

Hemispheric lateralization of speech perception in infancy and childhood: A systematic review

Erica Seely

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Committee:

Bonnie Lau

Adrian KC Lee

Sara Kover

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Erica Seely

University of Washington

Abstract

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Erica Seely

Chair of the Supervisory Committee:

Adrian KC Lee

Co-Chair of the Supervisory Committee:

Bonnie Lau

Speech and Hearing Sciences

Past neuroimaging research has shown left hemisphere dominance for the neural processing of speech in the mature adult brain. How this hemispheric asymmetry develops however, remains largely unknown. It is unclear whether this left lateralization is observed at birth, or whether this functional specialization develops with neural maturation and experience perceiving speech. This systematic review examined evidence from 13 papers that used a variety of neuroimaging modalities to investigate the neural processing of speech stimuli in infants and children. The two primary goals of this review were to identify at what age left hemisphere dominance emerges and to characterize the developmental trajectory of hemispheric lateralization from infancy to childhood. Of the papers that met inclusionary criteria, 5 used electroencephalography (EEG), 4 used functional magnetic resonance imaging (fMRI), 3 used functional near-infrared spectroscopy (fNIRS), and 1 used magnetoencephalography (MEG). The papers were divided

into three age groups: birth to 12 months, 1 to 8 years, and 8 to 18 years. Of the infant papers, significant variability in stimuli, methods, and findings made it difficult to determine whether the neural processes for speech perception are left lateralized in the first year, as many papers show left lateralization for both speech and nonspeech stimuli. Among the papers investigating lateralization among children, there was some evidence suggesting bilateral activation at younger ages with a shift to left hemisphere dominance as children develop. Two papers investigated lateralization in children with autism and concluded that, perhaps, it is more likely for children with autism to show atypical right lateralization.

INTRODUCTION

Prior neuroimaging studies have shown that when adults perceive speech, activation of a large and diffuse cortical network is observed and is lateralized predominantly to the left hemisphere. There is converging evidence from clinical studies, such as the Wada procedure, a determinate of lateralization used in pre-surgical planning, and observed deficits in left hemisphere (LHEM) lesions, that confirms this left hemisphere lateralization in most adults (Knecht et al., 2000; Loring et al., 1990; Szaflarski et al., 2006). Recent investigations have used differing methodologies to begin to investigate this in children (de Guibert et al., 2011; Finch et al., 2017; Flagg et al., 2005; Holland et al., 2007; Olulade et al., 2020; Szaflarski et al., 2006; Whitehouse & Bishop, 2008), and some papers have observed variations in lateralization in tandem with language impairments, often in individuals with autism (Finch et al., 2017; Flagg et al., 2005; Jouravlev et al., 2020; Sandbank et al., 2017; Whitehouse & Bishop, 2008). However, while atypical lateralization may or may not hold promise as a neural marker for language impairment, the origin of this functional asymmetry is not well understood. Many aspects of how left hemisphere lateralization for speech processing develops remains unknown and, without an understanding of the typical developmental trajectory, it is difficult to determine what would be considered atypical cortical specialization.

Researchers use a variety of methods to determine lateralization of various language functions. In many pediatric and adult studies, researchers choose to use verb generation or other expressive tasks to determine lateralization of expressive language. In these papers, participants are instructed to generate spoken language or think of words while researchers record activation patterns via neuroimaging (Holland et al., 2001). Much of the existing literature regarding lateralization of language functions utilizes these methods and provides clear evidence of

lateralization of expressive language. However, these tasks provide activation patterns only for expressive language and are impractical with infants and young children who do not yet speak.

To accurately determine lateralization for speech *perception*, neuroimaging data is recorded while subjects listen to speech stimuli. These methods can be done in infancy, and therefore, can give researchers a more complete picture of the developmental trajectory of activation for speech perception.

Though it's clear that language functions are left-lateralized in most typical adults, one fundamental question that remains unanswered is whether humans show left hemisphere specialization for speech at birth, or whether maturation of these mechanisms require experience with sound and/or speech. Influential papers by Dehaene-Lambertz and colleagues were among the first to investigate lateralization of speech perception in young infants (Dehaene-Lambertz et al., 2002; Dehaene-Lambertz, 2000). In a series of two papers, researchers played both forward and backwards speech to 3-month-old and 4-month-old infants while measuring activation via EEG and fMRI. These bold studies aimed to determine lateralization of speech perception in young infants. In both studies, Dehaene-Lambertz and colleagues found greater left activation for speech and nonspeech conditions in their participants. (Dehaene-Lambertz et al., 2002; Dehaene-Lambertz, 2000). While the researchers did observe left hemisphere activation in response to speech, similar hemispheric asymmetry was also found for backward speech in both papers. It is therefore unclear if this left-lateralization is speech-specific or can be observed for all sounds in infants of this age. We conducted a systematic review to investigate the current evidence regarding typical and atypical language lateralization, aiming to answer the question: *How does hemispheric lateralization for speech perception develop?* Understanding the typical developmental trajectory of hemispheric specialization for speech would facilitate our ability to

identify atypical patterns of neural response that could be a risk factor for later language impairments.

