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Early Childhood Stuttering and Electrophysiological Indices of Language Processing

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Abstract

We examined neural activity mediating semantic and syntactic processing in 27 preschool-age children who stutter (CWS) and 27 preschool-age children who do not stutter (CWNS) matched for age, nonverbal IQ and language abilities. All participants displayed language abilities and nonverbal IQ within the normal range. Event-related brain potentials (ERPs) were elicited while participants watched a cartoon video and heard naturally spoken sentences that were either correct or contained semantic or syntactic (phrase structure) violations. ERPs in CWS, compared to CWNS, were characterized by longer N400 peak latencies elicited by semantic processing. In the CWS, syntactic violations elicited greater negative amplitudes for the early time window (150–350 ms) over medial sites compared to CWNS. Additionally, the amplitude of the P600 elicited by syntactic violations relative to control words was significant over the left hemisphere for the CWNS but showed the reverse pattern in CWS, a robust effect only over the right hemisphere. Both groups of preschoolage children demonstrated marked and differential effects for neural processes elicited by semantic and phrase structure violations; however, a significant proportion of young CWS exhibit differences in the neural functions mediating language processing compared to CWNS despite normal language abilities. These results are the first to show that differences in event-related brain potentials reflecting language processing occur as early as the preschool years in CWS and provide the first evidence that atypical lateralization of hemispheric speech/language functions previously observed in the brains of adults who stutter begin to emerge near the onset of developmental stuttering.

Keywords

stuttering; ERP; language processing; N400; P600; semantic; syntactic

Introduction

Many preschool children display disfluencies in their speech, for example, repeating phrases or interjecting fillers such as “um, um, um.” These types of disfluencies are considered part of normal speech and language development. However, a subgroup of preschool-age

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children, approximately 4–5%, display stuttering-like disfluencies that include sound and syllable repetitions, sound prolongations, and silent blocks (Bloodstein & Bernstein Ratner 2008; Yairi & Ambrose, 2005). These children display developmental stuttering and are at risk for developing chronic stuttering.

Current theoretical accounts of stuttering view it as a multifactorial disorder in which a vulnerable speech-motor system interacts with neural mechanisms mediating language, cognitive, and emotional processes (Conture et al., 2006; DeNil, 1999; Howell, 2010; Smith, 1999; Smith & Kelly, 1997). The extent to which these factors produce, exacerbate, or maintain stuttering is likely to be weighted differently across individuals and may fluctuate in both the short term (e.g., in different situations) and the long term, for example, across the course of development (e.g., Smith, 1999). Within this framework, studies of the interactions between language processing demands and the control of speech movements indicate that the speech motor systems of many preschool children who stutter (CWS) show greater coordinative variability for language tasks compared to their typically fluent peers. For example, preschool-age CWS, compared to children who do not stutter (CWNS), were found to exhibit overall higher coordination variability for short and long sentence production and for sentences that had relatively simple syntactic structure (MacPherson & Smith, in press). In another study, many preschool-age CWS were also found to display higher variability for the production of novel phonological sequences than CWNS (Smith, Goffman, Sasisekaran, & Weber-Fox, 2012). The findings of greater speech-motor coordinative variability for preschool CWS were based on samples of children who displayed age-appropriate speech and language abilities as measured by standardized testing, and analyses were based only on speech samples that were perceptually fluent (MacPherson & Smith, in press; Smith et al., 2012). These results suggest that linguistic effects have a greater impact on the speech-motor coordination systems of many preschool CWS compared to preschool CWNS and point to the need for a better understanding of language processing in preschool-age CWS.

1.1. Behavioral Studies of Language Proficiency in CWS

Many researchers have examined aspects of language processing in CWS (e.g., Anderson & Conture, 2004; Anderson, Pellowski, & Conture, 2005; MacPherson & Smith, in press; Pellowski & Conture, 2005; Smith et al., 2012; Wagovich & Bernstein Ratner, 2007; Weber-Fox, 2001; Weber-Fox, Spruill, Spencer, & Smith, 2008). Research utilizing behavioral measures of language abilities in CWS indicated that a significant proportion of them have vulnerable semantic and syntactic language planning and production systems (Anderson & Conture, 2004; Anderson et al., 2005; Pellowski & Conture, 2005; Wagovich & Bernstein Ratner, 2007). Relative to semantic/lexical skills, some studies have reported that CWS perform more poorly on standardized measures of vocabulary than CWNS (Anderson & Conture, 2000; Murray & Reed, 1977; Pellowski & Conture, 2005; Westby, 1979). Some studies have not observed reduced vocabulary skills in CWS (Bernstein Ratner & Silverman, 2000; Ryan, 1992; Silverman & Bernstein Ratner, 2002); however, Silverman and Bernstein Ratner (2002) reported that CWS, compared to CWNS, demonstrated less lexical diversity in spontaneous speech. Relative to a specific class of the lexicon, Wagovich and Bernstein Ratner (2007) reported that preschool-age CWS produced fewer different and total verbs than CWNS. Also, in a lexical priming study, preschool-age CWS demonstrated slower picture naming when given a lexically related prime compared to an unrelated prime, whereas CWNS demonstrated the opposite, more expected pattern of naming pictures faster when primes were lexically related (Pellowski & Conture, 2005). In sum, behavioral studies indicate that there may be subtle differences in semantic/lexical processing between some children who stutter and their normally fluent peers.

Behavioral measures have also been utilized in the study of syntactic processing in CWS (Anderson & Conture, 2004; Howell & Au-Yeung, 1995). For example, in spontaneous speech, preschool-age CWS have been reported to use less complex syntax (Howell & Au-Yeung, 1995; Wall, 1980); though by school age, this difference is not evident (Silverman & Williams, 1967; Westby, 1979). In an experimental study of syntactic processing, CWS, compared to CWNS, demonstrated a greater syntactic priming effect (i.e., difference between the no-prime and prime conditions), as measured by speech reaction time, suggesting that some young CWS may have fewer computational resources available for syntactic construction (Anderson & Conture, 2004). Furthermore, CWS demonstrated fewer accurate responses than CWNS during the syntactic priming condition. These studies indicate that young children who stutter plan and produce syntax differently than their typically fluent peers. The converging evidence from studies utilizing behavioral language measures in CWS indicate the possibility that at least some aspects of semantic and syntactic processing may function atypically in a significant proportion of young children who stutter.

