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Modulation of auditory processing during speech movement planning is limited in adults who stutter

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Abstract

Stuttering is associated with atypical structural and functional connectivity in sensorimotor brain areas, in particular premotor, motor, and auditory regions. It remains unknown, however, which specific mechanisms of speech planning and execution are affected by these neurological abnormalities. To investigate pre-movement sensory modulation, we recorded 12 stuttering and 12 nonstuttering adults' auditory evoked potentials in response to probe tones presented prior to speech onset in a delayed-response speaking condition vs. no-speaking control conditions (silent reading; seeing nonlinguistic symbols). Findings indicate that, during speech movement planning, the nonstuttering group showed a statistically significant modulation of auditory processing (reduced N1 amplitude) that was not observed in the stuttering group. Thus, the obtained results provide electrophysiological evidence in support of the hypothesis that stuttering is associated with deficiencies in modulating the cortical auditory system during speech movement planning. This specific sensorimotor integration deficiency may contribute to inefficient feedback monitoring and, consequently, speech dysfluencies.

Keywords

stuttering; speech; sensorimotor integration; auditory cortex; movement planning

1. Introduction

Stuttering is a disorder of speech fluency associated with abnormal brain *activation* in a widespread network of pre-motor, motor, and sensory regions (Braun et al., 1997; Chang, Kenney, Loucks, & Ludlow, 2009; De Nil, Kroll, Kapur, & Houle, 2000; De Nil, Kroll, Lafaille, & Houle, 2003; Fox et al., 1996; Neumann et al., 2003; Watkins, Smith, Davis, & Howell, 2008). Across individual stuttering subjects, the involvement of specific brain regions appears to vary considerably (Ingham, Wang, Ingham, Bothe, & Grafton, 2013;

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Wymbs, Ingham, Ingham, Paolini, & Grafton, 2013). Nevertheless, several *structural* brain abnormalities have been reported, and these abnormalities include atypical white matter in pathways suggested to connect speech motor and auditory regions (Chang, Erickson, Ambrose, Hasegawa-Johnson, & Ludlow, 2008; Chang, Horwitz, Ostuni, Reynolds, & Ludlow, 2011; Cykowski, Fox, Ingham, Ingham, & Robin, 2010; Foundas et al., 2003; Sommer, Koch, Paulus, Weiller, & Buchel, 2002; Watkins et al., 2008). Accordingly, some of the most prominent contemporary theoretical views of stuttering suggest that the disorder may result from deficits in specific processes of sensorimotor integration that are critical for both early speech motor learning and mature speech motor control (Beal et al., 2010; Brown, Ingham, Ingham, Laird, & Fox, 2005; Cai et al., 2012; Chang et al., 2011; Daliri, Prokopenko, & Max, 2013; Hickok, Houde, & Rong, 2011; Kell et al., 2009; Liotti et al., 2010; Max, 2004; Watkins et al., 2008).

One aspect of sensorimotor integration that may be of particular theoretical importance in this regard is the central nervous system's (CNS) *prediction* of the sensory consequences (or, more generally, movement outcomes) of planned motor commands. In a recent study (Daliri, Prokopenko, Flanagan, & Max, 2014), we found that individuals who stutter accurately predict specific movement consequences in a ballistic reaching task (i.e., arm movements completed without relying on afferent feedback) in which those consequences could be fully compensated through anticipatory adjustments during movement planning. However, based on our overall theoretical framework (Max, 2004), stuttering individuals may be more likely to have difficulties with appropriately using such predictions to successfully "prime" task-relevant *sensory systems* for their subsequent role in (a) closely monitoring afferent inputs for online feedback control while (b) simultaneously preventing feedback-based motor responses that are undesirable during self-generated voluntary movements (note that the latter part of this hypothesis overlaps with ideas proposed by Zimmermann, 1980). Limited evidence consistent with this hypothesis was already provided by McClean (1996) who demonstrated that, as compared with fluent speakers, stuttering adults show less attenuation of mechanically-evoked lip muscle reflexes prior to the onset of speech (with lip muscle activity measured in speech trials vs. no speech trials). When participating sensory systems (auditory, somatosensory) are insufficiently modulated in terms of their response to self-generated afferent inputs, the triggered motor responses may interfere with, and disrupt, ongoing movements. To date, however, it remains completely unknown (a) whether stuttering individuals' atypical sensorimotor responses at speech onset are in fact due to a lack of *central modulation* of sensory neural systems, and, if so, (b) whether stuttering individuals show a lack of pre-speech sensory modulation in the *auditory cortical regions* that have been implicated in several, although not all, neuroimaging studies (see above).

