Auditory Temporal Processing in Children with Specific Language Impairment Compared to Same-Age Controls

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A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

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Compared to Same-Age Controls

(Thesis format: Monograph)

by

Elaine Yuen Ling Kwok

Graduate Program in Health and Rehabilitation Sciences

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science (Child and Youth Health)

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Abstract

It has been proposed that impaired language development in children with Specific Language Impairment (SLI) originates from immature auditory temporal integration (ATI), but results are inconsistent. We compared electroencephalographic data from 25 children with SLI aged 6-11 years to 25 typically developing peers. Participants’ neural responses to a 50ms tone presented alone were compared to their responses to two tones separated by silent gaps of 100, 200, 300 or 400ms. Amplitude and latency of P1 and N2 responses to single tones and tone pairs were compared across groups and gap conditions. The groups did not differ in the amplitude or latency of their responses to the second tone in any gap condition. Both groups showed attenuated, but present, responses to the second tone even in the shortest gap condition. Although results did not provide evidence for ATI impairments in SLI, further research using smaller gaps is required.

Keywords: Auditory Temporal Integration (ATI); Specific Language Impairment (SLI); language learning; child language development,
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Table of Contents

Abstract .......................................................................................................................... ii

Acknowledgements ..................................................................................................... iii

List of Tables ................................................................................................................ vii

List of Figures ............................................................................................................. viii

List of Appendices ...................................................................................................... ix

Introduction ................................................................................................................ 1

Characteristics of Specific Language Impairment (SLI) ........................................... 1

Auditory Temporal Integration (ATI) ......................................................................... 2

ATI and Language Learning ....................................................................................... 3

Event Related Potential Studies ................................................................................. 8

ATI studies focusing on Mismatch Negativity (MMN) .......................................... 8

ATI studies focusing on Cortical Auditory Evoked Potentials (CAEP) ............. 13

Purposes of This Study ............................................................................................... 16

Method ......................................................................................................................... 18

Participants ................................................................................................................ 18

Procedures .................................................................................................................. 20

Stimuli ......................................................................................................................... 21
Conditions……………………………………………………………….21

EEG Recording………………………………………………………………22

Data recording and online processing……………………………………23

Offline Processing and Data Analysis……………………………..……23

EEG waveform offline processing……………………………………23

Principle Component Analysis (PCA) of individually subtracted
waveforms……………………………………………………………….23

Results…………………………………………………………………………………..25

PCA on Second Tone Responses………………………………………25

Analysis of mean amplitude………………………………………………30

Analysis of peak latency…………………………………………………37

Analysis of maximum amplitude………………………………………41

Summary of Analyses………………………………………………………44

Discussion………………………………………………………………………..45

ATI Impairment in SLI Compared to Controls………………………46

Is ATI not impaired in SLI? ………………………………………..47

Are children with SLI only impaired at the level of auditory
discrimination?...............................................................48
Impaired detection of rapidly presented stimuli in SLI...........50

P1 and N2 as a Neural Indicator of ATI....................................53

Comparison of Our TD Data to the Literature..........................54

Difference in tonal frequency and duration.........................55

Difference in tone intensity (Loudness).............................56

Limitations and Future Directions........................................57

References...........................................................................61

Appendices..........................................................................69

Curriculum Vitae...................................................................78
List of Tables

Table 1. Expected result for P1 and N2 amplitude to the second tone in TT conditions analysis…………………………………………………………………………………………………………………………………………18

Table 2. Participant demographic information…………………………………………………………...20

Table 3. Mean amplitude of P1 over latency range 64 to 148ms for selected channels…33

Table 4. Mean amplitude of N2 over latency range 208-296ms for selected channels….36

Table 5. Summary of P1 and N2 latencies in TD and SLI (channel Fz only)……………39

Table 6. Maximum amplitude of P1 and N2 in subtracted two tone waveforms (channel Fz Only)………………………………………………………………………………………………………………………42
List of Figures

Figure 1. Stimuli Paradigm........................................................................................................22

Figure 2a. Grand average waveform of TD group across selected channels. ..............26

Figure 2b. Grand average waveform of SLI group across selected channels..............27

Figure 3a. Topographic images of subtracted waveform of TD group......................28

Figure 3b. Topographic images of subtracted waveform of children with SLI........29

Figure 4a. Grand average of OT and subtracted TT waveform of TD group.............31

Figure 4b. Grand average of OT and subtracted TT waveform of SLI group..........33

Figure 5. Grand average waveforms showing main effect of channels across conditions for the period 64ms to 148ms (P1).................................................................34

Figure 6. Interaction effect of channel by condition for mean P1 amplitude.........34

Figure 7. Grand average waveforms showing main effect of channels across conditions for the period 208ms to 296ms (N2).................................................................38

Figure 8. Interaction effect of channel by condition for mean N2 amplitude ..........38

Figure 9. P1 peak latencies at channel Fz across conditions......................................40

Figure 10. N2 peak latencies at channel Fz across conditions.................................41

Figure 11. Maximum P1 amplitude at channel Fz across conditions.........................43

Figure 12. Maximum N2 amplitude at channel Fz across conditions.......................44
List of Appendices

Appendix A: Matched TD and SLI participants information……………………………69

Appendix B: Quantile-Quantile plots of showing distribution of second tone P1 amplitude at TT100, N2 amplitude at TT100, N2 amplitude at TT200 condition……..70

Appendix C: Ethics approval……………………………………………………………………72

Appendix D: Letter of information and consent form………………………………………73

Appendix E: Assent form………………………………………………………………………76
Introduction

Characteristics of SLI

Specific language impairment (SLI) is a language disorder affecting 7% of individuals, with higher prevalence in males than females. These individuals experience difficulties acquiring language despite otherwise normal development in cognitive, neurological and hearing abilities and irrespective of socioeconomic status (Leonard, 2000). It has been reported that individuals with SLI have increased risk for difficulties in academic learning (Conti-Ramsden, Knox, Botting, & Simkin, 2000; Young et al., 2002) and establishing friendships (Fujiki, Brinton, & Todd, 1996).

Many studies have investigated and characterized the language impairment in SLI from different perspectives. Some studies have centered on biological origins. Familial studies showed some linkage of language impairment within family members, suggesting a role of genetics. For example, a region on chromosome 7 that contains a gene, *FOXP2*, has shown to be mutated in some families in which multiple members have language impairment (O’Brien, Zhang, Nishimura, Tomblin, & Murray, 2003). Neuroanatomical abnormalities have also been observed in individuals with SLI, particularly in language-relevant areas such as Broca’s area (Bishop, 2006). From a linguistic perspective, English-speaking individuals with SLI have been described as demonstrating a lesser extent of impairment in vocabulary and phonology development as compared to syntax and grammatical morphology (e.g., past tense), and to display more impaired expressive than receptive language (Leonard & Weber-Fox, 2008). Studies that focused on cognitive underpinnings have showed that these individuals demonstrate impairments in multiple areas of processing compared to typically developing peers. For example, children with
SLI have been noted to be impaired in both verbal short-term and working memory (Archibald & Gathercole, 2006) and to have slower response time to various processing tasks (Leonard & Weber-Fox, 2008; Miller, Kail, Leonard, & Tomblin, 2001). Other studies have suggested that individuals with SLI have poor attention (e.g., Shafer, Morr, Datta, Kurtzberg, & Schwartz, 2005).

One theory of particular interest to the present study relates to the auditory processing ability of individuals with SLI. Studies have indicated that children with SLI have poor frequency discrimination ability (McArthur & Bishop, 2004) and such ability, though maturing with age, shows persistent impairments into adolescence compared to age-matched controls (Hill, Hogben, & Bishop, 2005). Other studies have focused on the proposal that individuals with SLI are specifically impaired in their ability to process auditory stimuli that occur in rapid succession, a theory that is explored from a neurophysiological perspective in the present study. The sections that follow review literature on temporal integration of auditory stimuli, as well as behavioral and neurofunctional studies involving individuals with SLI that inspired the design of the present study.

**Auditory Temporal Integration**

Early behavioral studies of auditory processing involved measuring participants’ reports on the loudness and pitch of auditory signals that were presented at varying durations and with varying time gaps between stimuli. Results revealed that auditory signals are integrated if presented rapidly. This phenomenon was termed Auditory Temporal Integration (ATI) (Cowan, 1984). For example, Zwishlocki (1960) conducted an experiment in which adult participants were asked to report perceived loudness of two
successive tone bursts presented with varying time gaps between them. Participants reported an increased loudness when the two tone bursts were presented at gaps shorter than 200ms (Zwislocki, 1960). It was proposed that this perception of increased loudness resulted from auditory summation of the two tones. That is, when neurons are first activated in response to the primary tone, and before they return back to an inactivated state, the second tone stimulates them to fire again, resulting in overall signal summation. As a result, the activation of the second stimulus is combined with the residue activation of the first stimulus leading to a perceived increase in tone loudness (Zwislocki, 1969).

This and other behavioral studies estimated that integration occurs in typical adults when auditory stimuli are presented within a roughly 200-300ms window (see Cowan, 1984 for a review) and this window decreases with increasing age (Trehub, Schneider, & Henderson, 1995). Later neural evidence confirmed the existence of the window and showed that auditory signals are integrated as unitary percepts if presented within the integration window (i.e., cannot be distinguished as separate signals), but are processed independently if presented outside of the window (Winkler, Czigler, Jaramillo, Paavilainen, & Näätänen, 1998; Yabe, Tervaniemi, Reinikainen, & Näätänen, 1997). Therefore, a shorter window of ATI will provide higher resolution for the processing of auditory signals. Putatively, this higher resolution is important for language learning.

**ATI and Language Learning**

The importance of ATI to language acquisition has been proposed through a number of behavioral studies involving individuals with SLI. A number of studies have suggested that individuals with SLI have an immature ATI. For example, Tallal and Piercy (1973) asked 6-9 year old children to indicate whether two rapidly presented tones
were of the same or different pitch. Typically developing children performed significantly better than chance when the tones were separated with a silent gap as short as 8ms, whereas children with SLI required a significantly longer silent gap between tones (>300ms)\(^1\) to reach the same level of accuracy. A similar impairment in temporal processing ability has also been shown by other behavioral studies in individuals with SLI (reviewed by Leonard, 2000; Tallal, Miller, & Fitch, 1993).

The role of ATI in language development was further examined in longitudinal research conducted by Benasich and Tallal (2002). They studied ATI in infants at 6-12 months with or without a family history of language impairments, and later examined their language performance at 2-3 years of age. To study ATI in infants, an operant conditioning paradigm was used, where the infants were trained to turn their head towards a visual reinforcer when presented with a tone pair (left for 100Hz tone followed by 300Hz; and right for 300Hz tone followed by 100Hz). Blocks of randomized order tone pairs were presented with varying silent gaps between the tones to determine their threshold of ATI. When tones were presented at silent gaps shorter than their ATI window, infants performed no better than chance. Result indicated that the ATI window of infants with a family history of language impairment was longer than for those without. Importantly, the ATI window at this early age was predictive of later language performance on a standardized language test at 2 year of age, regardless of family history.

\(^1\) Different studies used different terminologies to describe the time separation of tone pairs in the experiment. Some studies (e.g. Wang et al., 2005) used stimuli-onset-asynchrony (SOA, measured from onset to onset of successive tones); while others (e.g. Tallal & Piercy, 1973. Fox et al., 2010) used inter-stimulus intervals (ISI, which is measured from offset of the first tone to onset of the second tone). For the purpose of this thesis, results from all studies as well as the estimated window of ATI are reported in terms of ISIs, which we termed silent gap for more intuitive understanding.
of language impairment (Benasich & Tallal, 2002). This study suggested that early
development in processing of rapidly presented fundamental auditory stimuli plays an
important role in language development.