IMAGING MODALITIES

The existing literature uses a variety of methodologies to investigate cerebral specialization for speech perception. The Wada (intracarotid amobarbital) test, although invasive, is considered the gold-standard for determining hemispheric lateralization for language functions (Abou-Khalil, 2007). The Wada test is used for presurgical planning in epilepsy patients to determine the boundaries of brain material to be removed (Binder, 1996). When performing the Wada test, sodium amytal is injected into the carotid artery, temporarily sedating one cerebral hemisphere. Patients are then asked to count continuously while the injection flows throughout different brain regions; if counting ceases, it can be determined that the brain regions necessary for verbal counting has been affected. While the sodium amytal injection is still active in the brain, subjects can be asked to follow verbal instructions and complete drawn memory tasks. Performance on these tasks allows surgeons to determine lateralization of language, memory, and other functions (Binder, 1996). The Wada test is historically considered to be the most reliable way to determine lateralization of language, though it is very invasive.

In addition to the Wada test, researchers have also investigated the hemispheric lateralization of speech perception through dichotic listening studies (Eling, Marshall, & van Galen, 1981). In dichotic listening studies, researchers present different auditory stimuli simultaneously in each of the participants' ears. The participants then verbally report which stimuli they heard. It is hypothesized that material presented to the right ear is better perceived because the crossed auditory pathways in the brain send the right ear auditory signals to the left

hemisphere, which is better prepared to process the stimuli (Eling et al., 1981). In these studies, researchers most often find a right ear, thus left hemisphere, advantage (Eling et al., 1981).

Though these studies offer a non-invasive alternative to the Wada test, they were excluded from this review due to their lack of neuroimaging.

fMRI can be used as a less invasive alternative to the Wada procedure (Binder, 1996). By measuring changes in blood oxygenation levels, also known as the hemodynamic response, fMRI shows neural activation with good spatial resolution (Glover, 2011). During fMRI, subjects are often asked to perform tasks, allowing researchers to create neural activation maps that show which areas of the brain were active during the task (Glover, 2011). For example, headphones or screens can be used to present auditory or visual stimuli and subjects may be asked to passively listen to or look at the stimuli. Participants may also be asked to do active speaking tasks, such as verb-generation, during fMRI.

fMRI has been found to be a reliable measure of lateralization, showing consistence with the Wada test, as shown by Binder and colleagues (1996). While fMRI may allow insight into activation during language tasks, too much motion by the subject often creates signal noise that is difficult to reliably remove from the raw data (Glover, 2011). Functional magnetic resonance imaging has only fair temporal resolution due to the limited response time of the hemodynamic response; peak responses generally occur 5-6 seconds following a stimulus (Glover, 2011). In addition, immaturities and differences in the hemodynamic response may exist in infants (Issard & Gervain, 2018). Due to differences in hemodynamic response and difficulties obtaining fMRI data from infants, few fMRI studies in infancy exist. However, fMRI has been shown to be an adequate measure of lateralization with high spatial resolution, though its limited temporal resolution and sensitivity to movement make it difficult to use effectively in children.

Some studies use EEG event-related potential (ERP) measures to determine laterality. EEG provides researchers with a non-invasive method to investigate the relative timing of neural activation in response to stimuli (Light et al., 2010). To collect EEG data, researchers place conductive gel-covered electrodes on the scalp and head that measure electrical neural activity produced by large numbers of neurons firing simultaneously (Light et al., 2010). EEG has precise enough temporal resolution to associate large neuronal activity spikes within milliseconds of stimuli presentation; this response to stimuli is measured as ERP (Light et al., 2010). EEG is desirable for its high temporal precision and ability to associate neural activity with a given stimulus; however, only signals generated by a large amount of synchronized neuronal activity can be measured at the scalp. Researchers must also consider the need to remove artifacts such as muscle movements and eye blinks from the raw data before analyses of brain activity (Light et al., 2010), though EEG preprocessing techniques are more efficient at filtering out motion artifacts than fMRI. One specific response EEG researchers have used to compare hemispheric activation is with the mismatch negativity (MMN). In MMN studies, researchers record brain activity in response to a repeated stimulus (Garrido et al., 2009, Näätänen et al., 2007). After the brain has habituated to that stimulus, they introduce a deviant stimulus and record the strength of the neuronal activity in response to the changed stimulus (Garrido et al., 2009). The resulting change wave is a representation of the brain's response to the change in stimuli (Garrido et al., 2009).

MEG is another imaging modality that has been used to acquire lateralization data in infants and children. The electrical activity of active neurons creates a magnetic field that is measured in MEG and provides high temporal and spatial resolution (Singh, 2014). Because it is silent, MEG is a good option for testing infants. MEG is also able to tolerate some movement of

the participant, and subjects can be seated in a typical infant seat in sight and touch of their caregivers, critical factors to ensure compliance while obtaining data. Breier and colleagues (2001) showed that MEG signals recorded during linguistic tasks were highly correlated with Wada findings. Moreover, MEG's superior temporal resolution in comparison to fMRI allows researchers to precisely correlate stimulus events with the neural responses (Breier et al., 2001). Because of its practicality for use with infants, high correlation with Wada, and precise timescales, MEG is a valid modality with which to investigate lateralization in infants and children.

Finally, functional near-infrared spectroscopy can be used to study lateralization of brain functions (Gallagher et al., 2012). It measures change in the brain's hemodynamic response by using increases in oxyhemoglobin and decreases in deoxyhemoglobin as measured by the absorption and reflection of near-infrared light (Gallagher et al., 2012). Much like fMRI, fNIRS has less temporal resolution than MEG or EEG because of the relatively slow response time of the hemodynamic response (Gallagher et al., 2012). However, fNIRS is often more easily performed in children than fMRI because it requires less equipment and a more relaxed testing environment.