1.2 Event-Related Brain Potential (ERP) Indices of Language Processing in Stuttering

ERP measures have been utilized effectively in previous studies of language processing in young typically developing children (e.g., Hahne, Eckstein, & Friederici, 2004; Hampton Wray & Weber-Fox, 2012; Holcomb, Coffey, & Neville, 1992; Pakulak, Sanders, Paulsen, & Neville, 2005; Weber-Fox, Spencer, Spruill, & Smith, 2004; Weber-Fox, Hart, & Spruill, 2006) and offer a direct measure of neural activity with fine temporal resolution (Nunez, 1995). However, ERP studies of children who stutter are few. One study of school-age CWS employed ERPs to examine aspects of phonological/rhyme processing using visually presented words (Weber-Fox et al., 2008). Results indicated that the neural processes related to phonological rehearsal and target word anticipation were atypical (possibly less mature) for the 9–12 year old CWS group. Additionally, the relative contributions of the left and right hemispheres in the linguistic integration stage of processing differed for the CWS compared to CWNS. Taken together, the results suggested that a significant proportion of CWS may be less able to form and retain a stable neural representation of the prime onset and rime as they anticipate the target presentation, which may have contributed to their lower rhyming judgment accuracy. Important for the current study, the findings for the CWS did not parallel those found in an earlier study of adults who stutter utilizing the same rhyming paradigm (Weber-Fox et al., 2004). The converging evidence from these two studies indicates that differences in neural processing associated with stuttering are not constant over the course of development and highlights the need for developmental studies of neural activity in stuttering.

To date, ERP studies of semantic and syntactic processing and stuttering have been conducted only in adults (Cuadrado & Weber-Fox, 2003; Weber-Fox & Hampton, 2008; Weber-Fox, 2001). The results from an ERP study of adults who stutter (AWS), which utilized a natural speech paradigm, indicated that AWS may display atypical language processing even in the absence of overt speaking demands (Weber-Fox & Hampton, 2008). AWS were found to exhibit both an N400 (indexing ease of lexical access and integration) and a P600 (indexing syntactic repair processes) to both unexpected semantic information contained in the verbs of sentences (semantic condition) and verb-agreement violations (syntactic condition) in relatively simple sentences. In contrast, the normally fluent speakers exhibited an N400 only to the violations in semantic expectation on the verb, and a P600 only to the verb-agreement violations. The biphasic (N400-P600) ERP pattern observed in the AWS has also been observed in typical speakers; however, in typical speakers this ERP pattern was elicited by complex online linguistic operations that rely more on semantic-syntactic interface processes (e.g., Friederici & Frisch, 2000; Kemmerer, Weber-Fox, Price, Zdanczyk, & Way, 2007; Kim & Osterhout, 2005; Kolk, Chwilla, van Herten, & Oor, 2003;

Kuperberg, Kreher, Stinikova, Caplan, & Holcomb, 2007). These ERP findings in the auditory modality converge with earlier studies using visual stimuli (Cuadrado & Weber-Fox, 2003; Weber-Fox, 2001) to indicate that, although linguistic abilities as measured by standardized testing are normal, underlying brain activity mediating some aspects of semantic and syntactic processing may function differently in adults who stutter (Weber-Fox & Hampton, 2008).

1.3 Approach of the Current Study

The current study focuses on the potential role of language processing demands in stuttering for preschool-age children. We employed a novel, ecologically valid ERP paradigm in which no overt speaking task or behavioral response was required. This allowed us to assess neural processes for language independent of the additional formulations required for overt speech or motor behavioral response planning and implementation stages in young children who stutter.

The experimental ERP paradigm of the current study allows for examination of neural functions for semantic and syntactic processing in preschool-age children who stutter. The specific paradigm utilized is well suited for preschool-age children, ecologically valid, and allows for examining both semantic and syntactic constraints on language during natural speech processing (Pakulak et al., 2005). These natural speech stimuli have already been shown to elicit well-known ERP components indexing semantic and syntactic processing (Pakulak et al., 2005; Neville, Pakulak, Yamada, & Hampton Wray, 2012; Yamada et al., 2012) that have been previously studied in typically developing children utilizing language processing paradigms (e.g. Hahne et al., 2004; Holcomb et al., 1992; Juottonen, Revonsuo, & Lang, 1996).

For the semantic condition, we examined the component known as an “N400” followed by a late positive component (LPC). The N400 is sensitive to cloze probability and is thought to index lexical access and integration (e.g., see Kutas & Federmeier, 2011, for review). The LPC, often observed to follow an N400, is also thought to be related to processing word meaning, but may be less automatic and more related to effortful integration of verbal meaning to semantic memory constructs than the N400 (Juottonen et al., 1996; Van Petten & Luka, 2012). For the syntactic condition, the current study examines two previously described ERP components shown to be elicited by phrase structure violations. These components include an “early negativity” that is thought to index parsing of syntactic structure (see Friederici, 2002, for review), followed by a P600, which indexes repair or reanalysis of syntactic violations (e.g., Friederici, Hahne, & Mecklinger, 1996; Yamada & Neville, 2007) or difficulty of syntactic integrations (Kaan, Harris, Gibson, & Holcomb, 2000).

Another important aspect of the current study is that the participants are preschool-age children who are closer to the onset of stuttering and are thereby less influenced by long-term experience with stuttering than participants in previous studies. Additionally, the current study combines comprehensive speech, language, and cognitive assessments to characterize and match proficiencies between the groups of preschool CWS and CWNS. This is the first ERP study examining neural processes mediating semantic and syntactic processing in preschool-age children who stutter.

In summary, the current study utilizes electrophysiological measures to explore semantic and syntactic processing of natural speech stimuli in preschool-age children who do and do not stutter. The specific goal of this study is to determine whether preschool-age children who stutter demonstrate atypical neural processing of natural speech stimuli containing semantic and syntactic violations. Based on previous findings in the behavioral testing and

ERP literature, we predict that neural indices of both semantic and syntactic processing will distinguish the CWS from their fluent peers. However, we predict that the nature of group differences may be different from those previously observed in AWS (Weber-Fox & Hampton, 2008), in part due to changes in stuttering, language abilities, and neural maturation over the course of development. Findings from this study will help to better understand the relationships between neural activity mediating semantic and syntactic processing and developmental stuttering near its onset.