Here, we addressed both these questions directly by using electroencephalographical (EEG) data and auditory evoked potential analyses to investigate, in stuttering vs. nonstuttering adults, the modulation of auditory cortical activity in response to probe tones presented prior to speaking (i.e., during speech movement planning) and in control conditions without preparation for motor activity[1]. Using an experimental paradigm that we previously developed for work with typically fluent speakers (Max et al., 2008), we recorded long

latency auditory evoked potentials (LLAEPs) in response to auditory stimuli presented during the delay phase of a delayed-response *speaking* task (seeing a word on a monitor, silently reading the word, and saying it aloud after a *go* signal), a *silent reading* task (seeing a word and silently reading it), and a *seeing* task (seeing nonlinguistic symbols). We also recorded the same LLAEPs in a standard eyes-closed rest condition to compare both groups in terms of basic auditory processing in the absence of an active task, and to verify, through comparison with these reference data, the validity of data processing and analysis procedures used in the three active tasks. Analyses focused on the amplitude and latency of the LLAEP components N1 and P2[2]. We hypothesized that if stuttering is associated with a lack of modulation of auditory cortical regions prior to speech onset, the stuttering group would fail to show the typical within-subject N1 amplitude attenuation that we have previously documented for normally fluent speakers (Max et al., 2008).

2. Methods

2.1.Participants

Twelve right-handed stuttering adults (eleven men and one woman; M_{age} = 27.32 years, age range: 18–46 years) and twelve right-handed nonstuttering adults (eleven men and one woman; M_{age} = 27.25 years, age range: 19–45 years) participated in the experiment after providing informed consent. Nonstuttering participants were individually matched with the stuttering participants based on age (± 3 years) and sex. All participants were naive to the purpose of the study.

Eligibility criteria for all participants included (a) being a native speaker of American English, (b) self-reported absence of psychological, neurological, or communication disorders (other than stuttering in the stuttering group), (c) not taking any medications with possible effects on sensorimotor functioning, and (d) pure tone behavioral hearing thresholds at or below 20 dB HL at all octave frequencies from 250 Hz to 8 kHz in both ears.

Using the Stuttering Severity Instrument, Fourth Edition (SSI–4; Riley, 2008), each stuttering participant's severity was determined by an American Speech-Language-Hearing Association-certified speech-language pathologist. Individual participant information for the stuttering group (age, sex, handedness, overall SSI–4 score, stuttering severity classification, and frequency of stuttering averaged across the SSI–4 speaking and reading tasks) are presented in Table 1.

[1]Note that, by investigating sensory systems during movement planning, this paradigm addresses neural processes that are distinct from those investigated with another recent paradigm in which stuttering and nonstuttering speakers have been compared in terms of auditory responses to their own speech during speech production (Beal et al., 2010, 2011; Liotti et al., 2010).

[2]The prominent LLAEP component that peaks ~70–130 ms after stimulus onset is typically labeled N100 or N1 in EEG recordings and M100 or N1m in magnetoencephalographic (MEG) recordings. This component is known to be generated by neuronal populations in the primary auditory cortex (Godey, Schwartz, De Graaf, Chauvel, & Liegeois-Chauvel, 2001; Näätänen & Picton, 1987; Zouridakis, Simos, & Papanicolaou, 1998). A similarly prominent component that peaks ~150–250 ms after stimulus onset is typically labeled P200 or P2 in EEG recordings and M200 or P2m in MEG recordings. The neural sources of the latter component have been shown to be located more anterior in auditory cortex (Papanicolaou, Baumann, Rogers, Saydjari, Amparo, & Eisenberg, 1990; Ross & Tremblay, 2009).