Researchers have employed a variety of imaging modalities to investigate the neural processing of speech in infants and children. Their differing methods, stimuli, and approach to determining laterality makes it difficult to compare findings across studies. By systematically reviewing cerebral specialization literature spanning across these imaging modalities, we hope to synthesize and better interpret existing literature by answering the question: *How does hemispheric lateralization for speech perception develop throughout infancy and childhood?*

GOALS

1. To identify at what age left hemisphere dominance emerges.
2. To characterize the developmental trajectory of hemispheric lateralization from infancy to childhood.

METHODS

We conducted a systematic search for empirical studies that used neuroimaging methods to investigate the cerebral specialization for speech perception in children and infants. The PRISMA protocol was followed to ensure transparent reporting of data collection for this systematic review (Moher et al., 2009). The search terms and procedures for selecting articles are included below along with the associated PRISMA flow diagram in Figure 1.

SEARCH PROCEDURE

Papers were identified based on computer searches of three online databases: PsychINFO, PubMed, and ASHAWire. The following search terms were used to identify these studies:

(newborn* OR neonat* OR infant* OR infancy OR child* OR pediatric)

AND

((("hemispheric lateralization" OR "functional specialization" OR "cerebral specialization" OR "language lateralization")

AND ("speech perception" OR ("auditory perception" AND language OR speech))))

Researchers also scanned references from relevant articles to identify additional eligible papers with the aim to identify pediatric and infant studies that investigated hemispheric lateralization for speech perception. Researcher 1 compiled a list of all search results and removed duplicates. They then screened the search results for eligibility based on title and abstract. Following the title and abstract screen, full articles were reviewed for eligibility by Researcher 1. Researcher 2 reviewed the list of selected papers, and disagreements in paper selection were discussed until a consensus was reached. Eligibility criteria are outlined below.

INCLUSION CRITERIA

Only empirical studies published in peer-reviewed journals were included; dissertations and theses were excluded. Subject age was restricted to 18 years and under. Studies which tested both adult and pediatric subjects were included only if pediatric data could be extracted from adult data. Papers were restricted to those that investigated hemispheric lateralization for speech using perceptual (listening) tasks and included neuroimaging data. Studies were not restricted by participant language abilities or impairments.

EXCLUSION CRITERIA

The focus of our review was on speech perception, therefore studies that involved an active speech production task, such as expressive verb generation were excluded, along with papers that involved a silent expressive task such as silent naming. Non-empirical research, such as dissertations, theses, and reviews, were also excluded.

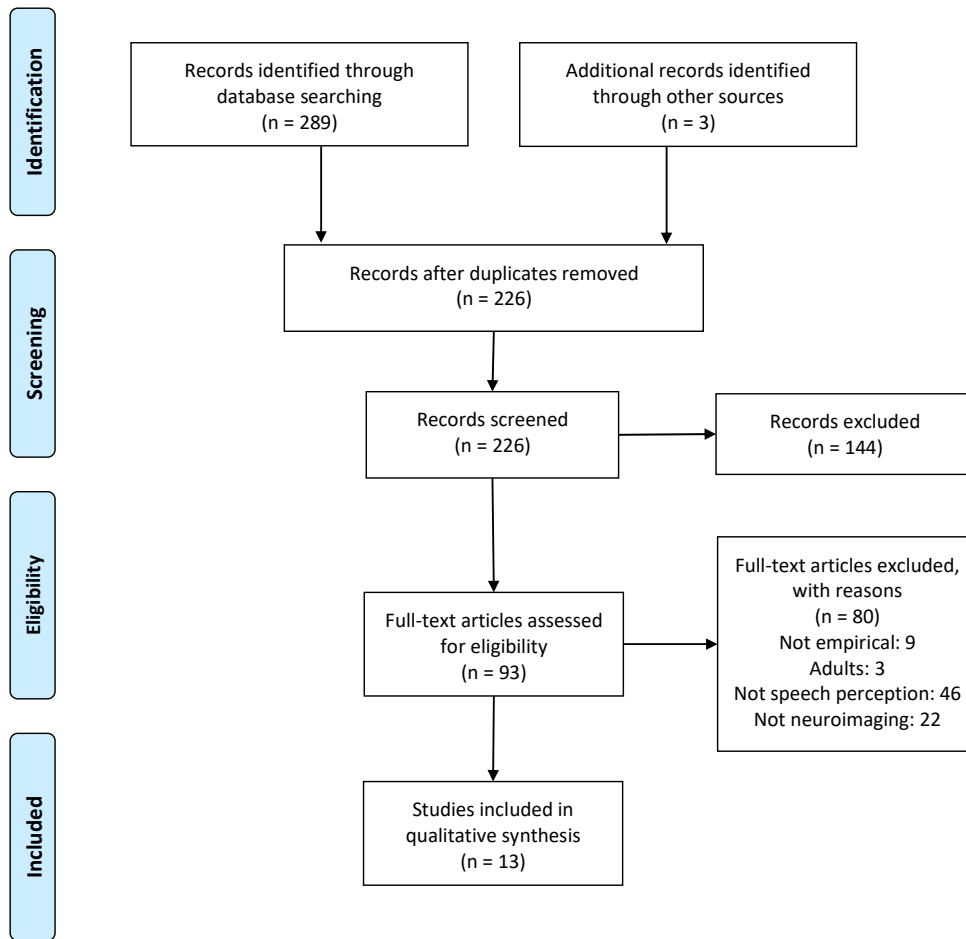


Figure 1 PRISMA Moher et al., (2009) flow diagram of systematic search methods.

RESULTS

A total of 13 papers were reviewed in this study. The studies involved typical children and children with autism. Participants across the 13 studies ranged from one day to 18 years old. Of the 13 studies, 5 used EEG, 4 used fMRI, 3 used fNIRS, and 1 used MEG.