Although a causal link between ATI and language acquisition has not been
established, one of mechanism has been proposed to account for the effect of immature
auditory temporal processing on language acquisition in individuals with SLI. Tallal et al.
(1993) suggested the link between the two lies in the less efficient processing of
phonemes, which are the smallest contrastive units in spoken language (Tallal et al.,
1993; Tallal, 1999). Tallal and Piercy (1974) conducted an experiment in which they
trained 6-9 year old participants (typically developing or SLI) to press buttons
corresponding to computer-generated speech stimuli. The first pair of stimuli was the
vowels /E/ and /æ/, which had steady-state frequencies throughout their presentation.
Participants with SLI performed no different from the controls in distinguishing this pair
of speech stimuli. The second pair of stimuli was the syllables /ba/ and /da/, which
differed only in the initial 40ms for the corresponding frequencies of consonants b and d.
Result showed that all 12 typically developing participants but only 2 out of 10
participants with SLI reached criterion (75% correct) after training. Participants with SLI
also reported hearing no difference between the two consonant syllables (Tallal & Piercy,
1974). Tallal and her group also performed more experiments on speech stimuli and
showed similar impairments in individuals with SLI (see Tallal et al., 1993 for a review).

Tallal, Stark and Mellits (1985) found a high correlation (r=0.85) between
performance on tasks for discriminating rapidly presented (speech and non-speech)
stimuli and performance on standardized tests of receptive language for individuals with
SLI (Tallal, Stark, & Mellits, 1985). Taken together, the evidence from speech and non-speech ATI experiments suggest that individuals with SLI may have an immature ATI window that restricts their ability to perceive rapid transitions of information in speech sounds, hence contributing to difficulties in learning language (Tallal et al., 1993).

Several other behavioral research studies were conducted to investigate the causal relationship between ATI and language impairment, however, not all results showed that individuals with SLI have impairment in ATI. A handful of studies found that individuals with SLI performed no different from TD controls on ATI tasks (see McArthur & Bishop, 2001 for a review). For example, Norrelgen et al. (2001) used a similar frequency determination task of two successive tones to that used in Tallal and Piercy (1973), involving shorter (20ms) and higher frequencies tones (878Hz and 1350Hz). Participants were asked to report if the two successive tones were same or different in pitch. A speech perception task was also included, where participants were presented two successive same or different consonant-vowel pairs (e.g. /pa/ followed by /ba/) with the same separation time gap as the tone pairs, and participants were asked to report if the vowel pairs were the same or different. In their first experiment, they assessed the correlation between the tonal and speech perception tasks. Result showed a normal distribution of performance on frequency determination of rapidly presented tones in the TD population, challenging the uniqueness of impairments of ATI to the language impaired population. In addition, the authors also found that performance on the rapid tones task was only weakly correlated ($r = 0.35$) with the speech perception task. The author argued that under the proposed causal relationship between ATI development and phonological awareness, a strong correlation should be found in the two experimental tasks. A weak correlation between the two
experimental tasks suggested an indirect relationship that involves other factors that the author did not examine, such as age of the participants.

In their second experiment, Norrelgen et al. investigated the relationship of ATI and language development. Performance of TD participants on rapidly presenting tones task was correlated to several language measures. Results revealed that only phonological awareness was significantly correlated with ATI task performance ($r = 0.47$). Results of this second experiment suggested that the relationship between ATI performance and language development is limited to level of phonological processing and may not be relevant to higher order language aspects such as lexical and receptive grammar development. Using the same tonal and consonant-vowel paradigm, Norrelgen, Lacerda and Forssberg (2002) compared the performance of a group of individuals with SLI to a same-age typically developing group. Results revealed that there was no group difference in performance. Both groups showed equal levels of difficulty in identifying the pitch of two successive tones that were presenting with a silence gap smaller than 64ms. Similarly, performances on the speech perception task greatly overlapped between the two groups and no group difference was observed.

Some other studies have suggested that only a subgroup of individuals with SLI have impairment in ATI compared to controls. For example, McArthur and Hogben (2001) found that only individuals with SLI who show poor reading performance have impairments in ATI compared to controls. Therefore, the proposed link between impaired ATI and impaired language development has not received consistent support from behavioural studies.
Some researchers have suggested that at least a subset of individuals with SLI may have poor attention or motivation, which could contribute to the inconsistency of findings in behavioral studies of auditory processes (McArthur & Bishop, 2005). One behavioral study demonstrated impairments of ATI in children with attention-deficit/hyperactivity disorder who do not have co-occurring SLI (Oram Cardy, Tannock, Johnson, & Johnson, 2010). This result highlighted that the use of behavioral responses as an indicator of ATI impairment may not reflect the underlying language or auditory processing impairment of an individual but rather the level of attention. Other traits of SLI that may also limit performance on behavioral tasks include immature motor control (see Hill, 2001 for a review) and slow processing speed (Miller et al., 2001). To avoid this potential confound, some studies employed a passive paradigm through the use of electroencephalography (EEG) to capture the brain’s response to auditory signals in the absence of a behavioural response.

**Event Related Potential Studies**

One neural marker for auditory processing is the late auditory evoked potentials (LAEP), which are electrical potentials generated from the brain in response to auditory stimuli, predominantly originating from auditory cortex in the temporal lobe (Picton, 2010). Of the many components in the LAEP, mismatch negativity (MMN) and cortical auditory evoked potentials (CAEP) such as P1 and N2 are often the focus in studies examining temporal integration.

**ATI studies focusing on Mismatch Negativity (MMN).** Mismatch Negativity is an evoked response occurring at roughly 100 to 200ms after the presentation of auditory stimuli (Hall, 2006), and is classified as a processing-contingent potential reflecting the
active involvement of the brain in discriminating auditory stimuli (Burkard, Don, & Eggermont, 2007). MMN was first reported by Näätänen, Gaillard and Mäntysalo in 1978 using an oddball paradigm where they presented, in a stream of standard stimuli, an infrequently occurring deviant stimulus (an auditory stimulus slightly louder or higher in pitch than the standard). MMN is the residual negative component after subtracting the auditory evoked potential of the standard stimuli from that of the deviant stimuli. It is suggested that MMN represents the brain’s discrimination of a stimulus as different from the short term auditory memory trace of what has come before (i.e., the standard; Näätänen, Paavilainen, Rinne, & Alho, 2007; Näätänen, 2003).

Some studies have used MMN as an indicator of auditory processing in typically developing children. Wang, Datta, and Sussman (2005) used a modified oddball paradigm where adults and typically developing children aged 5-8 and 9-11 years were presented with different blocks of trials, each varying in the length of a silent gap between two stimuli. A total of six gaps were studied: 100, 150, 200, 250, 300, and 350ms\(^2\). In each trial within the same block, all successive stimuli were presented at one of the six gaps. Standard stimuli (440Hz 80db) were presented 85% of the time. A double deviant stimulus, which was made up of a frequency deviant (490Hz 80db) followed by an intensity deviant (440Hz, 60db), randomly occurred 15% of the time. In trials of tones separated by a silent gap shorter than the participant’s ATI window (i.e., successive auditory stimuli will be perceived as unitary), the double deviant triggered only one MMN response. By contrast, two MMN responses were observed for stimuli presented

\(^2\) For participants aged 5-8 years old, only blocks with gaps of 250, 300, and 350 were presented because a pilot study revealed that this age group did not show a neural response to deviants at gaps shorter than 250ms.
with a silent gap longer than that participant’s ATI window. Results indicated a developmental maturation of the window of ATI in the typically developing population, with an estimated window in adults, 9-11 year olds, and 5-8 year olds to be less than 150, 250 and 300ms, respectively (Wang, Datta, & Sussman, 2005). A similar estimate of the window of ATI in adults (<200ms) was also observed in another MMN study using a similar paradigm (Winkler et al., 1998).

Only a few MMN studies have directly compared ATI in individuals with SLI and typically developing individuals. Using an oddball paradigm with a frequency deviant (standard 500Hz, deviant 553Hz), Korpilahti and Lang (1994) showed that children with SLI aged 7-13 years old had a significantly attenuated MMN amplitude at a presentation gap of 350ms compared to age matched, typical controls. Similarly, Benaisch et al. (2006) found that 6-month old infants at with a family history of language impairment produced a MMN response to a frequency deviant (standard 100Hz, deviant 300Hz) that was smaller in amplitude than that of infants without a family history of language impairment, for trials with shorter gaps between tones (70ms) but not longer gaps (300ms).

Consistent with behavioral studies, results of these MMN studies have indicated that the window of ATI matures with age, and individuals with SLI have an immature ATI window compared to age-matched typically developing individuals. One other MMN study has been conducted on individuals with SLI. Uwer, Albrecht, and Von Suchodoletz (2002) used both frequency deviants as well as duration deviants and found no significant difference in MMN amplitude between individuals with SLI and typically developing controls. However, the silent gap used in the experiment was relatively long
(around 900ms), so it may not have captured the developmental difference in auditory integration of the two groups.

What remains uncertain from the aforementioned MMN studies is whether individuals with SLI were impaired in their ability to detect or to discriminate rapidly presented tones. There is some debate as to whether MMN is a neural indicator of auditory detection of rapidly presented tones. The detection of a mismatch in auditory stimuli recruits two cognitive functions: first, the formation of an auditory memory trace of the standard stimulus, and second, the ability to detect a difference between the deviant stimulus and existing memory. An early study showed that the MMN response in an oddball paradigm did not vary in conditions where participants were asked to attend to the auditory signal or when they were distracted by performing a simultaneous visual task. This result and other studies suggested that MMN is an automatic response that does not require conscious attention (Alho, Woods, Algazi, & Näätänen, 1992). However, more recent evidence has suggested that MMN is not entirely attention-independent. When participants were asked to attend to different aspects (e.g., pitch or pattern) of the same oddball paradigm, MMN responses varied, and were not elicited in the condition where the participants’ attention was drawn to the presentation pattern of the paradigm (Sussman, Winkler, Huotilainen, Ritter, & Näätänen, 2002). This suggested the involvement of selective attention to the auditory stimuli in MMN production. Later on, it was further clarified that attention modulates the formation of auditory memory of the standard stimuli, in turn altering the deviance detection process and leading to varying MMN responses. Therefore, it has been recommended that future research should not consider MMN as an index of pre-attentive neural response (Sussman, 2007).
Bishop (2007) reviewed the auditory processing literature on SLI involving MMN studies, and commented that the choice of frequency deviants also contributed to the inconsistency in the literature. It has been shown that significant group differences in MMN between individuals with SLI and controls was only observed in paradigms that used a deviant that was less than 10% different in frequency compared to the standard stimuli; no group difference was observed for larger frequency differences. This is particularly concerning given that other studies have suggested individuals with SLI have poor frequency discrimination (e.g., McArthur & Bishop, 2004). There is debate as to whether the MMN difference between groups results from poor frequency discrimination or if it reflects the inability of individuals with SLI to detect the frequency deviant because of short presentation time. Many suggested that the focus of MMN experiments is on discrimination, rather than simple detection, of auditory signals (for example, Bishop & McArthur, 2005). Thus, MMN evidence showing an impairment of ATI in individuals with SLI may reflect a disability in auditory discrimination rather than the simple detection of auditory stimuli. Paradigms other than MMN, such as the one used in the present study, are required in order to determine whether children with SLI are also impaired at the level stimulus detection.

Another limitation with the use of an oddball paradigm for examining ATI is the necessity of collecting many trials. Since MMN is only observed during deviant trials, which must occur infrequently in any experimental blocks, MMN experiments contain many trials of standards in order to obtain enough deviant trials for analysis. In order to identify the gap durations at which a participant does versus does not show a MMN response, many gap conditions, each with many trials, are therefore required to pinpoint
the ATI threshold. However, a lengthy experiment is not readily tolerated by young children or functionally compromised participants. Bishop (2007) also pointed out that studies using MMN have generated inconsistent findings on the ATI ability of individuals with SLI due to a restricted number of trials available for analysis, thus, conclusions are often limited by noise in the data.