2. Method

2.1 Participants

Participants included 54 preschool-age children, 27 of these were children who do not stutter (CWNS; 9 girls) and 27 were children who stutter (CWS; 7 girls). The data were collected at two research sites with the same experimental setups, one at Purdue University and one at the University of Iowa. The participants' ages ranged between 4 years 1 month and 5 years 11 months for the CWNS group (mean age 5;1) and between 3 years 11 months and 5 years 11 months for the CWS group (mean age 5;1). Two participants in the CWNS group and three in the CWS group were left-handed as reported by the children's parents and confirmed by an abbreviated handedness inventory (5 tasks adapted from Oldfield, 1971). All participants passed a hearing screening at 20 dB HL for 1000, 2000, and 4000 Hz and had normal or corrected-to-normal vision according to parental report. The children had no history of neurological disorders and had never taken medications that might affect neural function (e.g., medications for depression, seizures, or attention-deficit hyperactivity disorder). All of the children also demonstrated normal nonverbal intelligence as assessed by the Columbia Mental Maturity Scale (Burgemeister, Blum, & Lorge, 1972), showed no symptoms of impaired reciprocal social interaction and restriction of activities (DSM IV criteria of autism and pervasive developmental disorder: American Psychiatric Association, 1994) as assessed by the Childhood Autism Rating Scale (Schopler, Reichler, & Renner, 1988), and according to parental report, had never been treated for emotional problems.

All of the children who were brought in to participate in the study were evaluated to determine whether they displayed developmental stuttering. For a child to be diagnosed with developmental stuttering he/she was required to meet the criteria established by Yairi and Ambrose (1999). These criteria included that the child was regarded as exhibiting a stuttering problem by his/her parent and at least one certified speech-language pathologist involved in the project; the child's stuttering severity was rated as 2 or higher on an eight point (0–7) severity scale by his/her parent and a speech-language pathologist; and the child exhibited at least three stuttering-like disfluencies per 100 syllables of spontaneous speech in a language sample. The coding reliability between two independent raters for the stutter-like and normal disfluencies was at least 85%. The stuttering-like disfluencies included part-word repetitions, monosyllabic word repetitions, and disrhythmic phonations such as sound prolongations and silent blocks.

All participants were administered a battery of tests to ensure that receptive language, expressive language, phonological abilities and verbal working memory were within normal limits. Language comprehension was measured by the Test for Auditory Comprehension of Language – 3 (TACL-3; Carrow-Woolfolk, 1999) and spoken language was assessed using the Structured Photographic Expressive Language Test – 3 (SPELT-3; Dawson, Stout, & Eyer, 2003). Phonological abilities were measured by the Bankson-Bernthal Test of Phonology (BBTOP; Bankson & Bernthal, 1990), and verbal working memory was assessed by the Test of Auditory-Perceptual Skills – Revised (TAPS-R; Gardner, 1996). All of the participants included in the current study scored within or above 1 standard deviation of the mean on each of these assessments. The mean (*SE*) performance scores for these

assessments, as well as the scores obtained for the Columbia Mental Maturity Scale, are presented for each group in Table 1. Previous research has shown that in young children, variations on these measures, even within normal range, can produce significant differences in the ERPs elicited by semantic and syntactic constraints (Hampton Wray & Weber-Fox, 2011; 2012). It is important to note that there were no significant group differences for any of these cognitive/behavioral indices, $p > .05$. Group comparisons on the Auditory Word subtest of the TAPS-R (Gardner, 1996) did not reach significance, $F(1, 52) = 3.916, p = .053$.

In addition, research indicates that socioeconomic status (SES) may have a significant influence on language proficiency, cognitive abilities, and ERPs (e.g., Hackman & Farah, 2009; Neville et al., 2012; Stevens, Lauinger, & Neville, 2009). We evaluated the level of maternal education employing the Hollingshead education scale (Hollingshead, 1975) as a measure of SES for each of our participants. According to this scale, a score of 4 was assigned for completed high school, 5 for partial college or specialized training (e.g., technical school), 6 for a completed college degree, and 7 for a graduate degree. The mean (*SE*) SES scores for the CWNS, 6.15 (0.22) and CWS, 5.85 (0.17), groups did not differ, $F(1, 52) = 1.185, p = .285$.

2.2 Sentence Stimuli

Sentence stimuli were developed to accompany visual displays of cartoon videos of “Pingu” the penguin (stimuli created in collaboration with the Brain Development Lab in Eugene, Oregon directed by Dr. Helen Neville). The naturally spoken sentences and accompanying visual displays were presented using Presentation software (9.70). The monitor displayed the ongoing cartoon with a visual angle of 4.9 degrees horizontally and 3.8 degrees vertically to minimize eye movement. At the same time, naturally spoken sentences that told the story of the video were presented via a speaker placed directly above the monitor at an average intensity of 70–75 db SPL. Each cartoon movie included 100 spoken sentences and was approximately 7–8 minutes in duration. Five movies were shown during the ERP recording session. Of the total 500 sentences heard by the participants, there were 50 semantic anomalies and their 50 control sentences as well as 50 phrase structure violations and their 50 control sentences. These 4 conditions were analyzed for the current study. (Additional conditions not included in the present report are irregular verb agreement, regular verb agreement and jabberwocky conditions.) Two scenarios were developed for each cartoon video so that a sentence that served as a violation condition in one scenario (e.g. story #2A, “The music box is on the name so Pingu can push it.”), would serve as control sentence in another scenario (e.g., story #2B “The music box is on the sled so Pingu can push it.”) The scenarios were counterbalanced across participants. All the words used to form the sentence stimuli were taken from the MacArthur Communicative Developmental Inventories: Words and Sentences (Fenson, Dale, Reznick, Thal, Bates, Hartung, et al., 1993) to ensure familiar vocabulary for the children. These stimuli were previously utilized in developmental studies of language processing (Pakulak et al., 2005; Neville et al., 2012; Yamada et al., 2012). Examples of sentences for each of the conditions, shown in Table 2, illustrate that the phrase structure violations were created by inserting a second closed-class word just before the target demonstrative (e.g., “that those”) or pronoun (e.g., “his her”). This type of insertion violation allows for comparisons of target words from the same word class in the control and violation cases. Insertion phrase structure violations have been utilized in previous studies of typically developing adults and children (e.g., Hampton Wray & Weber-Fox, 2012; Pakulak & Neville, 2010; Yamada & Neville, 2007).