QUALITY ANALYSIS

While it is difficult to rate or rank the quality of studies across different imaging modalities, our aim is to comment on the differing methodologies across each of the studies so that we may better understand the papers as a bulk of evidence and to critically assess the quality of the included studies. The papers are discussed with respect to six methodological features: number of participants, age, stimuli, control conditions, region of interest (ROI), and data exclusion. For this review, researchers assessed each paper separately and drew conclusions from each study in isolation. A meta-analysis was not completed due to the small number of studies, differing imaging modalities, and variety in stimuli and population; these variables do not allow for useful statistical analysis of the studies as a group.

Table 1: Neuroimaging studies that investigate hemispheric lateralization for speech perception in infancy and childhood. For papers that include adult data, entries are made based on pediatric subjects alone.

Source	Imaging Modality	N	Age / population	Stimuli / task	Control Stimuli	ROI	Data Inclusion/Exclusion criteria
Berl et al., (2014)	fMRI	57	4-12 years / Typically developing children	Sentences / Semantic decision task	Backward speech	Determined a priori	Excluded for motion artifacts, questionable task engagement
Cheng et al., (2012)	EEG (MMR) 8 electrodes used in analysis: F3, F4, C3, C4, T3, T4, P3, P4.	98	1-5 days / Typically developing children	Word / Passive listening	Synthesized nonvocal sounds	Determined a priori	Excluded for motion artifacts, technical failure
Dehaene-Lambertz et al., (2000)	fMRI	20	3 months / Typically developing children	Sentences / Passive listening	Backwards speech	Whole cortex	Excluded for motion artifacts
Dehaene-Lambertz, (2000)	EEG (ERP) 65 electrodes used in analysis: full cap	16	4 months / Typically developing children	Syllables / Passive listening	Timbre change within syllable stimuli	Determined after data collection	Excluded for motion artifacts
Finch et al., (2017)	EEG (ERP) 8 electrodes used in analysis: FC1, FC5, C3, C5, FC2, FC6, C4, C6;	96	12 months / Children with asd, children at high-risk for asd, children at low risk for asd.	Syllables / Passive listening	Native and nonnative deviant syllables	Determined a priori	Excluded for motion artifacts
Flagg et al., (2005)	MEG	12	8-17 years / Typically developing children and children with autism	Phonemes / Passive listening	n/a	Not determined: whole head used for analysis	Excluded for motion artifacts
Minagawa-Kawai et al., (2011)	fNIRS 5 incident and 4 detection probes in a 3x3 grid on temporal and frontal areas bilaterally	12	Age range not provided, average age 128 days (SDD 13.3) / Typically developing children	Sentences / Passive listening	Sentences in non-native language, emotional voice, monkey call, scrambled phonemes/ speech	Determined a priori	Excluded for motion artifacts, fuzziness, hair obstruction, sleepiness during testing
Molfese et al., (1975)	EEG Number of electrodes used in analysis not clearly defined: T3 and T4 locations	21	1 week-11 years / Typically developing children	Syllables and words / Passive listening	Piano chord, synthesized nonvocal sound	Determined a priori	Exclusion criteria not found

Norrelgen et al., (2015)	fMRI	19	8-18 years / children with intractable epilepsy	Sentences / Passive listening	Backwards sentences	Not determined: whole head used for analysis	Exclusion criteria not found
Olulade et al., (2020)	fMRI	39	5-13 years / Typically developing children	Sentences / Semantic decision task	Backwards sentences	Determined a priori	Excluded for motion, monitor during testing and cease imaging for motion
Sandbank et al., (2017)	EEG (ERP) 11 electrodes used in analysis: 6 electrodes at P3, 5 electrodes at T3	34	2-5 years / Typically developing children	Words / Passive listening	Nonwords	Determined a priori	Excluded for movement, lack of cooperation with testing
Sato et al., (2010)	fNIRS 5 incident and 4 detection probes on each side, total 12 recording channels on each side.	40	4 months , 10 months / Typically developing children	Words / Passive listening	Pure tone	Determined a priori	Excluded for crying, technical problems, motion
Vannasing et al., (2016)	fNIRS 8 recorded channels, 4 on each side between T3-T5 and T4-T6	29	1 day / Typically developing children	Sentences / Passive listening	Sentences in non-native language, backwards sentences in familiar and unfamiliar languages	Determined a priori	Excluded for motion

RESULTS OF THE QUALITY ANALYSIS

Number of Participants: Higher quality studies included more than 20 participants, though it is common for neuroimaging studies to have smaller participant numbers due to experiment time and cost. Four of the papers included less than 20 participants, while the remaining 9 included more than 20 participants. The papers by Flagg and colleagues (2005) and Minagawa-Kawai and colleagues (2011) had the smallest number of participants at 12 each, and the study by Cheng et al. (2012) had the largest number of participants at 98. In total, 493 participants were included in this review.

Age: Higher quality papers were those that included participants of multiple ages. To answer our research question, having participants of multiple ages or studying the same participants at multiple ages (longitudinal design) aids in interpreting results across development. However, researchers must be diligent when determining their age groups. Given the temporal nature of development, it is important that age groups be small enough to show change associated with age. Should an age group be too large, small age-related changes may be obscured by quantities of other data. In addition, it is important to include even numbers of participants across each age group. If an age group is unevenly distributed, results may not accurately represent the intended group. 6 papers included subjects of multiple ages and 7 papers included subjects of the same age (within 2 years). Among our 13 studies, subjects ranged in age from one day to 18 years.

