast and the scores of TOWRE depends on or ‘is moderated by’ the age-level moderator variable. Significant positive coefficient of the interaction between MMN amplitude in native condition and age-level moderator revealed that, the reading fluency is more positively correlated with the ERP amplitude of MMN to the native contrast among the individuals at younger age level (age 6 to age 11) comparing to the individuals at elder age level (age 12 to 17).

The different brain-behavioral relationship between MMN and reading fluency at different age levels indicates that, one’s pre-attentive auditory discrimination of native speech sounds plays a prominent role in the early stage of reading development. This finding seems to suggest that, elementary school readers may largely rely on their auditory discriminative processing to perform grapheme-to-phoneme phonological decoding of written words, whereas middle-school and high-school readers are less dependent on the brain function of auditory discrimination, possibly because they have acquired other strategies to achieve efficient reading beyond the phonological decoding of words.

Finally in Study 2, we examined the brain-behavioral relationship between the degree of one's auditory cortical narrowing to native speech and reading fluency. GFP difference between MMN to the native contrast and MMN to the non-native contrast was computed as the measure of the extent to which an individual's auditory discriminative processing is tuned to native speech. Significant positive relationship between the difference GFP of MMN and scores of TOWRE was found. This result supports our prediction that an individual's reading fluency is perhaps associated with the degree to auditory cortical narrowing i.e. how well the speech processing in brain is tuned to native language.

#### *Auditory cortical narrowing in poor readers*

In Study 3, we further investigated the association between auditory cortical narrowing and reading development by comparing the MMN native language effect between a group of poor readers (under the 25th percentile in reading fluency) and their matched controls. We found that, compared with the typical reading group, the poor reading group had reduced MMN to the native contrast /v-w/ and the acoustic contrast /b-t/, both of which are used phonetically in their native speech. Consistent with the 'basic auditory dysfunction' theory, this finding indicates that reading difficulty is associated with dysfunctions in auditory cortical discrimination of native speech sounds (Bishop, 2007; Bruder, et al., 2011a; Kujala, Lovio, Lepistö, Laasonen & Näätänen, 2006; Kujala, et al., 2000; Näätänen, et al., 2012; Pakarinen, et al., 2009; Schulte-Körne & Bruder, 2010).

Furthermore, Study 3 also revealed that the defectiveness of low-level sound processing in the brain is *not* the only attribute of the poor reading group. Beyond the prediction of 'basic

auditory dysfunction' theory for dyslexia, we found that, comparing to the typical reading group, the poor reading group showed even larger MMN to the non-native /j-q/ contrast, indicating that their auditory discrimination is not universally poor. Instead, the poor readers seem to suffer from hypersensitive to speech elements that are not relevant to their native language.