The sentences were spoken at a natural rate by male and female speakers. The onsets of the canonical and violation words were determined by independent judgments by three trained researchers in the Brain Development Laboratory in Eugene, Oregon. Based on visual

inspection of the waveforms and spectrograms, onset times were defined as the earliest indication of a new sound using Praat software (Boersma & Weenink, 2004) while at same time listening to the sentence segments using a gating procedure to confirm the onset times.

2.3 Procedures

Once appropriate electrode impedance levels were obtained ($< 5 \text{ k}\Omega$), the participants were seated comfortably in a sound-attenuating room and positioned 172 cm from a 47.5-cm monitor. Participants were given the following instructions: "While you sit in this chair, you will watch and listen to five stories about Pingu the penguin and his family and friends. It is important to keep your arms, legs, and head as still as you can while you are watching the stories. At the end of each story, you will have a break where you can move and stretch if you need to. You will also get to pick out a sticker and place it on your activity sheet at the end of each story. When you have five stickers on your sheet, you will be finished and will get to pick out a toy!" An experimenter sat next to the child throughout the presentations of the cartoons, helped re-instruct the participant to sit still when needed, and also helped the child with picking out a sticker after each story and putting it on an activity sheet.

2.4 Electroencephalographic Recordings

Electrical activity at the scalp was recorded from electrodes secured in an elastic cap (Quik-cap, Compumedics Neuroscan). Twenty-eight electrodes (Ag-AgCl) were positioned over homologous locations of the two hemispheres according to the criteria of the International 10–10 system (American Electroencephalographic Society, 1994). Locations were as follows: lateral sites F7/F8, FT7/FT8, T7/T8, TP7/TP8, P7/P8; medial sites FP1/FP2, F3/F4, FC3/FC4, CP3/CP4, P3/P4, O1/O2; and midline sites FZ, FCZ, CZ, CPZ, PZ, OZ. Recordings were referenced to linked electrodes placed on the left and right mastoids. Horizontal eye movement was monitored via electrodes (HEOG) placed over the left and right outer canthi. Electrodes over the left inferior and superior orbital ridge (VEOG) were used to monitor vertical eye movement. Electrode impedances were adjusted to $5 \text{ k}\Omega$ or less for all sites, with the exception for VEOG and HEOG channels which were adjusted to $10 \text{ k}\Omega$ or less. The electrical signals were amplified within a bandpass of 0.1 and 100 Hz and digitized on-line (Neuroscan 4.2) at a rate of 500 Hz.

2.5 ERP Analyses

The Neuroscan continuous EEG files were imported into EEGLAB (Delorme & Makeig, 2004) and downsampled (256 Hz). Eye movement artifacts were removed from the EEG waveforms using Independent Components Analysis (ICA) (EEGLAB; Delorme & Makeig, 2004). The EEG was then low-passed filtered at 30 Hz, and -200 to 2000 ms epochs for the semantic conditions and -1000 to 2500 ms epochs for the syntactic condition were created. The epochs were time-locked to the critical comparison words and were baseline corrected to the interval preceding the onset of the critical word. A longer baseline (1000 ms) was utilized for analyses of the ERPs in the syntactic (phrase structure) condition to accommodate for differences in timing of the prosodic phrase boundary (amplitude and pitch) and word type (preposition vs. pronoun) of the pre-target words that resulted in effects that began just prior to or at 0 ms . The longer baseline allowed us to view these differences more clearly in order to account for them in interpreting the findings (Neville et al., 2012; Yamada et al., 2012). After baseline correcting, any trials with remaining artifact exceeding $100 \mu\text{V}$ for the VEOG and HEOG channels or $200 \mu\text{V}$ for the remaining channels were automatically detected and these epochs were removed from further analysis. The remaining trials were averaged by condition for each participant (ERPLAB; Lopez-Calderon & Luck, 2010). The mean numbers of accepted trials for each condition for each group are summarized in Table 3.

The temporal windows used for measurements were selected to capture early, middle, and later time windows and are consistent with the existing literature on semantic and syntactic processing in young children (Hahne et al., 2004; Hampton Wray & Weber-Fox, 2012; Neville et al., 2012; Pakulak et al., 2005). The temporal windows utilized to measure the mean amplitudes and peak latencies of ERP components elicited in the semantic conditions were 400–700 ms for the N400 and 1250–1550 ms for the late positive component (LPC). Temporal windows for the phrase structure violation condition were 150–350 ms for the early negativity and 850–1550 ms for the P600. The mean amplitudes of components were computed relative to the baseline. For the semantic and syntactic conditions, separate omnibus ANOVAs with repeated measures were calculated for each of the ERP components with a between-subject factor of Group (CWNS, CWS) and four within-subject factors including Condition (Control, Violation), Hemisphere (Left, Right), Anterior/Posterior Distribution (Anterior: frontal, fronto-central; Posterior: central, centro-parietal, parietal), and Laterality (Lateral, Medial). Repeated measures ANOVAs were also calculated for the midline electrodes for Condition (Control, Violation), and Anterior/Posterior Distribution (Anterior: Fz, FCz; Posterior: Cz, CPz, Pz). Significance values were set at $p < .05$. In cases where the omnibus analysis produced a significant interaction with Group or Condition, the interaction was further evaluated with a step-down ANOVA based on the factors specific to the given interaction. For all repeated measures with greater than one degree of freedom in the numerator, the Huynh-Feldt (H-F) adjusted p -values were used to determine significance (Hays, 1994). Effect sizes, indexed by the partial-eta squared statistic (η_p^2), are reported for all significant effects.

3. Results

3.1 Processing Semantic Anomalies

The grand average ERPs elicited by the control and violation comparison words in the semantic condition are illustrated for the CWNS (Figure 1) and CWS (Figure 2) groups. As is evident in these figures, both groups of preschool children displayed robust increases in the N400 and LPC amplitude for the semantic anomalies relative to the control words. Below are the results of the statistical analyses of the ERP components (N400 and LPC) elicited in the semantic control and violation conditions.