**ATI studies focusing on cortical auditory evoked potentials (CAEP).** A handful of studies have investigated the use of a pre-attentive neural indicator of stimulus detection such as cortical auditory evoked potentials (CAEP). CAEP emerge starting around 50ms post-stimulus and last until 500ms post-stimulus, and reflect the earliest processing of stimuli in the auditory cortex (Picton, 2010). These potentials are considered sensory-evoked potentials, reflecting the fact that these potentials are obligatory and fundamentally dependent on the features of the auditory stimuli (Burkard et al., 2007).

Among the many components in the CAEP, P1 and N2 are the most prominent in the auditory evoked potential waveforms of children under 13 years and thus were chosen as the focus in this study. Although N1 and P2 are also found in adult CAEP, these components do not clear emerge until adolescence, so were not investigated in this study (Albrecht, Suchodoletz, & Uwer, 2000; Sussman, Steinschneider, Gumenyuk, Grushko, & Lawson, 2008). P1, a positivity that peaks around 80-110ms post-stimulus (Ponton, Eggermont, Kwong, & Don, 2000), is believed to be generated in Heschl’s gyrus (Albrecht et al., 2000), part of the secondary auditory cortex. Since P1 has been shown to be present even when participants are sleeping, it has been proposed to reflect pre-perceptual processing of auditory information (Čeponienė, Alku, Westerfield, Torki, &
Townsend, 2005). At 220-270ms post-stimulus onset, N2 is observed, which is a negative-going component reflecting perception of the auditory signal, and has been suggested to originate from primary auditory cortex (Ruhnau, Herrmann, Maess, & Schröger, 2011).

Fox et al. (2010) examined the ATI window in typically developing children aged 7-9 years and adults by observing the CAEP. Brain responses were recorded in children when presented with a single 1000Hz tone, and six conditions of two identical 1000Hz, 20ms tone pairs separated by varying length of silent gaps (25, 50, 100, 200, 400, and 800ms). Individual CAEP to the single tone was subtracted from the response to tone pairs, and the residual average P1 amplitude corresponding to the timing of the second tone presentation (i.e., P1 response to the second tone) was measured. In cases where the tone pair is presented within the child’s ATI window (two tones will be perceived as a unit) a second tone response will be absent, and thus no residual P1 amplitude should be observed. On the contrary, if the tone pair falls outside of the child’s integration window, the two tones will be perceived as separate units, hence, a second P1 response to the second tone will be present. Results revealed that the average P1 amplitude to the second tone increased with increasing silent gap duration between tones and was not significantly different from zero in typically developing children when the tones were separated by a gap of less than 200ms, suggesting that 200ms is the threshold of the window of temporal integration in children of this age group. Similar analysis on the N1 component was conducted on adult data and showed that the window of ATI was shorter in adults (<100ms).
Fox et al.’s (2010) findings were consistent with above mentioned Wang et al. (2005) MMN study. In addition to MMN, Wang et al. also analyzed P1 amplitudes on the grand averaged standard stimulus trials of different tone gaps. In adults and 9-11 year old children, P1 amplitude increased with increasing silent gap between tones and P1 amplitude from trials with shorter silent gaps between tones (<150ms) was significantly smaller than that from longer gaps (>200ms), suggesting the ATI window in children aged 9-11 years is less than 200ms. However, no such difference in amplitude was observed in 5-8 year old children across any tested silent gaps, possibly because the difference in P1 amplitude can only be observed in smaller tone gaps (e.g., 200ms) which were not included in the experimental procedure of this age group. Both Fox et al. and Wang et al. demonstrated the use of P1 as a neural indicator of processing of rapidly presenting tones. The same window of temporal integration was indicated in Fox et al. on a slightly younger group of typical children. This is likely due to the use of different auditory stimuli (Fox et al. used shorter and higher frequency stimuli compared to Wang et al.), highlighting that the window of temporal integration is specific to the stimuli properties.

Oram Cardy, Flagg, Roberts, Brian and Roberts (2005) conducted a magnetoencephalography (MEG) experiment on individuals with language impairment aged 8 to 17 years using two identical tones (1000Hz) presented with a separation gap of 150ms. They reported that a M50 response (a magnetic equivalent of P1) to the second tone in the pair was observed in significantly fewer individuals with SLI (34%) than same age typically developing controls (90%). Together with Fox (2010) and Wang (2005), these
studies suggest the possibility of using the P1 amplitude as an indicator of ATI in both a typically developing population and individuals with SLI.

In the Korpilahit and Lang (1994) MMN study mentioned above, the grand average waveforms of standard trials showed a significant positive peak at 100ms and a negative peak at 250ms (N2) post-stimulus that was observed in both SLI and control groups. P1 and N2 average amplitude and peak latencies in the standard trials were also analyzed. At a 350ms presentation gap between tones, children with SLI aged 7-13 years compared to their TD peers showed a significant delayed N2 peak but no group differences were observed in P1 amplitude, P1 latency, or N2 amplitude. Unlike the above mentioned CAEP studies, result from this study shows that P1 amplitude was not a sensitive neural indicator and that analysis on peak latency may reflects a group difference.

**Purposes of This Study**

The purposes of this study were 1) to further examine ATI in children with SLI compared to typically developing peers; and 2) to investigate the use of P1 and N2 as neural indicators of ATI at the level of stimulus detection. Past behavioral studies have suggested immature ATI in individuals with SLI, but methodology has possibly been limited by attention and motivation confounds. Using a passive paradigm, a few mismatch negativity (MMN) studies have suggested a similar impairment, however, the lengthy experimental procedure may not be readily tolerated by children. In addition, results reflect an impairment at the level of discrimination of auditory information, but do not indicate whether impaired ATI is also observable at a more fundamental level of stimulus detection. A few studies have used CAEP as a pre-attentive indicator of auditory
detection. Here, we further examined the role of ATI in SLI using a short and passive paradigm, and measured the cortical P1 and N2 responses, in order to characterize the ability of individuals with SLI to detecting rapidly presented tones.

Past studies showed that typically developing children aged between 5 and 8 years integrated auditory stimuli presented in a time gap smaller than 300ms (Wang, 2005) and children aged 7 to 9 years integrated stimuli presented with a gap less than 200ms (Fox, 2010). Therefore, we used four gaps ranging from 100 to 400ms to estimate the AWI in children aged 6-11 years old who were typically developing or had SLI. In order to isolate the neural response to the second tone from that to the first tone, we adopted the subtraction and Principal Component Analysis method reported by Fox et al. (2010, see Methods section for further detail). In addition to the four blocks of two tones with different time gaps between tones, every participant was also presented a block where only one tone was presented. Mean amplitude, maximum amplitude, and peak latency of the P1 and N2 responses to the second tone were compared across the four silent gap conditions and between the groups.

We hypothesized that children with SLI would demonstrate immature ATI compared to typically developing, same-age controls. Specifically, children with SLI would need a longer presentation time gap between two successive tones to elicit P1 and N2 responses to the second tone. Therefore, compared to same age peers, children with SLI would demonstrate a smaller average and maximum amplitudes of the P1 and N2 responses, as well as a delayed latency of the P1 and N2 peaks in response to the second tone in the 200ms gap condition, but no group differences would be observed in the shorter silence gap, 100ms condition (where both groups would fail to demonstrate P1
and N2 responses to the second tone) or the longer silent gap 300 and 400ms conditions (where both groups would show evoked responses to the second tone). In other words, we predicted that children with SLI would show evoked P1 and N2 responses to the second tone only when it occurred at least 300ms after the first tone, while children with typical development would show these responses at gaps of 200ms or greater (see Table 1 for a summary of our hypotheses). We also expected to see an increase in amplitudes of P1 and N2 responses to the second tone as the silent gap between tones increased.

Table 1

*Expected result for P1 and N2 amplitude to the second tone in TT conditions analysis.*

<table>
<thead>
<tr>
<th></th>
<th>100ms</th>
<th>200ms</th>
<th>300ms</th>
<th>400ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLI</td>
<td>×</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Typical developing</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Note: × represents an absence of P1 and N2 responses to the second tone. ✓ represents the presence of P1 and N2 responses to the second tone.

**Method**

**Participants**

A total of 50 children, aged between 6 and 11 years old, participated in the study. Of these, 41 were recruited from an existing database developed as part of a larger study examining language, reading, and math in school age children (Archibald, Oram Cardy, Joanisse, & Ansari, submitted) and nine through personal connections. A total of 25 children with typical development (TD; 10 males; age: $M = 9.23$ years, $SD = 1.14$) and 25 children with specific language impairment (SLI; 15 males; age: $M = 9.25$ years, $SD =$
1.44) participated. All participants in this study were reported by their parents to be primary English speakers, and to have no neurological, hearing, visual or global cognitive impairments. As well, all participants scored 85 or above on the Performance IQ (PIQ) scale from the *Wechsler Abbreviated Intelligence Scale* (WASI; Wechsler, 1999) administered within six months of the study. PIQ was computed from the child’s performance on two subtests: *Block Design*, in which the child arranged blocks to match a model, and *Matrix Reasoning*, which involved choosing a picture to complete a pattern. The two groups did not differ on age, $t(48) = 1.14, p = 0.951$, or PIQ, $t(48) = 0.904, p = 0.37$.

Within six months of the study, all participants completed the four subtests from the *Clinical Evaluation of Language Fundamentals*-4 (*CELF*-4; Semel, Wiig, & Secord, 2003) required to compute each child’s Core Language Score (CLS). In the *Concepts and Following Directions* subtest, the child pointed to pictures in accordance with a spoken instruction. For *Recalling Sentences*, the child repeated sentences immediately after hearing them, and for *Formulated Sentences*, orally created a sentence using a given word. Children under nine years completed the *Word Structure* subtest involving completing a sentence with the grammatically correct word form, and those nine years and over completed the *Word Classes 2* subtest involving identifying which two of four words had a related meaning. Children whose standard score on the CLS was below 85 were included in the SLI group, and those with scores at or above 85, in the TD group. As expected, the group with SLI had a significantly lower CLS than the group with TD, $t(48) = 10.803, p < 0.001$. Table 2 summarizes the descriptive statistics of participants in the two groups.
Table 2

Participant demographic information

<table>
<thead>
<tr>
<th></th>
<th>TD Group</th>
<th></th>
<th>SLI Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Number of participants</td>
<td>25</td>
<td></td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>(N)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (M:F)</td>
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<td></td>
<td>3:2</td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>9.23</td>
<td>1.14</td>
<td>9.25</td>
<td>1.44</td>
</tr>
<tr>
<td>PIQ from WASI</td>
<td>99.88</td>
<td>10.68</td>
<td>97.04</td>
<td>11.51</td>
</tr>
<tr>
<td>CLS from CELF-4</td>
<td>104.40*</td>
<td>10.53</td>
<td>77.4</td>
<td>6.73</td>
</tr>
</tbody>
</table>

*Note: TD – Typical development; SLI – Specific Language Impairment; *p < 0.001

Procedures

All participants completed one individual session of approximately three hours in the Siemens Hearing Research Clinic at Western University’s National Centre for Audiology. EEG recordings in response to auditory stimuli in each of five conditions were completed first. In cases when the most recent testing available in the database was older than six months, the standardized tests described above were administered. Upon arrival, the child and his/her parent(s) were given a tour of the lab and a brief description of the experimental procedure. Parents were asked to read and sign a consent form, and children signed an assent form. The child was given several breaks throughout the visit in order to avoid fatigue.
Stimuli. Auditory stimuli consisted of a single 50ms 440Hz pure tone presented either alone in the one tone (OT) condition, or followed by a second 50ms, 490Hz pure tone in the two tone (TT) condition. Both tones were recorded with a gradual 0-100% increase in amplitude within 10ms after the onset of the tone then a decrease in amplitude during the final 10ms of the tone (i.e., onset/offset ramps of 10ms). The auditory stimuli were created using Praat software (Boersma & Weenink, 2011) with a sampling rate of 41.1 kHz. Intensity of stimulus presentation was determined individually. Before presenting the experimental trials, participants performed an auditory threshold task in which the 440Hz tone was presented at varying volumes, starting at 50dB. The child was asked to press a button to indicate detection. The quietest threshold at which the child reliably responded to the tone was determined through a staircase procedure. Loudness was decreased by 10dB in cases of detection, and increased by 5dB in cases where no tone was detected, until the lowest intensity at which the child showed two correct detections was determined. The intensity of the auditory stimuli used in that child’s experimental trials was then presented as 50dB above this detection threshold (i.e., 50dB SL).