Stimuli: When studying speech perception, it is important that the stimuli resemble speech as closely as possible. Based on current evidence, it is unclear what length or complexity of stimuli is required to activate the neural networks involved in speech processing. Researchers may use

phonemes, syllables, words, or sentences as their spoken stimuli, but each example may or may not elicit the desired neural networks. Because there is no evidence-based standard, we erred on the side of caution and designated papers as having higher quality if they presented words and connected sentences as their stimuli. Lower ratings were given to papers with stimuli of words or shorter because it is more difficult to associate linguistic function at the phoneme or syllable level. High quality ratings were given to studies whose stimuli were sentences or longer. Six studies presented connected speech (full sentences, passages, or stories) as their stimuli, 3 presented words, 2 presented syllables, 1 presented phonemes, and 1 presented both syllables and words.

Control Condition: Control conditions are perhaps one of the most important methodological features we present in this review. Papers may have a control condition, such as backwards or scrambled speech or an unfamiliar language against which to compare. Control stimuli allow researchers to compare activation elicited by connected speech to activation elicited by non-speech acoustic stimuli, such as scrambled speech, backwards speech, or tones. The stimuli should be spectrally complex, therefore providing adequate acoustic variation in comparison to connected speech. 12 out of 13 papers included control conditions, though they varied in their acoustic complexity.

Region of Interest (ROI): Across imaging modalities, there are differing methods to select and analyze an ROI. Some studies analyzed data obtained from the whole cortex, while others select an ROI a priori. This data inclusion criteria may have a significant influence on the results observed. Researchers must be intentional in selecting their ROIs; well-selected ROIs can provide more relevant task-specific data without the need to filter out other neural activation in

unrelated parts of the brain. However, ROIs should be set a priori. ROIs that are determined after the collection of data could be influenced by existing analysis of the whole brain and can hinder or inflate effect size (Gentili et al., 2021). Higher quality papers were those that determined their ROIs prior to data collection. In the study by Sandbank et al., data was taken from ROIs only in the left hemisphere. Instead of comparing activation across hemispheres, they compared the amount of left activation across their word and nonword conditions.

Data Exclusion: Data exclusion can be conducted differently across researchers and modalities; however, it is expected that some data will be excluded due to noisy data or incomplete scans from infants and children. All 13 papers had clearly defined data exclusion criteria, a relative strength in the quality measures.

RESULTS

This review identified 13 papers that met inclusion criteria. As we are interested in the developmental trajectory from infancy to childhood, papers were grouped by age. Some papers included subjects from multiple age groups; these are discussed in multiple sections.

INFANTS 12 MONTHS AND UNDER

Our systematic review identified 8 papers that investigated hemispheric lateralization in infants 12 months and younger. Modalities among the 8 infant papers included fMRI, EEG, and fNIRS, with participants as young as one day old.

In their 2012 paper, Cheng and colleagues used EEG mismatch response (MMR) to investigate how the neonatal brain responds to emotionally spoken syllables vs synthesized nonvocal sounds. They compare happy syllables to nonvocal sounds in experiment 1, compare fearful to happy and neutral syllables in experiment 2, and happy vs angry syllables in experiment 3. This review will discuss only experiment 1. In this experiment, Cheng and colleagues compare activation to a happily spoken ‘dada’ syllable to a synthesized nonvocal sound in 0-5 days old. Specifically, they analyzed activation in a right temporal ROI vs left temporal ROI in each subject. They found that an MMR was elicited in their first experiment and was lateralized to the right hemisphere. The presence of an MMR suggests that either emotional characteristic of the happy tone or the linguistic characteristic of ‘dada’ elicited a significant neural response in the right hemisphere ROI. The use of word-level stimuli is a weakness of this paper, as it makes it perhaps unclear if the response was driven by language rather than emotional tone or acoustics. Though their stimuli are a potentially familiar English word, it is short in length and does not directly resemble connected speech. With 98 participants, N was a large strength, as was their explicit exclusion criteria. However, their syllable stimuli had an emotional component that is outside the scope of this review. The other experiments in the paper delved further into emotional lateralization and found that syllables spoken in fearful and happy manners also elicited a right hemisphere MMR. This replicated right hemisphere activation with emotional stimuli suggests that, in this paper, emotion may have driven results more than language.

Sato et al. (2010) investigated lateralization of lexical pitch-accent in 4- and 10-month-old infants using visual habituation and fNIRS in their experiment 2. Stimuli were sets of disyllabic Japanese word pairs differing only in pitch-accent (high to low vs low to high pitch)

and pure tone pairs whose fundamental frequencies were taken from the word token pairs; they measured responses to pitch changes correlating with semantic changes to Japanese words. In their 4-month-old group, researchers found bilateral activation for the pure tone and word conditions in both hemispheres. The 10-month-old subjects showed greater left hemisphere activation for the pitch change within word condition and no left side dominance for the tone condition. This result indicates that, by 10 months, infants are beginning to show a difference in how they perceive tone and speech signals that they did not show at 4 months. The use of control condition is a strength of this paper and allows for better interpretation of results, as does their use of subjects with different ages. Though it is not a longitudinal study, the use of 4- and 10-month-old subjects allows results are more easily interpreted across the developmental continuum. They also used predetermined ROIs consisting of 3 probes on each side of the superior temporal cortex, a strength of the paper. However, like the paper by Cheng et al. (2012), they presented word level stimuli and therefore may or may not have elicited activation like patterns seen via speech stimulation. Though the stimuli don't exactly resemble connected speech, the paper by Sato and colleagues provides some evidence that, perhaps, the language processes in the brain resemble acoustic processes at birth but shift to the left hemisphere as infants develop.