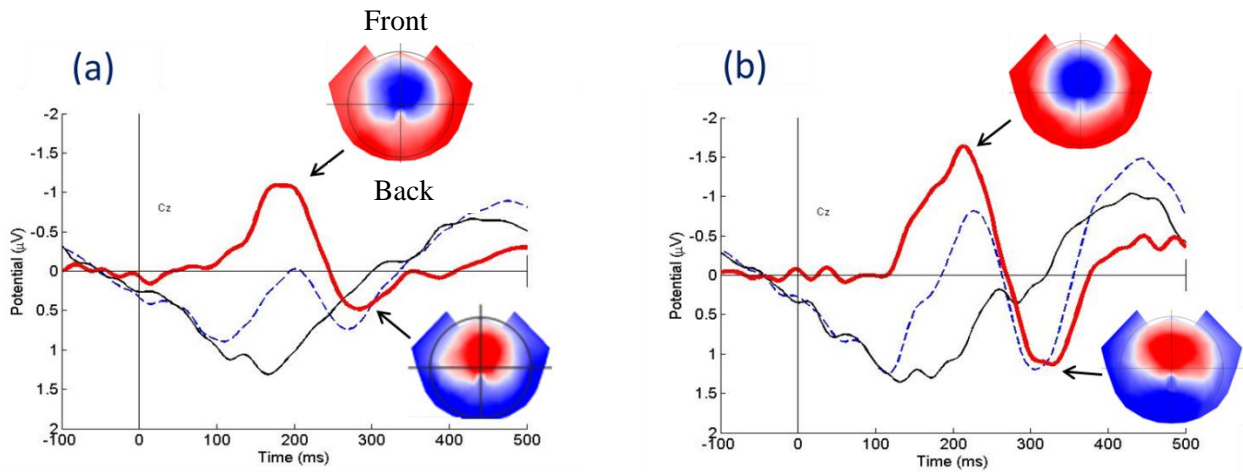
Study 3 revealed that school-age individuals with low reading fluency tend to have reduced MMN to native phonetic contrast along with excessive MMN to non-native contrast, i.e. a lack of MMN native language effect. It indicates that, some individuals with reading difficulty seem to suffer from hyposensitivity of auditory cortical discrimination to native phonemes but hypersensitivity of pre-attentive discrimination to non-native phonemes. The finding of insufficient cortical narrowing to native speech from the poor reading group indicates that brain specialization to native speech is perhaps fundamental for reading development, and insufficient cortical narrowing to native speech can be one of the attributes of individuals with reading difficulty.

### *Conclusion*

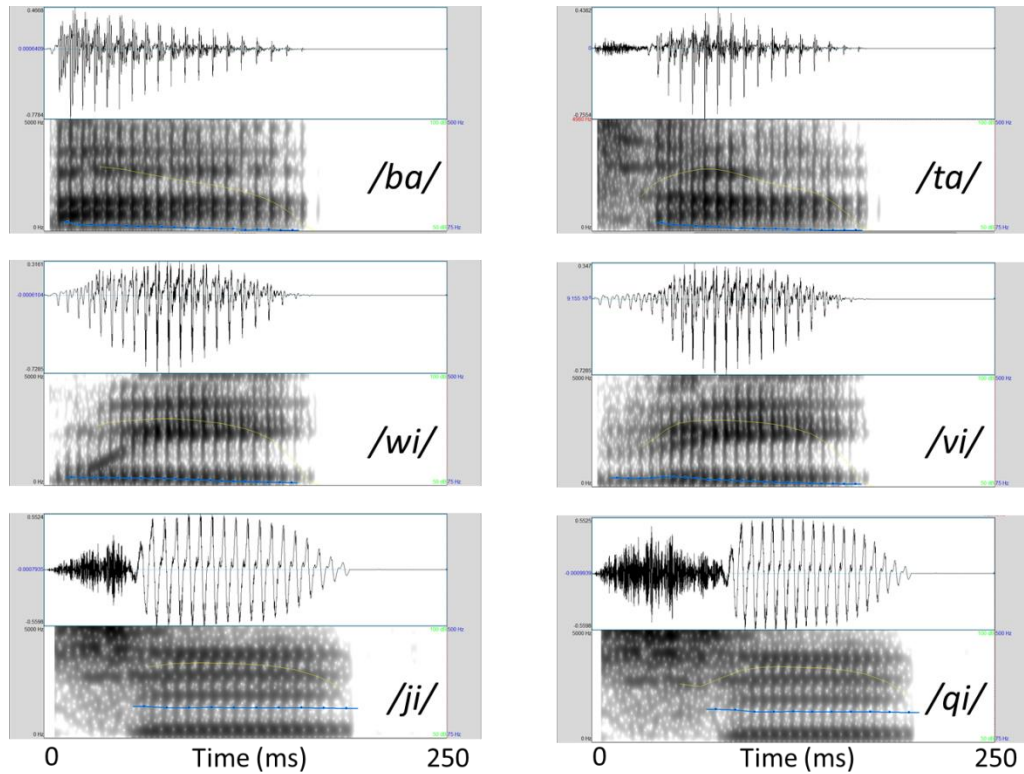
The current thesis advances our understanding of auditory cortical narrowing to native speech with development and its relationship with reading difficulty among school-age individuals. Findings from Study 1, Study 2 and Study 3 in the thesis shed lights on (a) how the MMN ERP component that indexes auditory discriminative processing in the brain is substantially influenced by one's native language experiences and (b) how a lack of MMN native language effect that reflects deficient auditory cortical narrowing to native speech is linked to reading problems. The current thesis will contribute to the scarce literature on these issues and