2.2.Procedure and Instrumentation

The experiment was conducted inside a sound-attenuated room. Wearing an electrode cap (details given below), participants were seated approximately 1 m from a 23-inch liquid crystal display (LCD) monitor with a refresh rate of 60 Hz. Participants' speech output was transduced and amplified (WL185, Shure Incorporated, Niles, IL; DPS II, ART ProAudio, Niagara Falls, NY) and, after amplification by a headphones amplifier (S-phone, Samson Technologies Corp., Syosset, NY), played-back to the participant in real-time through insert earphones (ER-3A, Etymotic Research Inc., Grove Village, IL). The insert earphones were also used to deliver binaural auditory stimuli (1 kHz, 50 ms duration, 10 ms rise/fall time, 75 dB SPL) during some trials. Before each recording session, this feedback system was calibrated such that speech input with an intensity of 75 dB SPL at the microphone (approximately 15 cm from the participant's mouth) resulted in 72 dB SPL output in the earphones (Cornelisse, Gagné, & Seewald, 1991). For calibration, the intensity of the auditory feedback in the earphones was measured using a 2 cc coupler (Type 4946, Bruel & Kjaer Inc., Norcross, GA) connected to a sound level meter (Type 2250A Hand Held Analyzer with Type 4947 ½" Pressure Field Microphone, Bruel & Kjaer Inc., Norcross, GA).

Continuous EEG was recorded in three conditions: *speaking*, *reading*, and *seeing*. Each condition consisted of 270 trials (3 blocks of 90 trials). In each block, binaural auditory stimuli were delivered through the insert earphones during one third of the trials (tone trials) whereas no auditory stimuli were presented in the remaining trials (no-tone trials). The order of the conditions was counterbalanced across participants in each group.

In the *speaking* condition (Fig. 1A), each trial started with the presentation of a word in white characters on a black background on the display. After 600 ms, the color of the word changed to green. This change of color constituted a *go* signal for the participant to say the word aloud. In the *reading* condition (Fig. 1B), the procedure was the same as in the speaking condition except that participants were instructed to read the word silently without any movements—thus, the motor component of the task was eliminated. In the *seeing* condition (Fig. 1C), the procedure was the same as in the *reading* condition except that nonlinguistic symbols ("++++") were shown rather than words—thus, both the cognitive-linguistic activity associated with reading and the motor activity were eliminated. For the tone trials in all three conditions, auditory stimuli were delivered 400 ms after presentation of the word/symbols in white color (Fig. 1D). Each trial ended 500 ms after the color of the word/symbols changed to green. The inter-stimulus-interval from the end of a trial to the beginning of the next trial was randomly selected from a set of five possible intervals (1500, 2000, 2500, 3000, or 3500 ms).

The words presented in the *speaking* and *reading* conditions were from two different word lists (list A and list B). Half of the participants in each group used list A for the *speaking* condition and list B for the *reading* condition; the other half of the participants used list B for the *speaking* condition and list A for the *reading* condition. Each list contained 90 different words. Only monosyllabic consonant-vowel-consonant (CVC) words were

included. All words were 3–5 letters long, and none of the words included consonant clusters.

In addition to the *speaking*, *reading*, and *seeing* conditions, we also recorded continuous EEG during an eyes-closed *rest* condition. The same binaural auditory stimuli (90 trials) were presented. Inter-stimulus intervals were randomly selected from the same intervals as listed above. These rest data mainly served to validate the morphology, amplitudes, and latencies of the other conditions' LLAEPs derived from the continuous EEG after the processing steps described below, but they also allowed a statistical comparison of the stuttering and nonstuttering groups' LLAEPs during rest.

2.3.Electroencephalographic Recordings

We used a Biosemi active-electrode EEG system, with electrodes mounted in a nylon head-cap (Biosemi Inc., Amsterdam, The Netherlands). EEG signals were recorded from 128 standard sites on the scalp (Fig. 1F) according to an extension of the international 10-10 electrode system (Gilmore, 1994; Oostenveld & Praamstra, 2001). Two electrodes were placed over the left and right mastoids for off-line re-referencing.

To record electrooculograms (EOGs), additional electrodes were placed below the lower eyelid and next to the outer canthus of the left eye. The EOG signals were used to detect and reject artifacts related to blinking and eye movements. Orofacial electromyograms (EMGs) were recorded by using four electrodes placed on the skin overlying muscles on the right side of the face (masseter: jaw elevation; anterior belly of the digastric: jaw depression; orbicularis oris: upper and lower lip elevation/rounding). The EMG signals were used to verify an absence of active muscle contraction prior to the *go* signal, and to estimate the onset time of speech movements in the speaking condition. The latter data showed that the average onset time for the stuttering group was not statistically significantly different from the average onset time for the nonstuttering group, $t(22) = 1.236$, $p = .229$.