In the paper by Vannasing et al. (2016) 1-day-old infants listened to a story in their native language of French forwards and backwards and another group listened to the forwards and backwards story in their non-native language of Arabic while undergoing fNIRS. In the forward speech condition, researchers found that the native language group showed activation in the left temporal ROI, while the subjects listening to a non-native language showed activation in the right temporal ROI. Both groups showed bilateral activation during the backwards speech

conditions. Methodological strengths of the paper include their relatively large number of subjects (29), ROI, and data exclusion in this paper. Stimuli was another significant strength of this paper; they used entire passages in a native and non-native language, along with passages of backwards speech as their stimuli. However, though they had a control condition, they did not present multiple conditions to their subjects. Instead, they presented one group of infants with the experimental condition and another group of infants with the control condition and drew conclusions based on group results. This is a weakness of the paper and therefore readers must interpret results with caution; variations in brain structure and function do not allow for easy comparison between groups. Despite the use of multiple groups for control and experimental conditions, Vannasing et al. (2016) provides evidence that perhaps neural networks for speech perception are intact and left lateralized from birth and are distinctly different from acoustic networks that perceive backwards speech and non-native language.

Minagawa-Kawai et al. investigated linguistic and non-linguistic stimuli using late-phase fNIRS in their 2011 paper. They presented 4-month-old full-term infants with short sentences in a familiar language (Japanese), unfamiliar language (British English), monkey calls, emotional non-linguistic voice, and scrambled speech. Looking at predetermined temporal and frontal areas of interest, they found that both sentences in both Japanese and English showed more left activation while the emotional voice showed more right activation. Scrambled sounds also showed left dominance while the monkey call was the only condition that showed bilateral activation. Stimuli and control conditions in this paper allow for robust conclusions to be drawn across multiple types of acoustic stimuli. They also used predetermined ROIs and included criteria for data exclusion. However, with only 12 participants, the number of subjects is a weakness in this study.

Dehaene-Lambertz et al. used forward and backward speech to elicit neural responses in infants 3-month-old infants. In their 2002 paper, participants were read a children's story forward and backward while undergoing fMRI. They found greater left activation in the forward speech condition, though backwards speech was also lateralized to the left. Researchers used whole-cortex fMRI on their 20 participants and did not predetermine their regions of interest. This makes it difficult to discern the significance of resulting activation patterns due to their post hoc ROI determination and small participant numbers, despite the use of connected speech stimuli and control condition.

In their 2000 paper, Dehaene-Lambertz used event-related potentials to investigate activation in response to /ba/ and /ga/ syllables and tones in 4 month-old infants. Like their 2002 study, the results showed left activation of both stimuli at 4 months. Neither condition was categorized as being more left activated than the other; both stimuli showed similar left activation in 4-month infants. As in their earlier study, participant numbers were small (20) and ROIs may have been selected after data collection. Unlike their later study, stimuli did not consist of connected speech. Instead, syllables were used. However, tones did act as a control condition against which to compare and clear criteria for data exclusion was defined.

Finch et al., (2017) was the only infant paper to investigate lateralization in non-typical infants. They used event-related potentials in left-central and right-central areas of interest in children at high risk for autism aged 12 months. Three groups were included in the study: children deemed at high-risk for autism (infants with autistic older siblings), high-risk children who were later diagnosed with autism, and controls with no autistic siblings. The infants were presented with standard consonant-vowel (CV) syllables, CV syllables with a native deviant, and syllables with a non-native deviant during EEG recording. The paper used 3 consonant-vowel

syllables as their stimuli that differed only by initial consonant. The study produced no main or interaction effects related to condition; the activation was the same across the syllable stimuli suggesting no difference in activation across their syllables. Both the control group and the group with autistic siblings showed more positive left lateralization for the syllable stimuli at 12m while the children with later autism diagnosis showed greater right lateralization. No significant difference in lateralization index was found between infants with autistic siblings and the control group. Despite their use of multiple stimuli, the deviant syllables do not directly resemble connected speech. ROI is also a relative weakness of this study, as regions of interest were constructed after data collection. However, the use of multiple groups is a strength of the paper, as is their inclusion of 96 participants.

In their 1975 paper, Molfese and colleagues used EEG to observe activation in a group of infants, 1 week to 11 months old, and a group of children, 4 to 11 years. The infant data will be presented here with the pediatric data to follow. In their paper, researchers played a series of syllables, 1-syllable words, a piano chord, and an electronically generated sound to their subjects while recording activation via EEG. In their infant group, researchers found greater left hemisphere activation for their combined speech condition (syllables and words) and increased right activation for the piano chord. Stimuli was a relative strength of this paper, as they included both syllable and word stimuli and had multiple nonspeech conditions. However, their results are difficult to interpret across development because of their temporally large age groups. The infant group spans 11 months and their pediatric group spans 7 years; with data analysis occurring among such a large range of ages, it is likely that temporally linked changes in activation may have been obscured by the differently aged participants in the same group. It is also unclear how many participants of each age were represented within the groups. Greater numbers of

participants at either end of an age group may have significantly impacted results. Additionally, the paper leaves out children aged 12 months to 4 years; it is reasonable to assume that any changes found between the younger and older group may have occurred during this span of development.

YOUNG CHILDREN (2y-8y)

This systematic review revealed 4 papers that investigated hemispheric lateralization in children whose ages were between 2 and 8 years. Three of these papers studied typically developing (TD) children and one studied children with autism. These papers represent our current evidence of lateralization patterns for speech perception in children during the critical period of language as revealed by our systematic literature search.