advance our understanding of auditory cortical narrowing to native speech and its relationship with developmental dyslexia.

## APPENDIX



Supplementary Figure 1. The ERP waveform of ‘Standard’ (solid black) and ‘Deviant’ (dash blue) and the difference waveform (solid red) on electrode Cz under the native contrast condition from Mandarin speaking adults (left, panel a) and English speaking adults (right, panel b). Both language groups showed MMN at 200 milliseconds (ms) and P3a at 300 ms. The 2-D ERP scalp maps showed the topographic distribution of MMN at 200 ms and P3a at 300 ms on the difference waveform. On each of the ERP scalp maps, the front of the head is at the top and the back of the head is at the bottom, crosshairs align with Cz, and negative ERP potential is in blue and positive ERP potential is in red.



Supplementary Figure 2. The sound spectrograms and waveforms of the acoustic contrast /b-t/, the English contrast /v-w/ and the Mandarin contrast /j-q/ used in the auditory oddball paradigm to elicit MMN.

The MMN stimulus contrasts in Study 1, Study 2 and Study 3 were natural speech recorded and edited using Adobe Audition 3.0 software. The stimulus contrast /v-w/ and /b-t/ (in Study 2 and Study 3 only) were produced by a male native English speaker (age 22) and /j-q/ were produced by a male native Mandarin speaker (age 26). The two syllables within a stimulus contrast pair were selected from 30 recorded tokens to match for pitch (blue line in the sound spectrograms) and sound duration. The selected syllables for MMN stimulus contrasts were edited to match for overall amplitude in Adobe Audition 3.0 software ('Match Clip Volume' function to match the sound loudness across source files).



## REFERENCES

- Best, C. T., McRoberts, G. W., & Goodell, E. (2001). Discrimination of non-native consonant contrasts varying in perceptual assimilation to the listener's native phonological system. *The Journal of the Acoustical Society of America*, 109(2), 775-794.
- Bishop, D. V. M. (2007). Using mismatch negativity to study central auditory processing in developmental language and literacy impairments: Where are we, and where should we be going? *Psychological Bulletin*, 133(4), 651-672.
- Bishop, D. V. M., Hardiman, M., Uwer, R., & Von Suchodoletz, W. (2007). Maturation of the long-latency auditory ERP: step function changes at start and end of adolescence. *Developmental Science*, 10(5), 565-575.
- Bishop, D. V. M., Hardiman, M. J., & Barry, J. G. (2010). Lower-Frequency Event-Related Desynchronization: A Signature of Late Mismatch Responses to Sounds, Which Is Reduced or Absent in Children with Specific Language Impairment. *The Journal of Neuroscience*, 30(46), 15578-15584.
- Bishop, D. V. M., Hardiman, M. J., & Barry, J. G. (2011). Is auditory discrimination mature by middle childhood? A study using time-frequency analysis of mismatch responses from 7 years to adulthood. *Developmental Science*, 14(2), 402-416.
- Bitz, U., Gust, K., Spitzer, M., & Kiefer, M. (2007). Phonological deficit in school children is reflected in the mismatch negativity. *NeuroReport*, 18(9), 911-915.
- Bruder, J., Leppänen, P. H. T., Bartling, J., Csépe, V., Démonet, J.-F., & Schulte-Körne, G. (2011a). Children with dyslexia reveal abnormal native language representations: Evidence from a study of mismatch negativity. *Psychophysiology*, 48(8), 1107-1118.
- Bruder, J., Leppänen, P. H. T., Bartling, J., Csépe, V., Démonet, J.-F., & Schulte-Körne, G. (2011b). An investigation of prototypical and atypical within-category vowels and non-speech analogues on cortical auditory evoked related potentials (AERPs) in 9-year old children. *International Journal of Psychophysiology*, 79(2), 106-117.
- Brunet, D., Murray, M. M., & Michel, C. M. (2011). Spatiotemporal Analysis of Multichannel EEG: CARTOOL. *Computational Intelligence and Neuroscience*, 2011.
- Čeponienė, R., Lepistö, T., Shestakova, A., Vanhala, R., Alku, P., Näätänen, R., & Yaguchi, K. (2003). Speech-sound-selective auditory impairment in children with autism: They can perceive but do not attend. *Proceedings of the National Academy of Sciences*, 100(9), 5567-5572.
- Čeponienė, R., Rinne, T., & Näätänen, R. (2002). Maturation of cortical sound processing as indexed by event-related potentials. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 113(6), 870-882.