Conditions. Each participant was presented with five blocks of stimuli, which included a OT block and four TT conditions. Tones in the TT conditions were separated by silent gaps of either 100, 200, 300, or 400ms. The OT condition was presented first (5 minutes), followed by the four TT blocks in random order. The lengths of the TT blocks were roughly 5 minutes each and the participants were given breaks in between blocks. Throughout the blocks, a soundless movie of the child’s choice was played on the computer screen located in front of the child. Children were instructed to ignore the
tones, and were encouraged to sit still and pay attention to the movie. Each block (OT, TT100, TT200, TT300, TT400) was composed of 250 trials of the tone or tone pair stimuli. The delivery gap between trials was randomly jittered between 800 to 1200 ms to avoid anticipatory ERP effects. Figure 1 illustrates the TT stimulus paradigm.

Figure 1. Stimulus Paradigm

**EEG Recording.** The EEG was recorded using a 128-channel DenseArray system with HydroGel Geodesic Sensors (Electrical Geodesics, Inc. Eugene, USA). First, the child’s head circumference was measured, and the center point of the scalp was measured and marked with a non-permanent pencil. A sensor net that best fit the child’s head circumference was soaked in soapy distilled water with KCl salt for 5 minutes before being placed on the participant’s head. The central electrode (VRCF) was placed above the marked center point of the scalp for positioning of the cap on the participant’s head. After placement of the net, the participant was asked to sit in a comfortable chair in an electrically shielded, sound proof testing booth throughout the experiment. Auditory stimuli were presented binaurally using E-Prime software (Psychology Software Tools Inc., Pittsburg, PA) through ER3A earphones (Etymotic
Research, Illinois, USA) that were inserted into both ears. Participants were given breaks in between every block, and impedance was checked after completion of every two blocks of experimental trials.

**Data recording and online processing.** The HydroGel Geodesic Sensor net was connected to an amplifier sending EEG recordings to a Mac computer running NetStation (Electrical Geodesics, Inc. Eugene, USA), the software used to record electrophysiological data during the experiment. Data were recorded at 250Hz, with an online bandpass filter of 0.1-100Hz and 60Hz notch filter. Impedance of the channels was adjusted to below a threshold of 75Ω.

**Offline Processing and Data Analysis**

**EEG waveform offline processing.** The raw EEG waveforms were processed offline. First, raw data were filtered through a 2-30Hz off-line finite impulse response filter. Then the filtered waveforms were segmented into epochs of 1200ms, from 200ms pre-stimulus to 1000ms after the presentation of the first tone. The epochs underwent physiological artifact removal for eye blinks (>140μV) and eye movement (>55μV), and rejection of bad channels (>200μV) for later analysis. Responses recorded in each channel were referenced to the average of all 128 channels. Individual trials in the same block of stimuli were averaged together individually (i.e., individual average waveforms for the OT and the four TT conditions were calculated for each participant).

**Principle Component Analysis (PCA) of individually subtracted waveforms.** PCA analysis was performed similar to that reported by Fox *et al.* (2010), with a focus on the positive component P1 and negative component N2 of the CAEP. Due to the short time separation between the first and second tones in the TT conditions, the second tone
ERP response overlaps with the first tone response. To extract the second tone response, each participant’s ERP response to the OT was subtracted from their TT response. The subtracted waveforms were baseline corrected to 50ms before onset of the second tone. Time was reassigned to zero at the onset of the second tone. Then, subtracted waveforms of all conditions at the midline and lateral sites (Fz, Cz, Pz, T7, T8) for all participants were entered into a PCA, a mathematical program that identifies patterns in data. A total of 1000 cases were entered into the PCA analysis (5 channels, 4 TT conditions, 50 participants). Mahalanobis distance was calculated for outlier identification with a critical threshold of 0.98, and 212 cases were rejected from the estimation of the PCA components. The number of outlier cases identified in our analysis was considerably higher than reported by Fox et al. (2010), however, it is unclear what outlier threshold they used. Based on the covariance matrix, with Varimax rotation of the factors, components were generated from a MATLAB program (The MathWorks, Inc). The latency range of components generated from PCA analyses that were consistent with previously reported latencies of P1 and N2 (Ponton et al., 2000) were chosen for further analysis. Average amplitude under these PCA-generated latency ranges of P1 and N2, was calculated using EGI Net Station Waveform Tools (version 4.5; EGI, Inc), and analyzed using repeated measures ANOVA in SPSS (version 20; IBM) for group effects (5 conditions x 5 channels x 2 groups). Greenhouse-Geiser Epsilon adjustments were applied in cases where sphericity was violated. Note that even though outlier cases were omitted from PCA estimation of the P1 and N2 time ranges, they were included in all later amplitude and latencies analyses. Post-hoc analysis including pair-wise comparison of second tone response amplitude to that elicited in the OT condition was also planned.
to investigate significant conditional effects, in order to determine if a second tone response was elicited in the TT conditions.

Further analyses at sites demonstrating particularly strong responses were planned, including analysis of component peak latency and maximum amplitude, which were also generated using Waveform Tools. Maximum amplitude analyses were included as a complimentary approach to average amplitude analysis due to the different advantages of the two measures in different waveforms. Handy (2005) pointed out that maximum peak amplitude is best for situations where a pronounced peak was being analysed, whereas mean amplitude is more suitable when peaks appears to be flatter or more diverse in morphologically. In addition, maximum and mean amplitude are sensitive to different features of the waveform being analysed; the former is more sensitive to noise in the data while the latter is more sensitive to changes in peak latencies in different conditions (Handy, 2005).

Results

Figure 2a (TD) and 2b (SLI) show the group grand average waveforms without OT subtraction over the time period of 50ms pre-stimulus to 1000ms after the presentation of the first tone.

Principle Component Analysis (PCA) on second tone responses

Figure 3a and 3b provides the topographic images of the subtracted waveforms from the groups with TD and SLI, respectively, over the time period of 50ms pre-stimulus to 400ms post-stimulus. Visual examination of the topographic image shows predominant frontal localization of P1 and N2 responses in both groups.
Figure 2a. Grand average waveform of TD group across selected channels. Grand average of ERP waveforms of TD group at Fz, Cz, T7, T8, Pz across OT and four TT conditions. X-axis represents time in ms, from 50ms pre-stimuli baseline to 1000ms post-stimuli onset was presented. Y-axis represents the amplitude measured in μV.
Figure 2b. Grand average waveform of group with SLI across selected channels.

<table>
<thead>
<tr>
<th>SLI</th>
<th>F2</th>
<th>Cz</th>
<th>T7</th>
<th>T8</th>
<th>P2</th>
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<tbody>
<tr>
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<tr>
<td>TT300</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
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<tr>
<td>TT400</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
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</tbody>
</table>
Figure 3a. Topographic images of subtracted waveform of TD group. The topographic images provide a top-down view of the recording of all channels from the onset of the tone in the OT condition and onset of the second tone in the TT condition. Intensity of the colour is proportional to the amplitude of responses recorded at the particular region of the scalp; red colour reflects positive amplitude relative to baseline measurement, blue represent negative amplitude with respect to baseline.
<table>
<thead>
<tr>
<th>SLI</th>
<th>0-50ms</th>
<th>50-100ms</th>
<th>100-150ms</th>
<th>150-200ms</th>
<th>200-250ms</th>
<th>250-300ms</th>
<th>300-350ms</th>
<th>350-400ms</th>
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</thead>
<tbody>
<tr>
<td>0T</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
<tr>
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<td><img src="image10.png" alt="Image" /></td>
<td><img src="image11.png" alt="Image" /></td>
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<td><img src="image32.png" alt="Image" /></td>
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<tr>
<td>ττ400-0T</td>
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<td><img src="image39.png" alt="Image" /></td>
<td><img src="image40.png" alt="Image" /></td>
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</tbody>
</table>

*Figure 3b.* Topographic images of subtracted waveforms of children with SLI.
The group averages of subtracted waveforms are shown in Figure 4a and 4b for the groups with TD and SLI, respectively. Visual inspection suggests that both groups showed a response to the second tone when it was presented as early as 100ms after the first tone, and the response magnitude increased with an increasing gap between the two tones.

The subtracted waveforms, over the period 0-400 ms, were entered into the PCA for P1 and N2 latency range identification. Maximal loadings on the first and second PCA components were at 64-148ms (eigenvalue = 64.9, explained variance = 23.9%) and at 208-296ms (eigenvalue =62.7, explained variance = 23.0%) consistent with the reported latencies of P1 and N2, respectively, in the CAEP (Ponton, 2000).

**Analysis of mean amplitude.** Mean amplitude over the latency range of P1 generated from the PCA is summarized in Table 3 for both TD and SLI.

A mixed ANOVA with group (TD/SLI) as the between subject factor and five conditions (OT/TT100/TT200/TT300/TT400) and five channels (Fz, Cz, T7, T8, Pz) as within subject variables, was completed on P1 mean amplitude. Results revealed a significant main effect of channel, $F(3.17, 151.93) = 113.63$, $p < 0.001$, partial eta-square, $\eta^2_p = 0.703$, and a significant interaction between channel and condition, $F(7.14, 342.5) = 6.51$, $p < 0.001$, $\eta^2_p = 0.119$. There were no significant effects involving group (group: $F(1, 48) = 2.66$, $p = 0.109$, $\eta^2_p = 0.053$, group x condition: $F(3.13, 150.27) = 0.54$, $p = 0.66$, $\eta^2_p = 0.011$; group x channel: $F(3.17, 151.93) = 1.09$, $p = 0.36$, $\eta^2_p = 0.022$; or group x condition x channel: $F(7.14, 342.54) = 0.91$, $p = 0.50$, $\eta^2_p = 0.019$. As well, the main effect of condition was non-significant, $F(3.13, 150.27) = 0.73$, $p = 0.54$, $\eta^2_p = 0.015$. Figures 5 and 6 below summarize the significant effects. For the main effect of
Figure 4a. Grand average of OT and subtracted TT waveforms of TD group. X-axis represents times in ms, and the Y-axis represents amplitude measured in μV.
<table>
<thead>
<tr>
<th>SLI</th>
<th>Fz</th>
<th>Cz</th>
<th>T7</th>
<th>TB</th>
<th>Pz</th>
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<tbody>
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<td><img src="image20" alt="Graph" /></td>
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Figure 4b. Grand average of OT and subtracted TT waveforms of group with SLI.
Table 3

*Mean amplitude of P1 over latency range 64 to 148ms for selected channels. (Data shown in μV: mean (SD))*

<table>
<thead>
<tr>
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<th>Pz</th>
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<td></td>
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<td>(0.95)</td>
<td>(0.90)</td>
<td>(1.08)</td>
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<td>-0.52</td>
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<tr>
<td></td>
<td>(2.21)</td>
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<td>(1.59)</td>
<td>(1.29)</td>
<td>(2.40)</td>
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<tr>
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<td>(2.07)</td>
<td>(2.20)</td>
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<tr>
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<td>(1.61)</td>
<td>(1.19)</td>
<td>(1.23)</td>
<td>(1.40)</td>
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<tr>
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<td>(1.76)</td>
<td>(1.78)</td>
<td>(1.53)</td>
<td>(1.29)</td>
</tr>
</tbody>
</table>
Figure 5. Grand average waveforms showing main effect of channels across conditions for the period 64ms to 148ms (P1).