As presented above, Molfese and colleagues presented young children aged 4-11 years with their syllable, word, chord, and noise stimuli during EEG recording. Individual participant data was not able to be further separated by age, therefore the entire pediatric group will be discussed here. Molfese and colleagues found greater left hemisphere activation in their speech conditions and greater right activation for their chord and electronic noise conditions. However, as previously discussed, weaknesses in age group assignments make it important to interpret these results with caution.

Sandbank et al., (2017) used event-related potentials in their study of 2–5-year-old children with autism who listened to words and nonwords during EEG recording. Researchers did not find a significant difference in left activation between words and nonwords, though their ROIs were different than any other paper in this review. They were the only study reviewed to not include right hemisphere data, and instead looked for differences in left activation between

word and nonword conditions in their predetermined left ROIs. Because there are no right hemisphere electrodes, it is difficult to determine left vs right activation. These methods instead allow us to see differences in left activation across their multiple conditions. Despite their unusual choice in regions of interest, the paper made good use of control stimuli and determined their ROIs before data collection. They had clear criteria for data exclusion and had 34 participants spanning multiple ages. However, as described above, researchers must be deliberate in their choice of age groups and distribution within those groups. Their results were unable to show a difference in left activation between their word and nonword stimuli.

In their 2020 study, Olulade et al. presented children and adults with forward and backward speech with a button task while undergoing fMRI. This review will only include their pediatric data. In their paper, typical children ages 4-13 were instructed to listen to sentences and press a button if the sentences correctly described the given object (e.g., “a big grey animal is an elephant”). The control condition consisted of reverse speech with beeps in which participants pressed a button upon hearing a beep. Children were divided into the following age groups: 4-6 years, 7-9 years, and 10-13 years. The youngest age group will be discussed here, the older age groups are found later in this review. In the 4 to 6-year-old group, researchers found activation largely in the left hemisphere for the speech condition but also showed some significant right activation. Their use of a button task is a strength of the study as it ensures that participants are engaged in listening to the stimuli. Their use of multiple age groups is another strength, though researchers must be careful when defining age groups. Should age groups be made too large, developmental changes may be obscured within the group. Connected speech stimuli and the control condition were additional strengths of this paper. Their results provide evidence that

neural activation in response to speech perception may be somewhat left-lateralized in children 4 to 6 years old.

In their study, Berl et al. (2014) presented children with forward and backward speech while they underwent fMRI with a button task. As in the paper presented above, children were instructed to listen to sentences and press a button if the sentence correctly described a given object. Their control condition consisted of backwards speech with similar button task. Their study consisted of three groups of children: 4-6y, 7-9y, and 10-12y. The youngest age group will be presented here, while the older age groups will be discussed later in this review. In their youngest age group, they found left activation for their receptive language condition in children 4-6 years old and no significant activation of their ROIs during the baseline backwards speech condition. Participant numbers, connected speech stimuli, control condition, and the inclusion of a button task are strengths of this study. Their use of multiple small age groups is another strength, as it shows activation patterns in different stages of development. ROIs were constructed based on large anatomical areas, and it is unclear if they were determined before or after data collection, a potential weakness of the study. This paper provides more evidence that neural activation while perceiving speech is at least partially left-lateralized in young children.

OLDER CHILDREN (8y-18y)

Our systematic review revealed 4 papers that investigated hemispheric lateralization of speech perception in children aged 8-18 years. Three of these papers used fMRI as their imaging modality while the third used MEG.

As introduced above (see pg. 22), Olulade et al. (2020) presented sentence stimuli with a button task to children of a variety of ages while undergoing fMRI. In addition to the left

activation they found in young children, Olulade and colleagues found stronger left activation in their older age groups. They also found that the right activation shown in their younger children decreased with age. Through their semantic decision task and fMRI data, the group showed left dominance in all their participant groups and showed fading right activation with age.

Berl et al. (2014) used fMRI to investigate lateralization of speech perception in typically developing right-handed children of varied ages, and included groups aged 4-6 years, 7-9 years, and 10-12 years. Their methods and results from their youngest age group are explained above (pg. 23). They calculated a lateralization index based on the activation across the entire cortex and found left activation during their task in the older age groups. All three of their age groups showed left dominance, although the older groups showed stronger activation on the left. As stated above, the use of multiple age groups is a strength of this study that allows us to draw conclusions throughout childhood in a single study using the same methods and stimuli. The results of this study suggest that, in typical children, speech perception is somewhat left lateralized by 4 years, though it appears to be shifting further left as children age.

Flagg et al., (2005) investigated lateralization of language in right-handed typically developing children and children with autism aged 8-12 and 8-17, respectively. In their MEG experiment, researchers presented subjects with the two vowels /a/ and /u/ presented with both typical male and typical female fundamental frequencies. In the typically developing group, researchers found left activation to the vowel stimuli that increased with age among their participants. However, they found that children with autism showed right activation to the stimuli that increased with age. The use of vowel stimuli is a weakness of this paper, as the vowel stimuli may not elicit the same neural responses as connected speech. Additionally, without the use of a control condition, it is increasingly difficult to determine the origin of the

elicited responses. In addition, the paper had only 12 participants, though they spanned multiple ages and allowed researchers to draw conclusions across a period of development, though their age groups had a large range that should be considered. The paper clearly outlined criteria for data exclusion and calculated laterality indices based on the number of dipole fits to late-phase MEG responses in each hemisphere.