3.1.1 N400 Measures—Relative to the control condition, the semantic anomalies elicited larger N400 amplitudes over the lateral/medial electrode locations, $F(1, 52) = 11.04$, $p = .002$, $\eta_p^2 = .175$, and midline sites, $F(1, 52) = 12.560$, $p = .001$, $\eta_p^2 = .195$. There were no significant group differences in the N400 amplitudes over lateral/medial or midline sites, $F(1, 52) < 1$, or interactions with group, $F(1, 52) < 2.91$, $p > .09$.

The peak latency of the N400 measured for the lateral/medial electrode sites occurred earlier in the ERPs of the CWNS group compared to the group of CWS, $F(1, 52) = 6.25$, $p = .016$, $\eta_p^2 = .107$. As can be seen in Figure 3, this effect was largely driven by earlier peak latencies for the CWNS for the N400 elicited by the control words at left medial and right lateral and medial sites, and for the violation condition at the left lateral sites, Condition X Hemisphere X Laterality X Group $F(1, 52) = 9.307$, $p = .004$, $\eta_p^2 = .152$. There were no significant group differences for the N400 peak latency for the midline electrode sites, $F(1, 52) < 1$.

3.1.2 Late Positive Component (LPC) Measures—The LPC mean amplitudes for lateral/medial and midline electrode sites were larger for the semantic anomaly compared to the control condition, $F(1, 52) > 10.64$, $p = .002$, $\eta_p^2 > .169$. There were no group effects on the mean amplitude of the LPC, $F(1, 52) < 1$. The LPC peak latency measures for lateral/

medial and midline electrode sites were similar for the semantic control and anomaly conditions, $F(1, 52) < 1$, and did not distinguish the CWNS and CWS groups, $F(1, 52) < 1$.

3.2 Processing Phrase Structure Violations

The grand average ERPs elicited by the control and violation comparison words in the syntactic (phrase structure) condition are illustrated for the CWNS (Figure 4) and CWS (Figure 5) groups. As is evident in these figures, both groups of preschool-age children displayed distinctions in their ERPs elicited by the violations in phrase structure relative to the control words. Below are the results of the statistical analyses of the early negativity and the P600 component elicited in the phrase structure control and violation conditions.

3.2.1 Measures of the Early Negativity (150–350 ms)—The phrase structure violations elicited an early increased negativity relative to the control words for lateral/medial $F(1, 52) = 9.90$, $p = .003$, $\eta_p^2 = .16$ and midline electrode sites, $F(1, 52) = 21.52$, $p < .001$, $\eta_p^2 = .293$. The early negativity effect for the violation condition was larger over medial sites for the CWS group compared to the CWNS, resulting in a significant interaction between Condition, Laterality, and Group, $F(1, 52) = 11.23$, $p = .002$, $\eta_p^2 = .178$. This effect is illustrated in Figure 6. The peak latencies of the early negativity did not distinguish the control and phrase structure violation conditions over lateral/medial or midline electrode sites, $F(1, 52) < 1$ and were similar for the CWNS and CWS groups, $F(1, 52) < 1$.

3.2.2. P600 Measures—The P600 was characterized by increased positivity elicited by the phrase structure violation relative to the control condition for lateral/medial, $F(1, 52) = 6.72$, $p = .012$, $\eta_p^2 = .114$, and midline electrode sites, $F(1, 52) = 8.82$, $p = .004$, $\eta_p^2 = .145$. While the P600 amplitude was larger over the left hemisphere for both groups, it was found that the P600 amplitude elicited by the phrase structure violations relative to the control words was larger over the left hemisphere for the CWNS group (Figure 7, left panel). In contrast, as plotted in Figure 7 (right panel), the condition effect was larger over the right hemisphere for the CWS group, Condition X Hemi X Group, $F(1, 52) = 4.91$, $p = .031$, $\eta_p^2 = .086$. P600 peak latencies did not differ between the phrase structure control and violation conditions for lateral/medial or midline electrode sites, $F(1, 52) < 1.08$, $p > .303$, and there were no group differences in the peak latency of the P600, $F(1, 52) < 1$.

4. Discussion

We examined semantic and syntactic processing in preschool-age children who stutter, independent of language and speech articulation planning and implementation stages. It should be noted, however, that recent evidence from transcortical magnetic stimulation (TMS) studies suggests that cortical areas for speech articulation typically show activity, or “resonate,” to auditorily perceived speech signals (Möttönen & Watkins, 2012). Therefore, it is possible that neural activity originating from speech-motor brain areas could have been involved to some extent in the current study, despite no overt speech planning or implementation. Four- and five-year-old children listened to sentences containing semantic and phrase structure violations embedded in a cohesive narrative and accompanied by a cartoon video. Children who stutter were matched for SES, nonverbal IQ, verbal working memory, and receptive and expressive language proficiency with typically fluent peers. Although both groups displayed robust N400 effects for semantic violations, longer peak latencies for the N400 for both the control words and semantic anomalies in the CWS group indicated less efficient and slower processes for lexical access and integration compared to CWNS. For syntactic processing, specifically insertion phrase structure violations, the CWS displayed similar timing of ERP components, but exhibited notable differences in the amplitudes or distributions of the effects. The early negativity elicited by the phrase