- Chandrasekaran, B., Krishnan, A., & Gandour, J. T. (2007). Mismatch negativity to pitch contours is influenced by language experience. *Brain Research*, 1128(0), 148-156.
- Cheour, M., H.T. Leppänen, P., & Kraus, N. (2000). Mismatch negativity (MMN) as a tool for investigating auditory discrimination and sensory memory in infants and children. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 111(1), 4-16.
- Cheoura, M., Korpilahti, P., Martynova, O., & Langa, A. H. (2001). Mismatch Negativity and Late Discriminative Negativity in Investigating Speech Perception and Learning in Children and Infants. *Audiology and Neurology*, 6(1), 2-11.
- Csépe, V. (2003). Auditory event-related potentials in studying developmental dyslexia Dyslexia: Different brain, different behavior (pp. 81-112). New York, NY, US: Kluwer Academic/Plenum Publishers.
- Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, 134(1), 9-21
- Dupoux, E., Pallier, C., Sebastian, N., & Mehler, J. (1997). A distressing "deafness" in French? [Article]. *Journal of Memory and Language*, 36(3), 406-421.
- Escera, C., Alho, K., Winkler, I., & Näätänen, R. (1998). Neural mechanisms of involuntary attention to acoustic novelty and change. *J Cogn Neurosci*, 10(5), 590-604.
- Escera, C., & Corral, M. J. (2007). Role of mismatch negativity and novelty-P3 in involuntary auditory attention. *Journal of Psychophysiology*, 21(3-4), 251-264.
- Heim, S., & Keil, A. (2004). Large-scale neural correlates of developmental dyslexia. *European Child & Adolescent Psychiatry*, 13(3), 125-140.
- Horváth, J., Winkler, I., & Bendixen, A. (2008). Do N1/MMN, P3a, and RON form a strongly coupled chain reflecting the three stages of auditory distraction? *Biological Psychology*, 79(2), 139-147.
- Jacquemot, C., Pallier, C., LeBihan, D., Dehaene, S., & Dupoux, E. (2003). Phonological Grammar Shapes the Auditory Cortex: A Functional Magnetic Resonance Imaging Study. *The Journal of Neuroscience*, 23(29), 9541-9546.
- Kirmse, U., Ylinen, S., Tervaniemi, M., Vainio, M., Schröger, E., & Jacobsen, T. (2008). Modulation of the mismatch negativity (MMN) to vowel duration changes in native speakers of Finnish and German as a result of language experience. *International Journal of Psychophysiology*, 67(2), 131-143.
- Kraus, N., Koch, D. B., McGee, T. J., Nicol, T. G., & Cunningham, J. (1999). Speech-Sound Discrimination in School-Age Children: Psychophysical and Neurophysiologic Measures. *J Speech Lang Hear Res*, 42(5), 1042-1060.