Finally, specialization of speech perception in older children was also investigated in the paper by Norrelgen et al. (2015). Their fMRI study consisted of children aged 8-18 with intractable focal epilepsy and included a forward and backward story listening task, a dichotic listening task, and a verb-generation task. All tasks were included in the analysis, but this review will comment only on the listening task. Out of 19 participants, 15 had enough voxels to complete analysis. Of these 15, 2 subjects showed clear left activation (left LI for 2/3 regions of interest – frontal, temporal, parietal), 5 showed clear left activation, and the remaining 8 had either only 1 ROI with conclusive laterality data or had results in multiple areas that opposed each other. 2 participants had at least 2/3 lobes showing left activation, 5 participants had at least 2/3 lobes showing right activation. Stimuli, span of age ranges, and ROI were strengths of this paper. Three ROIs were determined before data acquisition and participants spanned a range of ages. Given that participants had intractable focal epilepsy, a control condition would have allowed for better generalization of conclusions; the paper also would have benefited from including more than 19 participants. Though it is out of the scope of this review, the inclusion of receptive and expressive language tasks gives this paper a unique perspective of the full scope of language lateralization.

DISCUSSION

Many details surrounding the development of hemispheric lateralization of language remain unknown. Due to the large variation in methodologies and small number of papers, it is unclear what typical lateralization of speech perception looks like in infants and throughout development. Papers by Dehaene-Lambertz et al., (2002), Dehaene-Lambertz, (2000), Finch et al., (2017), and Minagawa-Kawai et al., (2011) show left lateralization for speech in the first year of life but also show left lateralization for nonspeech conditions. Perhaps there is no differentiation in speech and non-speech acoustic stimuli in infancy. Papers by Sato et al. (2010), Vannasing et al. (2016), and Molfese et al., (1975) show conflicting trajectories of language lateralization. Sato et al., (2010) found bilateral activation for tones and words in 4-month-old infants, but left activation for the word condition in 10-month-old infants, making it the only infant paper to show a shift in lateralization during the first year of life. Vannasing et al., (2016) found left lateralization for native language, right lateralization for non-native language, and bilateral activation for backwards speech, and Molfese et al found left activation for speech and right activation for nonspeech stimuli. These two papers are inconsistent with other papers in this review because they show lateralization within the first year of life. There is conflicting evidence regarding lateralization of speech perception in the first year of life and trajectories within this year remain unknown.

This review revealed few studies involving young children, making it difficult to definitively determine the development of lateralization during early childhood. The evidence by Sandbank et al., (2017) is difficult to interpret due to the lack of imaging data from the right hemisphere; their left hemisphere results showed no difference in activation among their two conditions. Berl et al., (2014) suggests that speech perception is left lateralized by 4-6 years, and

Olulade et al., (2020) showed activation that was left lateralized in their 4 to 6-year-old group, though their results included some lesser right activation. This small number of papers may not be significant enough evidence from which to draw conclusions about an entire age group.

Overall, more high-quality research is needed in this age range of language development.

Stronger evidence for left lateralization was found in the older children age group than in any other group of papers. Despite the small number of studies and differing modalities, there is evidence to suggest that speech perception is left lateralizing during these ages (Berl et al., 2014; Flagg et al., 2005; Olulade et al., 2020). One paper looked extensively into the lateralization of both receptive and expressive language but had inconclusive results in non-TD children (Norrelgen et al., 2015). The papers with older typically developing participants showed stronger left activation of speech vs nonspeech stimuli suggesting that, perhaps, left lateralization is intact in older children; there is also some evidence to suggest that lateralization strengthens as children age.

Two papers investigated lateralization of speech perception in children at risk for autism (Finch et al., 2017; Flagg et al., 2005). The paper by Flagg et al., (2015) suggests that perhaps children with autism have atypical activation patterns when compared to their typically developing peers between the ages of 8-17. It is possible that this pattern is present in younger children remains unclear if this pattern is present in younger children as Finch et al. (2017) also found right activation in their infants with autism.

Despite the inconsistency in evidence presented thus far, it is perhaps possible that language is not fully lateralized at birth, and instead shifts throughout childhood. The developmental trajectory is not yet clear and many aspects of functional specialization for speech processing in children and infants remain ripe for investigation.

LIMITATIONS

Due in part to the cost and time demands of neuroimaging studies, many of the papers in this review present small participant numbers. Some papers in this review also use methodologies that are less desirable, such as presenting different stimuli to different groups of participants or foregoing the use of a control condition. Overall, there is an overall lack of longitudinal papers, or papers that track development of its subjects over time.

There is additional evidence regarding lateralization in childhood that use expressive methodologies, such as the verb generation paradigm, that may provide further evidence for lateralization of language functions. Because of their expressive nature, they remain outside the scope of this review and were excluded. However, their data may help provide a better picture of lateralization of broader language functions. Finally, the search terms used in this review were designed to reveal any papers investigating the lateralization of or specialization for speech perception, though due to the lack of consistent terminology in this area of research, some relevant papers may have been excluded from the initial search.

FUTURE DIRECTIONS

There are many other directions that research should take. In future studies, researchers should take care to ensure that they use connected speech stimuli matched with an acoustically complex control condition. By using sentence or paragraph stimuli, we can be sure that the activation resembles that of connected speech. With the addition of a control condition, researchers can assure that differences in activation are a direct result of their speech stimuli in comparison to complex acoustics.

Longitudinal studies will also be beneficial when further investigating hemispheric lateralization for speech perception. Longitudinal study design allows researchers to track changes over time within the same group of subjects. By using a longitudinal design, researchers will be better able to identify changes in lateralization that may or may not be revealed by the current literature.

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