Figure 6. Interaction effect of channel by condition for mean P1 amplitude.
channels, a positive peak was observed at the PCA-generated latency that corresponded to the expected polarity of P1 at channels Fz and Cz, however, at all other electrodes (T7, T8, Pz), a negative response was observed (see Figure 5). For the interaction effect between channel and condition (see Figure 6), an increasing gap between tones corresponded to an increase in average amplitude with a drop at TT300 for channels Fz and Cz. Inversely, channel T7 and T8 showed negatively deflecting average amplitude with the exception of TT300.

In order to further investigate the significant channel by condition effect, responses at Fz were analyzed in a separate ANOVA, given that the biggest P1 response was recorded at Fz. A main effect of condition was found, $F(3.01, 147.64) = 5.78, p = 0.001, \eta^2_p = 0.11$. To determine if P1 was elicited in the TT conditions, post-hoc pairwise comparison of second tone P1 average amplitude in all TT conditions to that of OT was conducted. A significant difference was observed for average P1 amplitude between OT ($M = 1.86, SD = 1.12$) and TT100 ($M = 0.62, SD = 2.04$), $t(49) = 3.67, p = 0.001$, as well as OT and TT300 ($M = 0.85, SD = 1.58$), $t(49) = 3.77, p < 0.001$. A t-test against a test value zero suggested that second tone P1 amplitudes at TT100 and TT300 were significantly different from zero ($p \leq 0.036$).

The second component from the PCA analysis emerged at time 208-296ms post-stimulus, which corresponded to the latency of an N2 in the CAEP. Table 4 below summarizes the average amplitude of N2 at the five selected channels for all conditions and both groups at the time period generated from the PCA analysis. Similar to P1, a 2 (group: TD/SLI) x 5 (condition: OT/TT100/TT200/TT300/TT400) x 5 (channel: Fz, Cz,
Table 4

Mean amplitude of N2 over latency range 208-296ms for selected channels. (Data shown in μV: mean (SD))

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Fz</th>
<th>Cz</th>
<th>T7</th>
<th>T8</th>
<th>Pz</th>
</tr>
</thead>
<tbody>
<tr>
<td>TD SLI</td>
<td>TD</td>
<td>SLI</td>
<td>TD</td>
<td>SLI</td>
<td>TD</td>
</tr>
<tr>
<td>OT</td>
<td>-2.59</td>
<td>-2.35</td>
<td>-0.89</td>
<td>-0.80</td>
<td>2.03</td>
</tr>
<tr>
<td></td>
<td>(1.80)</td>
<td>(1.33)</td>
<td>(1.21)</td>
<td>(1.16)</td>
<td>(1.53)</td>
</tr>
<tr>
<td>TT100-OT</td>
<td>-0.70</td>
<td>-0.96</td>
<td>0.23</td>
<td>-0.87</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>(1.63)</td>
<td>(1.33)</td>
<td>(1.22)</td>
<td>(1.47)</td>
<td>(1.37)</td>
</tr>
<tr>
<td>TT200-OT</td>
<td>-1.27</td>
<td>-0.64</td>
<td>-0.46</td>
<td>-0.20</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>(2.46)</td>
<td>(1.52)</td>
<td>(2.28)</td>
<td>(1.25)</td>
<td>(1.70)</td>
</tr>
<tr>
<td>TT300-OT</td>
<td>-2.66</td>
<td>-2.04</td>
<td>-1.57</td>
<td>-1.81</td>
<td>2.14</td>
</tr>
<tr>
<td></td>
<td>(2.04)</td>
<td>(1.78)</td>
<td>(1.49)</td>
<td>(1.87)</td>
<td>(1.82)</td>
</tr>
<tr>
<td>TT400-OT</td>
<td>-2.10</td>
<td>-1.70</td>
<td>-1.03</td>
<td>-0.60</td>
<td>1.71</td>
</tr>
<tr>
<td></td>
<td>(2.15)</td>
<td>(1.43)</td>
<td>(1.92)</td>
<td>(1.13)</td>
<td>(1.94)</td>
</tr>
</tbody>
</table>

Pz, T7, T8) mixed ANOVA was completed on N2 mean amplitude. Results indicated a significant main effect of channel, $F(1.64, 78.79) = 76.34, p < 0.001$, $\eta^2_p = 0.61$, and a significant interaction between channel and condition, $F(9.17, 440.30) = 7.75, p < 0.001$, $\eta^2_p = 0.139$. There were no significant effects involving group, $F(1, 48) = 0.59, p = 0.45$, $\eta^2_p = 0.012$; group x condition, $F(3.13, 150.43) = 0.75, p = 0.53, \eta^2_p = 0.015$; group x channel, $F(1.64, 78.79) = 0.60, p = 0.52, \eta^2_p = 0.012$; or group x condition x channel: $F$
(9.17, 440.30) = 0.90, \( p = 0.52, \eta^2_p = 0.018 \). As well, the main effect of condition was non-significant, \( F(3.13, 150.43) = 1.26, \ p = 0.29, \eta^2_p = 0.026 \). The significant effects are shown in Figures 7 and 8. At the N2 time period generated by the PCA, Fz and Cz involved negative components, while T7, T8, and Pz were positive (see Figure 7). The N2 response was strongest in the OT condition. For the TT conditions, as the gap between the two tones increased, a gradual increase in average N2 amplitude was observed at Fz and Cz (see Figure 8). Such increments were also observed at T7 and T8 with the opposite polarity.

The significant channel and condition interaction was further examined in an ANOVA completed on the Fz data only, given that the maximum N2 response was recorded at Fz. Results revealed a significant main effect of condition, \( F(4, 196) = 12.39, \ p < 0.001, \eta^2_p = 0.20 \). Post-hoc pairwise comparisons with Bonferroni correction (\( \alpha/4 \)) of the TT conditions against OT showed significant differences in average N2 amplitude between OT (\( M = -2.47, SD = 1.57 \)) and TT100 (\( M = -0.83, SD = 1.48 \)), \( t(49) = -5.62, p < 0.001 \), as well as OT and TT200 (\( M = -0.96, SD = 2.05 \)), \( t(49) = -5.02, p < 0.001 \). Further analysis on the amplitude of the second tone N2 responses at TT100 and TT200 showed that the responses were significantly different from a test value of zero (\( p \leq 0.002 \)).

**Analysis of peak latency.** In addition to average amplitude, peak latencies of P1 and N2 were also analyzed. These data are summarized in Table 5.

Given that P1 and N2 responses were strongest at Fz, analyses only focused on Fz. The latency at which P1 and N2 peaked within the time periods suggested by PCA were generated and analyzed separately using 2 (group: TD/SLI) x 5 (condition: OT/TT100/TT200/TT300/TT400) ANOVAs. Analysis of P1 peak latency showed
Figure 7. Grand average waveforms showing main effect of channels across conditions for the period 208ms to 296ms.

Figure 8. Interaction effect of channel by condition for mean N2 amplitude.
Table 5.

Summary of P1 and N2 latencies (ms) in TD and SLI groups (channel Fz only)

<table>
<thead>
<tr>
<th></th>
<th>TD</th>
<th></th>
<th>SLI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>P1 Latency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OT</td>
<td>111.5</td>
<td>20.3</td>
<td>121.9</td>
<td>20.1</td>
</tr>
<tr>
<td>TT100-OT</td>
<td>109.6</td>
<td>24.1</td>
<td>113.0</td>
<td>21.9</td>
</tr>
<tr>
<td>TT200-OT</td>
<td>107.7</td>
<td>26.7</td>
<td>102.9</td>
<td>20.7</td>
</tr>
<tr>
<td>TT300-OT</td>
<td>113.8</td>
<td>19.9</td>
<td>113.6</td>
<td>22.5</td>
</tr>
<tr>
<td>TT400-OT</td>
<td>117.8</td>
<td>19.8</td>
<td>120.3</td>
<td>22.4</td>
</tr>
<tr>
<td>N2 Latency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OT</td>
<td>263.4</td>
<td>25.3</td>
<td>264.0</td>
<td>22.3</td>
</tr>
<tr>
<td>TT100-OT</td>
<td>246.7</td>
<td>26.0</td>
<td>253.9</td>
<td>28.6</td>
</tr>
<tr>
<td>TT200-OT</td>
<td>246.2</td>
<td>24.1</td>
<td>243.2</td>
<td>28.2</td>
</tr>
<tr>
<td>TT300-OT</td>
<td>244.3</td>
<td>24.6</td>
<td>254.7</td>
<td>21.7</td>
</tr>
<tr>
<td>TT400-OT</td>
<td>250.4</td>
<td>20.3</td>
<td>249.0</td>
<td>19.6</td>
</tr>
</tbody>
</table>

a significant main effect of condition, $F(4, 192) = 3.41, p = 0.01, \eta^2_p = 0.06$ (see Figure 9).

However, there were no significant effects involving group, $F(1, 48) = 0.431, p = 0.515,$ $\eta^2_p = 0.01,$ or group x condition, $F(4, 192) = 0.93, p = 0.45 \eta^2_p = 0.02.$ Post-hoc pairwise analysis examining the condition effect was conducted with Bonferroni correction for multiple comparisons. Result showed that latency of the second tone P1 was significantly different between the OT ($M = 116.72, SD = 20.69$) and TT200 ($M = 105.28, SD = 23.73$)
$p = 0.045$, as well as TT200 and TT400 ($M = 119.04, SD = 20.96$) conditions, $p = 0.013$, $p \geq 0.05$ for the other comparisons.

Similarly for N2, results showed a significant effect of condition $F(4, 192) = 4.34$, $p = 0.002$, $\eta^2_p = 0.083$ (see Figure 10) but not significant effects involving group $F(1, 48) = 0.789$, $p = 0.379$, $\eta^2_p = 0.016$, or group x condition, $F(4, 192) = 0.72$, $p = 0.582$, $\eta^2_p = 0.015$. The condition effect was examined using post-hoc pairwise comparison with Bonferroni correction. Result revealed a significant delay in N2 peak latencies in the three shortest TT conditions: OT ($M = 263.68, SD = 23.59$) and TT100 ($M = 250.32, SD = 27.29$) $p = 0.049$, OT and TT200 ($M = 244.72, SD = 26.01$) $p = 0.006$, OT and TT300 ($M = 249.52, SD = 23.53$) $p = 0.037$. No significant differences were found in any other comparisons, $p \geq 0.05$ for the other comparisons.
Figure 10. N2 peak latency at channel Fz across conditions

Analysis of maximum amplitude. Maximum amplitude of P1 and N2 was generated from EGI Waveform Tools, and summarized in Table 6.

Maximum amplitude difference in the two tone conditions was analyzed using repeated measures ANOVA on 5 conditions (OT/TT100/TT200/TT300/TT400) with group as between subject factor. Analysis of maximum P1 amplitude showed a significant main effect of condition, $F(4, 192) = 7.38, p < 0.001, \eta^2_p =0.13$ (see Figure 11). However, there were no significant effects involving group, $F(1, 48) = 0.64, p = 0.43, \eta^2_p =0.01$, or group x condition, $F(4,192) =0.24, p = 0.91, \eta^2_p = 0.01$. To examine the conditional effect, post-hoc comparison with adjusted significance level 0.0125 using Bonferroni correction ($\alpha/4$) based on apriori hypothesis was conducted on P1 amplitude between OT and the second tone response in the four TT conditions using a paired sample t-test. Result revealed a significantly reduced P1 maximum amplitude compared to OT ($M = 3.59, SD = 1.49$) in TT conditions with a 100ms gap ($M = 1.91, SD = 2.02$),
Table 6

*Maximum amplitude (μV) of P1 and N2 in subtracted two tone waveforms (channel Fz only)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>TD</th>
<th>SLI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>OT</td>
<td>3.41</td>
<td>1.45</td>
</tr>
<tr>
<td>P1 Maximum Amplitude</td>
<td>TT100-OT</td>
<td>1.94</td>
</tr>
<tr>
<td></td>
<td>TT200-OT</td>
<td>3.04</td>
</tr>
<tr>
<td></td>
<td>TT300-OT</td>
<td>2.13</td>
</tr>
<tr>
<td></td>
<td>TT400-OT</td>
<td>3.08</td>
</tr>
<tr>
<td>OT</td>
<td>-4.47</td>
<td>2.17</td>
</tr>
<tr>
<td>N2 Maximum Amplitude</td>
<td>TT100-OT</td>
<td>-1.98</td>
</tr>
<tr>
<td></td>
<td>TT200-OT</td>
<td>-2.08</td>
</tr>
<tr>
<td></td>
<td>TT300-OT</td>
<td>-3.97</td>
</tr>
<tr>
<td></td>
<td>TT400-OT</td>
<td>-3.34</td>
</tr>
</tbody>
</table>
Figure 11. Maximum P1 amplitude at channel Fz across condition

t(49) = 4.61, p < 0.001; as well as between OT and 300ms gap (M = 2.07, SD = 1.73),
t(49) = 4.65, p < 0.001. To determine if any P1 response was elicited in these two TT
conditions, the maximum amplitude of these conditions was further compared to a test
value of zero. A statistically significant evoked potential was observed at TT100, t(49) =
6.14, p < 0.001, and TT300 t(49) = 8.47, p < 0.001.