- Kraus, N., McGee, T. J., Carrell, T. D., Zecker, S. G., Nicol, T. G., & Koch, D. B. (1996). Auditory neurophysiologic responses and discrimination deficits in children with learning problems. [Article]. *Science*, 273(5277), 971-973.
- Kuhl, P., & Rivera-Gaxiola, M. (2008). Neural substrates of language acquisition *Annual Review of Neuroscience* (Vol. 31, pp. 511-534). Palo Alto: Annual Reviews.
- Kujala, T., Lovio, R., Lepistö, T., Laasonen, M., & Näätänen, R. (2006). Evaluation of multi-attribute auditory discrimination in dyslexia with the mismatch negativity. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 117(4), 885-893.
- Kujala, T., Myllyviita, K., Tervaniemi, M., Alho, K., Kallio, J., & Näätänen, R. (2000). Basic auditory dysfunction in dyslexia as demonstrated by brain activity measurements. *Psychophysiology*, 37(2), 262-266.
- Leppänen, P. H., & Lyytinen, H. (1997). Auditory event-related potentials in the study of developmental language-related disorders. *Audiol Neurootol*, 2(5), 308-340.
- Leppänen, P. H. T., Lohvansuu, K., Bartling, J., Bruder, J., Honbolygó, F., Hämäläinen, J. A., . . . Csépe, V. (2012). Language-specific effects on auditory brain responses in children with dyslexia in four European countries. *International Journal of Psychophysiology*, 85(3), 322.
- Lovio, R., Halttunen, A., Lyytinen, H., Näätänen, R., & Kujala, T. (2012). Reading skill and neural processing accuracy improvement after a 3-hour intervention in preschoolers with difficulties in reading-related skills. *Brain Research*, 1448(0), 42-55.
- Lovio, R., Näätänen, R., & Kujala, T. (2010). Abnormal pattern of cortical speech feature discrimination in 6-year-old children at risk for dyslexia. *Brain Research*, 1335(0), 53-62.
- Maurer, U., Bucher, K., Brem, S., & Brandeis, D. (2003). Development of the automatic mismatch response: from frontal positivity in kindergarten children to the mismatch negativity. *Clinical Neurophysiology*, 114(5), 808-817.
- May, P. J. C., & Tiitinen, H. (2010). Mismatch negativity (MMN), the deviance-elicited auditory deflection, explained. *Psychophysiology*, 47(1), 66-122.
- Murray, M., Brunet, D., & Michel, C. (2008). Topographic ERP Analyses: A Step-by-Step Tutorial Review. *Brain Topography*, 20(4), 249-264.
- Näätänen, R. (2001). The perception of speech sounds by the human brain as reflected by the mismatch negativity (MMN) and its magnetic equivalent (MMNm). *Psychophysiology*, 38(1), 1-21.
- Näätänen, R., Kujala, T., Escera, C., Baldeweg, T., Kreegipuu, K., Carlson, S., & Ponton, C. (2012). The mismatch negativity (MMN) – A unique window to disturbed central auditory processing in ageing and different clinical conditions. *Clinical Neurophysiology*, 123(3), 424-458.