structure violations was larger over medial electrode sites in the CWS compared to CWNS, indicating that some young CWS have less mature processing of early parsing of syntactic structure (Hahne et al., 2004; Neville et al., 2012; Pakulak & Neville, 2010; Yamada et al., 2012). Also, the distribution of the P600 was left lateralized in both groups, however, the condition effect, elicited by the phrase structure violations, differed between groups. The increase in the amplitude of the P600 was more robust over the left hemisphere in the CWNS, but the reverse pattern was observed for the CWS group, as the P600 condition effect was evident over the right hemisphere in CWS. These findings suggest possible differences in the functional neural organization for processing of phrase structure violations in CWS compared to their typically fluent peers. In summary, both semantic and syntactic processing distinguished the CWNS and CWS groups, however, the quality and degree of the differences in ERPs for the two groups were not parallel across the conditions. These findings may be consistent with behavioral measures that indicate a greater dissociation across language domains in CWS (e.g., Coulter, Anderson, & Conture, 2009). Taken together, the current findings indicate that, despite similar proficiencies in IQ, language, and verbal working memory abilities compared with CWNS, some preschool-age children who stutter demonstrate subtle alterations in their neural functions for processing semantic and phrase structure constraints occurring in natural speech within cohesive narratives. We emphasize that “some” CWS show subtle differences in hemispheric organization for language processing, because CWS are highly heterogeneous (e.g., Bloodstein & Bernstein Ratner, 2008; Yairi & Ambrose, 2005), and we do not wish to suggest that all CWS in the current sample would show the same underlying patterns for neural processing of linguistic stimuli. Also, because the number for females in our sample of participants is relatively small, we are not able to comment on prior work that continues to debate sex differences in language lateralization (e.g., Kansaku, Yamaura, & Kitazawa, 2000; Sommer, Aleman, Somers, Boks, & Kahn, 2008). However, visual inspection of individual the ERP records in the current study did not indicate subgroups within our sample based on sex. Nonetheless, our findings can be interpreted as strong evidence that early in the development of stuttering, the neural networks mediating language processing are developing sufficiently atypically that the overall group data for the CWS reflect these underlying differences.

4.1 Aspects of semantic processing may be less efficient in preschool CWS

4.1.1 N400 indices—The N400 is thought to index ease of lexical access and integration (e.g., Holcomb et al., 1992; Kutas & Federmeier, 2011; Kutas & Hillyard, 1980; Kutas & Van Petten, 1994; Neville, Mills, & Lawson, 1992). This ERP component has been shown to decrease in amplitude and have shorter peak latencies with development, a process which is thought to reflect increased ease of integration of lexical information, or less dependence on semantic context for sentence processing (e.g., Holcomb et al., 1992). In the current study, the N400 components elicited in preschool-age children who stutter displayed longer peak latencies for both canonical and violated semantic content compared to their normally fluent peers. These findings suggest that lexical access and integration requires more time for a significant proportion of CWS when the meaning of a content word is correct and when it is anomalous.

The present ERP evidence of slower initial semantic processing (as indexed by the N400) in preschool-age CWS may be consistent with behavioral performance in AWS, indicating that they retrieve semantic information more slowly than their normally fluent peers (e.g., Bosshardt & Fransen, 1996). Earlier ERP findings for semantic processing in AWS suggested reduced efficiency in processing unexpected semantic information because both semantic and syntactic processing streams may have been engaged (Weber-Fox & Hampton, 2008). The longer peak latencies of the N400 in the preschool-age CWS in the current study may also indicate reduced efficiency in processing semantic information; however, these

ERP results in CWS are qualitatively different from findings in AWS (Weber-Fox & Hampton, 2008). Although the studies in AWS and CWS both used natural speech stimuli, there were several methodological differences between the study in AWS and the current study in CWS that could have contributed to the differences in findings. The study in AWS focused on the semantics of verbs instead of nouns and also required a button press after each sentence to measure judgment accuracy. Therefore, differences in findings may be, in part, due to methodological variations; however, both studies used natural speech stimuli and elicited classic N400 components. The differences in findings between AWS and CWS are consistent with previous ERP findings for phonological processing (Weber-Fox et al., 2004; 2008) that indicate that differences in neural processing for language functions may not be constant over the course of development. We examined neural processes for language in preschool-age children who are close to the onset of stuttering (1–2 years) and who also have less developed linguistic skills compared to adults. In contrast, the AWS had stuttered for at least 15 years. Additionally, in the study of AWS, all of the participants displayed persistent developmental stuttering, whereas in the current participants, it is expected that approximately 50% or more of the participants could eventually recover from stuttering (Yairi & Ambrose, 2005). It is reasonable to assume that the children who will eventually recover may display differences in their neural functions for language processing compared to those who will develop chronic stuttering (Chang, Erickson, Ambrose, Hasegawa-Johnson, & Ludlow, 2008). Therefore, we can speculate that the current group of CWS may be more heterogeneous than the group of AWS studied previously. A longitudinal comparison of children who persist and recover is currently under way.

The present ERP findings are also consistent with behavioral studies of semantic priming in children within a similar age range. These studies reported longer overall picture-naming latencies for preschool-age CWS compared to their normally fluent peers (Hartfield & Conture, 2006; Pellovski & Conture, 2005). Pellovski and Conture (2005) reported an atypical pattern of preschool-age CWS naming pictures more slowly given a related compared to an unrelated semantic prime. As with the present study, these behavioral findings reflect differences in semantic processing even when these preschool-age children score normally on speech and language tests. However, for the priming studies, it is possible that speech motor planning or implementation difficulties may have contributed to the finding of increased picture-naming latencies for all priming conditions in CWS. The current findings of CWS demonstrating increased ERP latencies to semantic stimuli, in the absence of any speech-language production or planning requirements, provide evidence of underlying semantic processing differences in some preschool-age CWS.

4.1.2 CWNS and CWS demonstrate similar LPC indices of semantic memory

integration—The late positive component (LPC) following the N400 component showed effects of semantic manipulations for both CWNS and CWS groups and was similar for the two groups in both amplitude and peak latency measures. As reported previously, although the N400 and LPC both play a role in semantic processing, they may index somewhat different neural processes (Juottonen et al., 1996). The current findings are consistent with the idea that the N400 and LPC components may index related, but different semantic processes (Juottonen et al., 1996; Van Petten & Luka, 2012) and suggest that reduced efficiencies observed in CWS for semantic processing are earlier, somewhat more automatic computations associated with the N400. The robust LPC condition effect elicited in these preschool-age children is not consistent with the findings of Juottonen and colleagues (1996), who studied processing of semantic anomalies in Finnish school-age children and adults. Juottonen and colleagues observed an LPC condition effect in their adult participants, but only a small late positive deflection was recorded for the child subjects (aged 5–11 years) that did not distinguish the canonical and violation conditions. An important methodological difference across the two studies is that children in the current study, by

watching the accompanying video as they heard the sentences, were supplied visual information, which provided additional contextual information to the auditory stimuli. It is possible that the rich information contained in the stimuli of the current study resulted in clearer distinctions of semantic integration processes compared to the previous study by Juotinen and colleagues (1996). The current findings suggest that the later, less automatic semantic integration processes related to activation of the semantic memory, may function similarly for preschool-aged CWS and CWNS who display similar cognitive and language abilities.