For N2, the repeated measures ANOVA showed a significant main effect of
condition, F(4, 192) = 13.67, p < 0.001 ,partial $\eta^2_p = 0.22$ (see Figure 12). Effects
involving group were non-significant: group, F(1,48) = 1.42, p = 0.239, $\eta^2_p = 0.029$,
group x condition $F(4,192) = 0.91, p = 0.46, \eta^2_p = 0.019$. A significant attenuation in
maximum N2 amplitude compared to OT (M = -4.06, SD = 1.95) was observed in post-
hoc paired t-test analysis in conditions where the silent gap between tones was 100ms (M
= -2.00, SD = 1.44), $t(49) = -6.09, p < 0.001$, 200ms (M = -2.16, SD = 2.25), $t(49) = -$
4.79, $p < 0.001$, and 400ms (M = -3.01, SD = 1.92), $t(49) = -2.94, p < 0.005$. Further
Figure 12. Maximum N2 amplitude at channel Fz across condition

analysis on maximum N2 amplitude in these three conditions against a test value zero showed a statistically significant N2 response at TT100 ($t(49) = -9.8, p < 0.00$), TT200 ($t(49) = -6.8, p < 0.00$), and TT400 ($t(49) = -11.1, p < 0.00$).

Summary of Analyses

To summarize the repeated measures analyses, there were no significant group differences in the average or maximum amplitude of the P1 component. Generally, larger, positive P1 amplitudes were found as the gap between tones increased for the Fz and Cz electrodes, whereas the same pattern but reversed polarity was recorded at lateral channels T7 and T8, in all conditions with the exception of TT300. A significant conditional effect was observed in P1 peak latency, with post-hoc analysis revealing that an earlier P1 peak was observed in the TT200 compared to OT and TT400 condition. Mean and maximum amplitude of P1 at channel Fz showed a conditional effect. Significant but attenuated second tone P1 responses were observed in conditions where
tones were separated by silent gaps of 100ms or 300ms. For average and mean N2 amplitude, there were no significant differences involving group. Generally, increasingly larger, negative N2 amplitudes were recorded as the gap between tones increased for the Fz and Cz electrodes, whereas a positively increasing amplitude was observed at channels T7 and T8. Delayed peak latency of the second tone N2 response was observed in the three shortest gap conditions (TT100, TT200, TT300) compared to OT, but no latency differences were found amongst the TT conditions. A significant condition effect on mean and maximum amplitude of second tone N2 responses at channel Fz was observed. Attenuation of N2 peak amplitude was found compared to OT at TT conditions with shorter time gaps (i.e., 100ms, 200ms).

**Discussion**

In the present study, a passive ERP paradigm was used to assess processing of rapidly presented tones in children who have specific language impairment (SLI) compared to their age-matched typically developing peers (TD). We measured cortical auditory evoked potentials (CAEP), that is, amplitude and latency of P1 and N2 responses to the second tone in a tone pair, as an indicator of auditory temporal processing. Participants in the present study were presented with one block of one tone trials, and four blocks of trials with two tones separated by silent gaps of 100ms, 200ms, 300ms and 400ms, while their evoked potentials were recorded using EEG. The methodology used by Fox et al. (2010) was employed to analyze the amplitude and latencies of P1 and N2 responses to the second tone in the tone pairs. Briefly, the children’s one tone responses were subtracted from those from the tone pair conditions, and the residual waveforms were time-adjusted according to the onset of the second tone
in the tone pair. Then all subtracted waveforms from five selected channels (Fz, Cz, T7, T8, Pz) were entered into a principle component analysis (PCA), which generated the P1 and N2 time frames. Group differences in average amplitude of P1 and N2 in the five selected channels were analyzed using mixed ANOVA. Maximum amplitudes, as well as latencies of P1 and N2 for the Fz channel were separately analyzed using repeated measures ANOVA. No significant group effect was observed in our data, but significantly attenuated P1 and N2 responses were observed for the TT conditions in which tones were separated by shorter time gaps.

**ATI Impairment in SLI Compared to Controls**

The primary aim of the present study was to investigate the immature auditory temporal integration window in children with SLI that has been previously reported in the literature. Based on past research, we hypothesized that, compared to age-matched controls, children with SLI would require a longer time gap between two tones in order to show an identifiable second tone response. However, analysis of P1 and N2 responses across all conditions showed no group differences. Instead, both groups showed comparable levels of attenuation in their evoked responses to the second tone in the conditions with shorter gaps. Follow-up analyses revealed that these attenuated P1 and N2 responses were nonetheless present (i.e., were significantly larger than zero). Although there was a pattern of increasingly reduced amplitude in the neural responses with decreasing gap duration between the tones, this pattern did not differentiate between groups. Three possible explanations, outlined below, may account for the discrepancy between the results of present study and those of prior literature in which ATI was impaired in children with SLI relative to those without.
Is ATI not impaired in SLI? In the present study, participants in the group with SLI responded not differently from the TD group in detecting rapidly presented tones. One possible interpretation of these data would suggest that individuals with SLI are not impaired in their development of ATI compared to age-matched controls. As reviewed in the introduction section of this thesis, the literature on ATI impairment and language development has mainly involved measuring behavioral responses of participants; neural evidence is available but scarce. Within the behavioral studies, conclusions of ATI impairments in SLI, as well as the relationship of ATI with language development, have been inconsistent. McArthur and Bishop (2001) reviewed behavioral studies of ATI in individuals with reading and language impairments, and argued that, although most studies have shown an impairment of ATI in these populations, most of the experiments had design limitations. The most common limitations were the task requirements for attention, motivation and other motor abilities in order to learn as well as produce the correct behavioral response. Other factors that may have interfered with behavioral responses in these studies were poorer reaction time and motor control of the individuals with SLI (Hill, 2001; Miller et al., 2001). Therefore, these artifacts may have confounded the performance of the group with SLI and led to a false conclusion of ATI impairment. Hence, this may explain why when a study, like the present study, employs a passive paradigm that requires no active participation or attention from the participants, no group difference in ATI is observed.

There are, however, results of some other studies that cannot be explained under this account. As discussed in the Introduction, there is neural evidence from EEG and MEG experiments that used passive paradigms and identified an impairment of ATI in
children with SLI (e.g., Korpilahti & Lang, 1994; Oram Cardy et al., 2005). McArthur and Bishop’s review of ATI studies (2001) also pointed out that most behavioral studies reporting an ATI impairment in SLI required participants to report the difference (in terms of pitch or intensity) of two rapidly presented tones. That led us to consider another possible account for the lack of group differences in our study. Is it possible that individuals with SLI are only impaired at the level of discriminating differences between auditory stimuli, but not at the level of detecting the stimuli?

**Are children with SLI only impaired at the level of auditory discrimination?**

Since the majority of prior studies examining the window of ATI measured participants’ judgements about frequency differences in auditory stimuli, it is possible that an impairment only manifesting at the discrimination level may be linked to the language impairment in SLI. The obligatory P1 and N2 responses to auditory stimuli measured in the present study putatively reflected the fundamental detection of auditory stimuli in the auditory system, which is thought to precede the differentiation of auditory stimuli. Our lack of group difference between the groups with SLI and TD may reflect a similar developmental level of fundamental detection of auditory stimuli of the two groups.

There is some evidence of frequency discrimination (FD) disability in the SLI population. Hill, Hogben and Bishop (2005) found that participants with SLI varied greatly in their performance, but, as a group, showed significantly higher thresholds than participants with TD in detecting the difference in frequencies of two tones. This FD impairment did not appear to be a result of behavioural artifacts, such as lack of attention (McArthur & Bishop, 2004). Further analysis in this study provided some evidence for a FD impairment in the group with SLI that correlated with poorer language performance.
These studies provided some evidence that FD disability is an alternative explanation for the poor performance of children with SLI on ATI experiments. However, in most behavioral studies of ATI, a training phase was included in which participants learned the correct responses to slowly presented stimuli, in order to demonstrate and control for the groups’ ability to differentially respond to tones of different frequencies. McArthur and Bishop (2001) argued that auditory discrimination (e.g., FD) impairments in SLI may only become apparent when time constraints are added in the experimental phase, and that just controlling for performance in the learning phase without the pressure of timing limited the conclusions about ATI in these behavioral studies.

If individuals with SLI are only impaired at the level of auditory discrimination, this could also account for neural studies using MMN as an indicator of ATI. For example, Korpilahti and Lang (1994) showed a significant MMN amplitude attenuation in children with SLI when a deviant was presented 350ms after standard tones. Importantly, analysis of the P1 and N2 responses elicited by the standards at the same separation gaps revealed no difference in amplitude between groups. MMN is thought to result from discrimination of changes in auditory stimuli, whereas P1 and N2 are considered to reflect the detection level of auditory stimuli. Therefore, the lack of group difference in P1 and N2 amplitudes may have reflected a comparable level of detection of the rapidly presented tones between the group with SLI and controls, whereas the attenuated MMN response of the group with SLI reflected impairment at the discrimination level. This account, however, fails to explain some other neural evidence
of impairments at the level of detecting two rapidly presented tones (e.g., Oram Cardy et al., 2005).

**Impaired detection of rapidly presented stimuli in SLI.** An alternative way of interpreting our data is that our experimental paradigm failed to reflect an ATI impairment in children with SLI, that does occur at the level of detection. That is, it is possible that we did not have a gap condition that was small enough to capture a difference in ATI threshold for the groups in our sample. Our choice of auditory stimuli as well as duration of the silence gaps of this experiment was inspired by the Wang et al. (2005) MMN study on a TD population, where they estimated the ATI window in response to two 440 and 494 Hz tones to be less than 250ms and 300ms for children aged 9-11 years and 5-8 years, respectively. Analyses of P1 amplitudes on standard trials in their study also estimated the ATI window of TD children aged 9-11 to be between 150 and 200ms. Hence, we had hypothesized that the window of ATI would be around 200ms in our TD participants aged 6-11 years, and slightly longer for our SLI group, when using tones of similar frequencies and durations to those used by Wang and colleagues.

Data from the present study suggested that for both groups in the current study, significant P1 and N2 responses were identified in all two tone conditions, indicating some level of detection was present even when two tones were separated by as little as 100ms. Attenuation, but not absence, of a response was observed at 100 and 300ms for the second tone P1 response when compared to a single tone. Two explanations for the attenuated second tone P1 amplitude can be considered. First, attenuation may reflect the lower sensitivity of the brain’s detection of the second tone because of the refractory period of the auditory nervous system after the presentation of the first tone. Another
possible explanation would be that there is within-group variability in the window of ATI, in which a proportion of participants showed a comparable response to the second tone at TT100 compared to a single tone, whereas others did not show a second tone response at all. Under both circumstances, it would explain why the group average amplitude appeared smaller than what was observed in the single tone condition.