- Naatanen, R., Lehtokoski, A., Lennes, M., Cheour, M., Huotilainen, M., Iivonen, A., Alho, K. (1997). Language-specific phoneme representations revealed by electric and magnetic brain responses. [10.1038/385432a0]. *Nature*, 385(6615), 432-434.
- Näätänen, R., Paavilainen, P., Rinne, T., & Alho, K. (2007). The mismatch negativity (MMN) in basic research of central auditory processing: A review. *Clinical Neurophysiology*, 118(12), 2544-2590.
- Näätänen, R., Pakarinen, S., Rinne, T., & Takegata, R. (2004). The mismatch negativity (MMN): towards the optimal paradigm. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 115(1), 140-144.
- Noordenbos, M. W., Segers, E., Serniclaes, W., Mitterer, H., & Verhoeven, L. (2012). Neural evidence of allophonic perception in children at risk for dyslexia. *Neuropsychologia*, 50(8), 2010-2017.
- Pakarinen, S., Lovio, R., Huotilainen, M., Alku, P., Näätänen, R., & Kujala, T. (2009). Fast multi-feature paradigm for recording several mismatch negativities (MMNs) to phonetic and acoustic changes in speech sounds. *Biological Psychology*, 82(3), 219-226.
- Schulte-Körne, G., & Bruder, J. (2010). Clinical neurophysiology of visual and auditory processing in dyslexia: A review. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 121(11), 1794-1809.
- Skrandies, W. (1990). Global field power and topographic similarity. *Brain Topography*, 3(1), 137-141.
- Tsang, Y.-K., Jia, S., Huang, J., & Chen, H.-C. (2011). ERP correlates of pre-attentive processing of Cantonese lexical tones: The effects of pitch contour and pitch height. *Neuroscience Letters*, 487(3), 268-272.
- Tsao, F.-M., Liu, H.-M., & Kuhl, P. K. (2006). Perception of native and non-native affricate-fricative contrasts: Cross-language tests on adults and infants. *The Journal of the Acoustical Society of America*, 120(4), 2285-2294.
- Werker, J. F., & Tees, R. C. (2002). Cross-language speech perception: Evidence for perceptual reorganization during the first year of life. *Infant Behavior and Development*, 25(1), 121-133.
- Werker, J. F., & Tees, R. C. (2005). Speech perception as a window for understanding plasticity and commitment in language systems of the brain. *Developmental Psychobiology*, 46(3), 233-251.
- Wetzel, N., Widmann, A., Berti, S., & Schröger, E. (2006). The development of involuntary and voluntary attention from childhood to adulthood: A combined behavioral and event-related potential study. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 117(10), 2191-2203.

- Winkler, I., Lehtokoski, A., Alku, P., Vainio, M., Czigler, I., Csépe, V., Näätänen, R. (1999). Pre-attentive detection of vowel contrasts utilizes both phonetic and auditory memory representations. *Cognitive Brain Research*, 7(3), 357-369.
- Xi, J., Zhang, L., Shu, H., Zhang, Y., & Li, P. (2010). Categorical perception of lexical tones in Chinese revealed by mismatch negativity. *Neuroscience*, 170(1), 223-231.
- Zevin, J. D., Datta, H., Maurer, U., Rosania, K. A., & McCandliss, B. D. (2010). Native language experience influences the topography of the mismatch negativity to speech. [Original Research]. *Frontiers in Human Neuroscience*, 4.
- Zhang, L., Xi, J., Wu, H., Shu, H., & Li, P. (2012). Electrophysiological evidence of categorical perception of Chinese lexical tones in attentive condition. *NeuroReport*, 23(1), 35-39
- Zhang, Y., Kuhl, P. K., Imada, T., Iverson, P., Pruitt, J., Stevens, E. B., Nemoto, I. (2009). Neural signatures of phonetic learning in adulthood: A magnetoencephalography study. *NeuroImage*, 46(1), 226-240.
- Zhang, Y., Kuhl, P. K., Imada, T., Kotani, M., & Tohkura, Y. (2005). Effects of language experience: Neural commitment to language-specific auditory patterns. *NeuroImage*, 26(3), 703-720.
- Zhang, Y., Zhang, L., Shu, H., Xi, J., Wu, H., Zhang, Y., & Li, P. (2012). Universality of categorical perception deficit in developmental dyslexia: an investigation of Mandarin Chinese tones. *Journal of Child Psychology and Psychiatry*, 53(8), 874-882.