4.2 Group differences in ERP indices for the syntactic condition

4.2.1 Early negativity differences may indicate less mature neural activity for CWS—Phrase structure violations elicited early negativities that were larger over medial electrode sites for the CWS compared to the CWNS. A study of ERP development in typical children indicates that with increased age, earlier negativities become more focal and left lateralized (Hahne et al., 2004). Additionally, a study of typical adults reveals similar patterns, with more focal and left lateralized early negativities in the adults with higher language proficiency (Pakulak & Neville, 2010). Therefore, the larger amplitude early negativity over more medial electrode sites in the CWS suggests that early syntactic parsing may be less mature or proficient in CWS compared to typically fluent peers. Less mature neural processes for syntactic parsing may help to account for findings from behavioral studies indicating that preschool-age CWS, compared to typically fluent peers, use less complex syntax (Howell & Au-Yeung, 1995; Wall, 1980) and demonstrate a stronger syntactic priming effect, perhaps reflecting fewer computational resources available for syntactic construction in CWS (Anderson & Cunture, 2004). It is important to note that the present electrophysiological findings indicating differences in functional neural processing in CWS, as well as the previously cited behavioral differences, were observed even in the absence of clinically detectable speech, language, or cognitive deficits. As proposed by Bernstein Ratner (1997), subtle, rather than clinically discernible, linguistic differences may be more likely to contribute to stuttering in young CWS who do not have a frank concomitant language or speech-sound disorder (Yairi & Ambrose, 2005).

It is likely however that the larger early negativity over medial sites observed in the ERPs of the CWS also reflect processes related to differences in the timing of the prosodic boundary preceding the prepositional phrase containing the target words in the control and phrase structure violation conditions, as the effects were visible near the onset of the target words. Similar near-onset effects have been observed in the ERPs of preschool children who were part of a large scale developmental study that included older children and adults and employed the same stimuli (Neville et al., 2012; Yamada et al., 2012). Interestingly, these ERP effects (i.e., near-onset differences between control and violation conditions) were not observed in the ERPs of the older children and adults for these same stimuli, suggesting that the prosody related effects visible at the onset of the target words may also be an indication of less mature neural processing of prosody (Neville et al., 2012; Yamada et al., 2012). Thus, it is not clear whether the larger amplitude early negativity observed in the preschool-age CWS group reflects processing differences for prosody or syntax, or a combination of effects. However, the current findings indicate that the neural functions mediating prosodic and/or syntactic aspects of language processing may be less mature in a significant proportion of CWS. More work is needed to disambiguate whether one or both of these language functions may be less mature in CWS.

4.2.2 Hemispheric distribution of the P600 effect may differ for CWS—The hemispheric distribution of the condition effect on the P600 mean amplitudes differed between the CWS and CWNS, with CWNS exhibiting a robust condition effect over the left

hemisphere while CWS displayed a larger effect over the right hemisphere. This finding of greater right hemisphere engagement for the CWS compared to CWNS is consistent with many previous findings suggesting that some individuals who stutter may engage right hemisphere neural functions differently than their normally fluent peers (e.g. Braun et al., 1997; Fox et al., 1996; 2000; Preibisch et al., 2003; Weber-Fox et al., 2004). It has been proposed that this atypical right hemisphere engagement, even in the absence of overt speaking requirements, reflects a compensatory mechanism for less than optimal functioning of left-hemisphere language functions (Preibisch et al., 2003). The current observations of atypical lateralization of the P600 syntactic condition effect in children close to stuttering onset suggests that at least some aspects of compensatory neural processes may be engaged early in the development of the disorder rather than resulting from years of chronic stuttering.

On the other hand, the differences in lateralization of the P600 syntactic condition effect may also be related to more immature reliance on prosodic cues in the children who stutter, as discussed above for the syntactic negativity. Results from an fMRI study of 5 and 6 year children revealed that their right hemisphere was more engaged for syntactic processing compared to adults (Brauer & Friederici, 2007). Because the right hemisphere is thought to play a greater role in prosodic processing, these findings were interpreted as supporting the view that young children rely on prosodic cues for processing syntactic structure to a greater extent (Brauer & Friederici, 2007). Thus, it is possible that a greater right hemisphere condition effect for the CWS in the current study reflected a more immature pattern, that is a greater reliance on prosodic cues, but the underlying mechanism is not clear. While the posterior corpus callosum has been found to play a crucial role in coordinating the information flow necessary for processing of syntactic and prosodic interactions (Sammler, Kotz, Eckstein, Ott, & Friederici, 2010), recent voxel-based morphometry (VBM) findings indicate that white matter volume of both the overall and posterior corpus callosum are similar for children who do and do not stutter (Choo, Chang, Zengin-Bolatkale, Ambrose, & Loucks, 2012). It is possible that similar morphology, or volume, of the corpus callosum across groups, however, does not indicate the same white matter integrity. A previous study of both VBM and fractional anisotropy (FA) comparing children with persistent stuttering, children who had recovered from stuttering, and typically fluent children revealed that while volume of the corpus callosum was comparable across groups of children, FA measures of the corpus callosum were larger in the recovered compared to persistent groups (Chang et al., 2008). Thus, the current ERP measures, which index more functional aspects of language processing, suggest that reduced FA measures of the white matter integrity of the corpus callosum, perhaps across posterior regions, in children who stutter may reveal less coherent (less mature) organization.

4.3 Conclusions and implications

Present findings indicate that a significant proportion of preschool-age children who stutter exhibit atypical neural processes for integrating semantic and syntactic violations in natural speech stimuli. The ERP results show that CWS exhibit robust condition contrast effects for semantic and syntactic processing that are similar in overall pattern to the CWNS. However, differences in the ERP measures of peak latencies, mean amplitudes, and hemispheric distribution suggest potentially important distinctions in neural activations that implicate less efficient semantic processing, less mature neural functions for prosodic/syntactic process, and atypical hemispheric involvement for processing phrase structure constraints.