However, when exploring the distribution of the amplitude of P1 of the 50 participants at TT100 using a quantile-quantile (Q-Q) plot (see Appendix B), there was no indication of clustering of participants showing amplitudes around the upper or lower ends of the distribution. The distribution of data from the present study suggests that the attenuated P1 amplitude in the TT100 condition was unlikely to be explained by within-group ATI variability, leaving a refractory process as the more likely explanation for response attenuation.

A similar pattern of increasing second tone N2 peak amplitude was observed when separation between the two tones increased, with the exception of TT300. Again, attenuation, but not absence, of the N2 peak compared to that from a single tone was observed at shorter separation time gaps between tones (100 and 200ms). The attenuation of the second tone amplitude was not different between groups at the separation gaps chosen in this study. Distribution of N2 amplitude in these TT conditions did not suggest a subgroup explanation (see Appendix B), hence, attenuation was again likely attributable to the refractory period of the neural generators associated with the first tone response. It is noted that the second tone P1 and N2 amplitude in the TT300 condition slightly deviated from the pattern of increasing amplitude with increasing time gap between tones, however, the reason for this difference is unclear.
The data from the present study showed no difference in the second tone response of the two groups. However, Oram Cardy et al. (2005) measured the M50 (magnetic P1) and found that a higher proportion of children with language impairments failed to show an evoked response to a second tone in a condition with a 150ms silent gap. The disparate results between the Oram Cardy et al. study and the current findings may be a result of the different analysis methods of the two studies. In Oram Cardy et al. study, an expert reader determined the presence or absence of M50 response from individual participants’ waveforms by visual inspection. Then group performance was reported in terms of the percentage of participants showing identifiable second tone M50 responses. In the present study, amplitude data was generated automatically using EGI Waveform Tools on subtracted waveforms, and group performance was compared at the level of absolute amplitude. Given that the two tones were close to each other in the current study as well as in the study by Oram Cardy et al., visual inspection of the waveforms may be limited by the overlapping first and second tone responses. It is also known that some individuals with SLI have an overall more heterogeneous and attenuated AERP (Bishop, Hardiman, Uwer, & Von Suchodoletz, 2007; Neville, Coffey, Holcomb, & Tallal, 1993) compared to TD peers, which may confound visual inspection and lead to the conclusion of a group difference.

It is, however, premature to conclude, based on these results, that the group with SLI is not impaired in ATI, because we were unable to identify the threshold of ATI, even in our TD group. It is unknown whether there would be a group difference in the window of ATI at smaller time windows or with different (duration, frequency) stimuli than those included in the present study. In the future, it would be beneficial to use
shorter separation gaps (e.g. 25ms, 50ms) that might better capture the window of auditory detection of the two groups (i.e., a shorter gap for which there would be no second tone response because it falls within the temporal integration window). Until then, it would be premature to rule out a difference in maturation of ATI between individuals with SLI and those who are typically developing.

**P1 and N2 as a Neural Indicator of ATI**

Another purpose of the current study was to investigate the use of the second tone P1 and N2 responses in children as a neural indicators of ATI. We analysed three aspects of the CAEP (mean amplitude, maximum amplitude, and peak latency) based on the PCA-generated time range from the subtracted two tone waveforms. In terms of mean and maximum amplitudes, our data suggested a trend of increasing amplitude with increasing gap between tones. Such a pattern of modulation by gap duration suggests that amplitude is a sensitive measurement of the brain’s response to rapidly presented tones. In terms of peak latency, our data suggested there was a general trend of an earlier peak in response to the second tone compared to the corresponding component in the single tone condition. This may have resulted from the subtraction of the OT from TT waveforms, where the peak latencies of the P1 and N2 response to the single tone was not identical to the corresponding responses to the second tone in the TT conditions. Therefore, the resultant peak in the subtracted waveforms was not reflective of the absolute peak of the second tone. The lack of variation of peak latencies between the four TT conditions suggested that there was little effect of silence gap between tones on the peak latencies in these subtracted waveforms; hence latency measures were not a useful indicator of ATI in the current analysis approach.
Comparison of Our TD Data to the Literature

Although not explicitly the purpose of this study, we compared our TD data to that reported by Fox et al. (2010), who studied children with typical development and employed a similar paradigm to ours. There are some methodological differences that should be pointed out before directly comparing the results. In Fox et al. study, a 40-channel cap was used to measure mean amplitude of P1 and Ta in typically developing children (N = 28). These responses were compared across seven conditions: single tone, and two tones with silent gaps of 25, 50, 100, 200, 400, and 800 ms. Since measurements of all the channels were mastoid referenced, P1 amplitude in the four selected channels (Fz, Cz, T7, T8) were all positive at the PCA-generated time range. Hence, the P1 amplitude was averaged across the four selected channels for conditional effect analysis. However, in the present study, a 128-channel system was used and average referencing was applied to all the collected data, in which case P1 amplitude at T7 and T8 after referencing was opposite in polarity compared to that at channels Fz, Cz and Pz. Thus, when we analysed for effect of conditions, a mixed ANOVA of condition by channels was employed.

Conclusions about the size of the ATI window in children are different based on our data and those from the Fox et al. (2010) study. Our analysis suggested a statistically significant (i.e., identifiable) second tone P1 response at 100ms, which was attenuated compared to a single tone response. A clear second tone P1 response was observed at 200ms that was no different in amplitude from a single tone response. Taken together, our TD group participants showed some level of detection of the second tone at a 100ms gap separation between tones, and a complete response when tones were separated by
200ms, suggesting that the window of ATI in our TD group was less than 100ms. Fox et al. found that their children with TD showed a significant second tone response that was no different from the single tone condition when tones were separated by 200ms, and a greatly reduced second tone response when tones were separated by 100ms. These results were consistent with ours. However, the second tone response at 100ms in Fox et al was so attenuated that it was not different from zero. The authors therefore concluded that in their sample, the window of ATI was in between 100 and 200ms. Our estimated window of ATI of less than 100ms in a broader age group of TD participants (6-11 years old) is shorter than that estimated by Fox et al. on their 7-9 year old participants.

Two methodological differences may have contributed to the discrepancy in the estimated window of ATI: 1) the frequency and duration, and 2) intensity of the tones used in the paradigms.

**Difference in tonal frequency and duration.** Compared to the identical first and second tone (1000Hz, 20ms with 2ms rise/fall time) used in Fox et al. (2010) study, our stimuli were lower in frequency and longer in duration (first tone: 440Hz, second tone: 490Hz, both 50ms with 10ms rise/fall time). It is likely that the difference in frequencies in the two tones used in our paradigm facilitated the detection of the second tone. The auditory central nervous system is organised with tonotopic representation from the cochlear to auditory cortical levels (Bear, 2007). It is possible that when two tones of the same frequency were presented in rapid succession as in Fox et al., it created more interference in detection of the latter tone. Two tones of the same frequencies recruit the same neural generators of the nervous system, and the activation from the second tone may fall into the refractory period of the neural generators activated by the first tone. In
our paradigm where two successive tones were different in frequency, different or partially overlapping neural sets may have been recruited, hence causing less interference in activation of the two tones.

In terms of the duration of the tones used, the present study involved slightly longer tones than those used by Fox et al. (2010). There is some evidence from studies involving healthy adults that has shown amplitude of CAEP increasing as a function of increase in tone duration (Alain, Woods, & Covarrubias, 1997). Such effects of tone duration on amplitude of the CAEP have been less well-characterized in children. If amplitude of the CAEP in children follows the same pattern of tone duration modulation, it may explain why more pronounced P1 and N2 responses were recorded at 100ms in the present study compared to that reported by Fox et al.

**Difference in tone intensity.** In the Fox et al. (2010) study, all participants were presented with tones at 75 dB SPL. To ensure tones were presented at equal perceptual loudness across participants, in our experiment, effort was made to identify the auditory threshold of individual participants, and all tones were presented at 50dB above each participant’s hearing threshold. There is evidence that amplitude of obligatory auditory ERPs is modulated by intensity of the auditory stimuli. A study by Dince and Sussmann (2008) on typically developing 9-11 years olds showed that P1 amplitude increased with increasing intensity of the tones presented (range 66-86 dB SPL). The authors speculated that louder tones capture the attention of the participants, which in turn modulated the overall amplitude of auditory ERPs. The perceived loudness of tones presented in Fox et al. (2010) study would likely have varied from participant to participant, while it was kept relatively consistent across participants in this experiment.
Data from the present study suggested that the second tone P1 response in the TT100 condition was significantly smaller compared to that in single tone condition, but was significantly greater than zero; whereas at the same time gap condition in the Fox et al. study, no statistically significant second tone P1 was observed. This discrepancy may be due to the participants’ overall higher perceived loudness of tones in the present study as compared to that in Fox et al. study, which lead to a general amplitude modulation because of better attention. This, however, cannot be validated without information on participants’ hearing thresholds from the Fox et al. study. With the auditory threshold data, it would be possible to look for clustering patterns of participants’ responses at TT100, and examine factors for any subgroup (such as auditory threshold).

**Limitations and Future Directions**

There are some limitations of this study that must be considered in the interpretation of the data. The time gaps chosen in this study was based on the prior ATI thresholds found by Wang et al. (2005) and Oram Cardy et al. (2005), suggesting a window in the 200ms range for typically developing children and longer for children with language disorders. The stimulus properties (duration of 50ms, frequency of 440 and 490Hz) for our two-tone paradigm were selected to match the frequency and duration of Wang et al.’s MMN stimuli, so that their double-deviant MMN paradigm could also be used for comparison. The Fox et al. (2010) study, which suggested smaller thresholds than Wang and Oram Cardy et al., was published when most of our data was already collected. In hindsight, it would have been beneficial to have included the 25ms and 50ms silence gaps used by Fox et al. In that case, we may have identified a gap duration for which a second tone response would not be elicited for our two groups of participants.
Another possible limitation of this study was the imbalanced distribution of genders in the groups with TD and SLI. However, it is unlikely that this impacted the rapid tone detection result of the two groups, because the neural indicator chosen was a fundamental obligatory evoked response. Gender differences in CAEP to rapidly presented tones have not been well characterized in the literature. One study showed that these fundamental auditory brain responses have no gender difference in typically developing children. Research by Freedman, Adler and Waldo (1989) investigated the difference in the P1 response amplitude ratio when two identical tones were presented with a silent gap of 500ms in between. The ratio was not significantly different between the two genders of participants within two age groups, 1-8 years old and 9-11 years old. Although this study investigated the second tone response at a slightly longer time gap compared to our study, it provides some level of evidence that gender differences did not affect our findings.

Another possible limitation was the relatively high number of outliers for cases excluded from our PCA analysis as compared to Fox et al. (2010). We had chosen a conservative threshold for outlier rejection of greater than two standard deviations from the mean. It is possible that Fox et al. had fewer outliers because they used a more liberal threshold (e.g., 3 SD). However, they did not indicate what threshold they chose for their PCA analysis. We considered age as a contributing factor in our outlier cases. We found that younger participants (≤ 9.25 years old, \( N = 26 \)) has significantly more condition by channel cases rejected as outliers compared to the older participants (> 9.25 years old, \( N = 24 \)), \( p = 0.017 \). Since the age range of participants in the current study (6 - 11 years) is wilder than that in Fox et al. study (7 – 9 years), having a more varied participants’ age
distribution in the current study may have contributed to the relatively higher number of outliers. It should be noted that in the current study, although outlier cases were rejected from the analysis of latency range estimation of P1 and N2, these cases were included in later amplitude and latency analyses. There are two possible explanations for why waveforms were rejected as outliers. Participants’ waveforms could be rejected as outliers because of noisiness of the waveform, which made it difficult to identify P1 and N2 components. Another possibility would be that the P1 and N2 peaks in a waveform marked as an outlier were exceedingly delayed or advanced compared to majority of the data. In both cases, not including these outlier cases in the estimation of P1 and N2 components latencies would be preferred to avoid skewness in the PCA components estimation, so as to maximize the proportion of the dataset being explained. Note that even though in the outlier cases the response peaks were out of the range of the PCA estimated P1 and N2 range, some part of the P1 and N2 response could still be captured within the PCA-generated time range during amplitude and latency measurement.