Our findings are important for a better understanding of the underlying mechanisms that contribute to the behavioral reports of sub-clinical language deficits observed in CWS (e.g., Anderson & Conture, 2004; Anderson et al., 2005; Hartfield & Conture, 2006; Howell & Au-Yeung, 1995; Ntourou, Conture, & Lipsey, 2011; Pellowski & Conture, 2005; Wagovich

& Bernstein Ratner, 2007; Wall, 1980). The present findings are the first to show that differences in electrophysiological measures of language processing occur near the onset of stuttering and thus may play an important role in the development of stuttering. These findings extend recent findings from near-infrared spectroscopy (NIRS) that demonstrated differences in neural functioning in CWS for phonemic and prosodic processing (Sato, et al., 2011). While these studies suggest atypical neurophysiology mediating language processing in children who stutter, future studies are needed to determine if these differences in neural functions underlying language in CWS have a causal link to stuttering. In the context of a larger framework for understanding important factors for the development of stuttering, the current findings provide further evidence that language factors are necessary for a comprehensive model of stuttering (DeNil, 1999; Howell, 2010; Smith, 1999; Smith & Kelly, 1997; Walden et al., 2012). In conclusion, preschool children who stutter have speech motor control systems that are more variable and vulnerable to breakdowns in the face of higher speaking demands (MacPherson & Smith, in press; Smith et al., 2012); the present findings provide the first evidence that, even in the absence of any speaking demands, these children display electrophysiological differences underlying language processing that are distinctive from their typically fluent peers.

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Highlights

We examined neural indices (ERPs) of language processing in young CWNS and CWS.

Both groups were matched for age, SES, IQ, working memory, and language skills.

CWS demonstrated slower, less efficient lexical access and integration than CWNS.

Hemispheric P600 (syntactic processing) distribution differed between groups.

Preschool-age CWS display subtle differences in brain processes for language.

Figure 1. Grand Average ERPs Elicited for Semantic Control and Violation Conditions in Preschool-Age Children Who Do Not Stutter (CWNS). Robust N400 and LPC components elicited by semantic anomalies can be observed. Negative potentials are plotted upward in this and subsequent figures.

Figure 2. Grand Average ERPs Elicited for Semantic Control and Violation Conditions in Preschool-Age Children Who Stutter (CWS). Robust N400 and LPC components elicited by semantic anomalies can be observed.

Figure 3. N400 Peak Latency Group Means (and Standard Errors) for the Semantic Control and Violation Conditions. Values are plotted for the left and right hemisphere lateral and medial electrode sites.

Children Who Do Not Stutter – Syntactic Conditions

Figure 4. Grand Average ERPs Elicited for Syntactic Control and Violation Conditions in Preschool-Age Children Who Do Not Stutter (CWNS). Early Negative and P600 components elicited by phrase structure violations can be observed.

Children Who Stutter – Syntactic Conditions

Figure 5. Grand Average ERPs Elicited for Syntactic Control and Violation Conditions in Preschool-Age Children Who Stutter (CWS). Early Negative and P600 components elicited by phrase structure violations can be observed.

Figure 6. Early Negative Component Group Mean Amplitudes (and Standard Errors) for the Syntactic Control and Violation Conditions. Values are plotted for the lateral and medial electrode sites.

Figure 7. P600 Group Mean Amplitudes (and Standard Errors) for the Syntactic Control and Violation Conditions. Values are plotted for the left and right hemispheres.

Table 1

Mean and Standard Errors for Participant Characteristics and Test Scores

Group	CMMS	TACL-3	SPELT-3	BBTOP-CI	BBTOP-PPI	Aud #	Aud Word	Dollaghan NWR
CWNS	113.78 (1.69)	113.78 (2.98)	109.00 (1.95)	101.96 (1.49)	102.96 (1.56)	102.30 (3.50)	95.93 (2.41)	79.16% (2.36)
CWS	109.93 (1.63)	116.85 (2.43)	104.52 (1.51)	99.93 (1.41)	99.37 (1.77)	102.96 (2.48)	89.85 (1.90)	78.56% (2.54)

Note. CMMS = Columbia Mental Maturity Scale; TACL-3 = Test of Auditory Comprehension of Language – 3; SPELT-3 = Structure Photographic Expressive Language Test – 3; BBTOP-CI = Bankston-Bernthal Test of Phonology Consonant Inventory; BBTOP-PPI = Bankston-Bernthal Test of Phonology Phonological Process Inventory; Aud # = Test of Auditory-Perceptual Skills – Revised, Auditory Number Memory Forward; Aud Word = Test of Auditory-Perceptual Skills – Revised, Auditory Word Memory; Dollaghan NWR = Nonword Repetition Task from Dollaghan & Campbell (1998).

Table 2

Examples of the sentence stimuli for each condition

Sentence Type	Example Sentences
Semantic Control	She closes her <u>door</u> on Pingu.
	Daddy is holding another <u>present</u> for Pingu.
	They play a <u>game</u> in the snow.
	Pingu is building a <u>castle</u> on the floor.
	Pingu wants to play <u>music</u> , too.
Semantic Anomaly	She closes her <u>head</u> on Pingu.
	Daddy is holding another <u>backyard</u> for Pingu.
	They play a <u>hand</u> in the snow.
	Pingu is building a <u>music</u> on the floor.
	Pingu wants to play <u>hat</u> , too.
Phrase Structure Control	Mommy and Daddy look at <u>their</u> son.
	He makes lots of noise with <u>that</u> accordion.
	Pingu sits on top of <u>this</u> igloo.
	Pinga walks back to <u>her</u> sled with her head down.
	Pingu chews with <u>his</u> mouth open.
Phrase Structure Violation	Mommy and Daddy look at that <u>their</u> son.
	He makes lots of noise with this <u>that</u> accordion.
	Pingu sits on top of their <u>this</u> igloo.
	Pinga walks back to their <u>her</u> sled with her head down.
	Pingu chews with that <u>his</u> mouth open.

Table 3

Means and Standard Errors for Trials Accepted for Semantic and Syntactic Conditions

Group	Semantic Condition		Syntactic Condition	
	Control	Violation	Control	Violation
CWNS	34.33 (1.17)	33.33 (1.10)	34.52 (1.05)	32.67 (0.92)
CWS	34.30 (1.26)	34.81 (1.25)	34.33 (1.13)	33.81 (0.90)