To better characterize the window of ATI in children with TD and SLI in future studies, it would be of interest to include 25ms and 50ms silence gaps. Alternatively, shorter tones or two tones with identical frequencies could be used, such as those employed Fox et al. (2010). In addition, additional effort to apply Wang et al.’s (2005) MMN paradigm to groups with SLI and TD would be helpful in clarifying the impairment at the level of discrimination and simple detection in the SLI population. Our P1 and N2 results from 6-11 year olds with SLI suggested some level of second tone detection at 100ms, and a definite response at 200ms. Wang’s study suggested typically developing children aged between 5-11 years showed attenuated discrimination at 250-
300ms time gaps. Considered in concert with behavioural evidence of frequency discrimination impairments in children with SLI (for example McArthur & Bishop, 2004), it would be fruitful to investigate the MMN response of children with SLI in this age group when two tones of different frequencies were presented with separation gaps ranging from 200 to 400ms. Although the detection level of auditory stimuli was not significantly different between children with SLI and the TD group at these presentation gaps, it is possible that group differences would be found in the MMN at these rates, reflecting a frequency discrimination impairment.

Another focus of future studies could be to look at the auditory window of integration in subgroups of children with SLI. Some previous experiments suggested that impairment in ATI is only observed in a subgroup of children with SLI (e.g., SLI with a reading impairment, suggested by McArthur & Hogben, 2001). We had not collected other language measures for the purpose of this study, but it would be of interest to identify different aspects of language as a predictor of performance on an ATI task in the future.

In conclusion, even though our experiment failed to show an impairment of auditory temporal integration of individuals with SLI compared to same-age controls, a group difference in ability to detect rapidly presented auditory stimuli cannot be ruled out. Future research should look into the use of more refined separation time gaps to better characterize ATI development in the SLI population.
References


### Appendix A

**Table**

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Appendix B

Figure: Quantile-Quantile plot showing the distribution of second tone P1 amplitude at 100ms silence gap between tones condition

Figure: Quantile-Quantile plot showing the distribution of second tone N2 amplitude at 100ms silence gap between tones condition
Figure: Quantile-Quantile plot showing the distribution of second tone N2 amplitude at 200ms silence gap between tones condition.
Appendix C

Office of Research Ethics
The University of Western Ontario

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. J. Cardy
Review Number: 15660E
Review Date: May 14, 2010
Revision Number: 1
Approved Local # of Participants: 120

Protocol Title: Brain markers of auditory integration in autism spectrum and language disorders

Department and Institution: Communication Sciences & Disorders, University of Western Ontario
Sponsor: Scottish Rite Foundation Grant

Ethics Approval Date: May 14, 2010
Expiry Date: December 31, 2011
Documents Reviewed and Approved: Revised Study End Date

Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB’s as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB’s periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g., change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB: Dr. Joseph Gilbert
FDA Ref. #: IRB 00000940

Ethics Officer to Contact for Further Information

This is an official document. Please retain the original in your files.

UWO HSREB Ethics Approval - Revision
V.2008-07-01 (nttApprovalNotice/HSREB_REV)
15660E
Page 1 of 1
Appendix D

LETTER OF INFORMATION AND CONSENT FORM

Title of Research Project:
Brain markers of auditory integration in autism spectrum and language disorders

Investigators:
Janis Cardy, PhD, S-LP(C)
Marc Joanisse, PhD
Rob Nicolson, MD, FRCP(C)

Purpose of the Research and this Letter of Information:
You and your child are being invited to participate in research investigating how the brains of children with Autism Spectrum Disorders, Specific Language Impairment and typical development process what they hear. By examining the electrical signals emitted from the brain when different sounds are presented, we can see if there are differences between these groups of children in the way their brains process this information. In the future, we hope this kind of technique may help earlier diagnosis and suggest new treatments for children with Autism Spectrum and language disorders. This study aims to test 120 children.

This letter of information contains information to help you decide whether or not to participate in this research study. It is important for you to be aware of why the study is being conducted and what it will involve. Please take the time to read this carefully and feel free to ask questions if anything is unclear or there are words or phrases you do not understand.

Description of the Research:
If you agree to participate, you and your child will visit [redacted] for 2½ -3½ hours for this study.

In the first part of the session (1-1½ hours), your child will complete tests of thinking and language if these tests have not been recently administered. During this time, you will be asked to complete questionnaires about your child’s past and present socialization, communication, and behaviour.

In the second part of the session (1½-2 hours), your child will be tested using electroencephalography (EEG) while sitting in a comfortable chair in a sound-dampened room. EEG is a recording of brain waves, or the electrical activity of the brain cells, made using a cap with wires that is placed on the head. Before your child begins, s/he will practice wearing a net cap. Once s/he is comfortable wearing the practice cap, we will place the real net cap on his/her head. This cap is dipped in saline (salt water) solution before placing it on your child’s head, and a small amount of saline remains. A towel will catch any saline that might drip onto your child’s clothes during placement. Your child will be instructed to keep still and listen to a series of sounds for 5 to 20 minutes at a time. A DVD movie will be projected on a computer screen for
your child to watch (but not listen to) while the sounds are being presented. S/he will not be required to do anything but sit still and watch the movie.

If, during the course of this study, new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the investigator.

**Potential Harms, Injuries, Discomforts or Inconvenience:**

There are no known harms or injuries associated with participating in this study. The testing session will take up to one half day, which may be inconvenient. Some of the questions your child will be asked may be too easy or too difficult (e.g., challenging problem solving, remembering long sentences), which may cause some boredom or anxiety. The examiner will make every effort to reduce frustration and provide breaks when needed. During the EEG portion, your child may find the cap slightly uncomfortable or become tired of sitting still. We will make every effort to reduce any discomfort.

**Potential Benefits to Individual Participants:**

You and your child will not benefit directly from participating in this study.

**Potential Benefits to Society:**

What we learn from this study may help us gain new knowledge that may benefit children with autism spectrum or language disorders in the future.

**Confidentiality:**

We will respect your privacy. No information about who you or your child are will be given to anyone or be published without your permission, unless required by law.

Representatives of The University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your child’s study-related records to monitor the conduct of the research. By signing this consent form, you agree to let these people look at your child’s study-related records.

The data produced from this study will be stored in a secure, locked location. Only members of the research team (and maybe those individuals described above) will have access to the data.

If the results of the study are published, your child’s name will not be used. At the end of the study, we will send you a copy of the overall results of this study.

The results of the tests we describe in this form will be used only for this study. If another professional caring for your child needs to see these results, you will have to give us your permission. We will ask you to sign a form saying that you agree that this person can see your child’s results. We recommend that only a registered psychologist or doctor tell you what the results of these tests mean.

**Reimbursement:**

You will be reimbursed $20 to help cover your travel and other incidental expenses. Parking at Elborn College is free.
Participation:

Participation in this study is voluntary. You and your child may refuse to participate, refuse to answer any questions, or withdraw from the study at any time with no effect on your future care.

During this study we may create new tests or other things that may be worth some money. Although we may make money from these findings, we cannot give you or your child any of this money now or in the future because your child took part in this study.

We will give you a copy of the consent form for your records. A separate Assent Form will be obtained from your child.

Your signing the consent form does not interfere with your legal rights in any way. The staff of the study and any people who gave money for the study are still responsible, legally and professionally, for what they do.

Sponsorship:

The sponsor/funder of this research is the Scottish Rite Charitable Foundation of Canada and the University of Western Ontario.

Consent:

I have read the Information and Consent document, have had the nature of the study explained to me and I agree to that my child ___________ and I may take part in this study. All questions have been answered to my satisfaction.

Printed name of Parent/Legal Guardian ____________________________ Parent/Legal Guardian’s signature & date

Printed name of person who explained consent ____________________________ Signature & date

Printed witness’ name (if the parent/legal guardian does not read English) ____________________________ Witness’ signature & date

If you have any questions about this study, please call Dr. Janis Cardy [Contact Information]

If you have questions about your rights as a research participant or the conduct of the study, please contact the Office of Research Ethics [Contact Information]
Appendix E

ASSENT FORM

Title of Research Project:

Brain markers of auditory integration in autism spectrum and language disorders

Investigators:

Janis Cardy, PhD, S-LP(C)
Marc Joanisse, PhD
Rob Nicolson, MD, FRCPC

Why are we doing this study?

Some kids have trouble understanding what we say. We want to know why. You will listen to sounds while you watch a movie. We will use a special cap to look at your brainwaves while you listen. This will help us learn about how kids understand what they hear and see. Then we may be able to help kids who have problems learning to listen and speak properly.

What will happen during the study?

You will come to the University of Western Ontario for a half day. First, you will do some jobs to check your thinking, listening and talking. While you are working, your parent will answer some questions on a paper. They will answer questions about what you were like when you were little and what you are like now.

Next, we will look at your brainwaves using a special machine. We will put a special stretchy cap on your head. You will wear it for a while to get used to it. When you are ready, we will put another cap on your head. This cap will measure your brainwaves. It is just like the first cap but it will have some water in it. A little bit of water might drip on your head. We will wipe the water up with a towel. You will sit in a comfortable chair with the cap on your head. Then you will do eight jobs. For these jobs, you will wear earplugs and listen to lots of sounds. You will watch a movie without words while you listen to the sounds. You will have to keep very still.
Are there good things and bad things about the study?

Here is a good thing about being in this study. You can help us learn about why some kids have problems learning to listen and speak properly.

Here are some bad things about this study. The cap might feel funny on your head. It might be a bit hard to keep still in the chair. Some of the jobs might be boring or tricky.

Who will know about what I did in the study?

If we talk about this study to other people, we will not tell them your name. Only if you or your parents ask us to.

Can I decide if I want to be in the study?

If you do not want to be part of this study, that is OK. You can say yes now, but change your mind later. You can say no at any time. Nobody will be angry or upset if you do not want to be in the study. We are talking to your parent about the study. You should talk to them about it too. Ask them questions if you are not sure about what you have read or heard. They will help you.

Assent:

I was present when ________________ read this form and said that he or she agreed, or assented, to take part in this study.

______________________________
Printed name of person who obtained assent

______________________________
Signature & Date

I want to participate in this study:

______________________________
Signature of child

______________________________
Age

______________________________
Date
Elaine Yuen Ling Kwok

**Education**

2011-present  **University of Western Ontario**, London, Ontario, Canada
- Master of Science, Health and Rehabilitation Science
- Child and Youth Health (expected graduation: August 2013)
  
  *Thesis: Auditory temporal integration in children with SLI compared to same-age control*

2007-2011  **Chinese University of Hong Kong**, Hong Kong, China
- Honor Bachelor of Science, Molecular Biotechnology
  
  *Thesis: Functional genetics study of dyslexia susceptibility gene-KIAA0319*

2009-2010  **McGill University**, Montreal, Canada
- Exchange Student (One Year), studying Psychology and Biology

2008-2009  **University of California**, Los Angeles, United State
- Summer Course

**Honours/Awards and Scholarships**

2011-2013  Western Research Graduate Scholarships

2008-2011  Dean’s Honors List (Faculty of Science)

2009-2010  Ho Hing Kee Memorial Exchange Award

2010-2011  Chung Chi College Postgraduate Scholarships (Chinese University of Hong Kong)

2009-2010  Yasumoto International Exchange Scholarships

2008-2009  Chung Chi College Class Scholarship (Chinese Christian Universities Alumni Scholarship)

2007-2008  Robert Fu Memorial Scholarship
Conference and Poster Presentations


Selected Experience

2011-2013  Teaching Assistant
Professor Shauna Burke, University of Western Ontario

2009-2010  Lab Trainee
Professor Maurice Ptito, University of Montreal, Canada

2008-2009  Summer Lab Trainee
Professor Mary Waye, Chinese University of Hong Kong

2007-2008  Summer Lab Trainee
Professor Edwin Chan, Chinese University of Hong Kong