The acoustic signal from an additional microphone (SM58, Shure, Niles, IL) was recorded together with the EEG data. All signals (EEG, EMG, EOG, and speech acoustics) were recorded with a sampling rate of 1024 Hz.

2.4.Data analysis

Data analyses were conducted using the EEGLAB toolbox (Delorme & Makeig, 2004) and custom-written MATLAB scripts (The MathWorks, Inc., Natick, MA). The EEG signals were first re-referenced to an off-line reconstructed average mastoids reference. The signals were then filtered off-line using a low-pass filter with cut-off frequency of 50 Hz. Next, the continuous signals were segmented into epochs ranging from 100 ms before to 400 ms after the onset of the auditory stimulus (and the equivalent time window in the no-tone trials). For each epoch, the mean amplitude of the pre-stimulus period (100 ms) was subtracted from the whole epoch to remove baseline differences. Epochs with EEG amplitudes greater than ±70 μV were excluded. Trials were visually inspected to exclude epochs contaminated by artifacts associated with (a) speech movements that started before the *go* signal—based on EMG activity, and (b) blinking or eye movements—based on the EOG signal.

After these processing steps, the averaged response for the tone trials reflected auditory as well as non-auditory activity (e.g., activity related to motor, linguistic, cognitive, and visual processes), whereas the averaged response for the no-tone trials reflected solely the non-auditory activity. Hence, to isolate the auditory activity evoked by the probe tones, each participant's averaged response for the no-tone trials from each condition was subtracted from the averaged response for the tone trials of the same condition (Fig. 1E). This subtracted signal was then used for all LLAEP analyses as it provides the best estimate of the true auditory response (Baess, Jacobsen, & Schroger, 2008; Baess, Horvath, Jacobsen, & Schroeger, 2011; Martikainen, Kaneko, & Hari, 2005; Max et al., 2008). In the rest condition, the LLAEPs were obtained directly by averaging epochs time-locked to the auditory stimuli. The final LLAEPs for each channel were low-pass filtered with a cut-off frequency of 15 Hz.

In the last step, overall LLAEPs for each of three regions of interests (ROIs) were obtained by averaging the LLAEPs from 6 electrodes over the left hemisphere (Left ROI: electrodes D11, D12, D19, D20, D27, D28), 6 electrodes over the central region (Central ROI: electrodes A1, A2, B1, C1, D1, D15), and 6 electrodes over the right hemisphere (Right ROI: electrodes B17, B18, B21, B22, B30, B31). The three ROIs and the included individual channels are illustrated in Fig. 1F. As dependent variables, the latency and amplitude of the N1 and P2 components were extracted for each participant's ROI LLAEPs. N1 was defined as the largest negative peak between 70 and 130 ms following the onset of the auditory stimulus. P2 was defined as the largest positive peak between 150 and 250 ms following the onset of the auditory stimulus. Surface distribution maps of the brain's auditory responses were also created, using the data from all 128 electrodes.

2.5.Statistical analyses

Statistical analyses were performed using the IBM SPSS Statistics 19 software package (IBM, Armonk, NY). Given that EEG data show large inter-subject variation that results not only from neurophysiological differences but also from skin, skull, and brain anatomical differences (Nunez & Srinivasan, 2006), our hypotheses and analyses focused on within-subjects effects and group-by-condition interactions (Coulson, 2007; Luck, 2014). Thus, N1 and P2 amplitude and latency data were subjected to analysis of variance (ANOVA) for repeated measures with Condition (speaking, reading, seeing) and ROI (left, central, right) as within-subjects variables and Group (stuttering, nonstuttering) as a between-subjects variable. Due to the differences in recording procedure between these conditions and the rest condition (i.e., absence of visual stimuli), N1 and P2 amplitude and latency for the rest condition were analyzed separately. For the rest condition, we used repeated measures ANOVA with ROI as the within-subjects variable and Group as a between-subjects variable. For all within-subjects tests, degrees of freedom were adjusted using the Huynh-Feldt correction to account for potential violations of the sphericity assumption (Max & Onghena, 1999). Statistically significant interactions involving the Group variable were followed up with post-hoc analyses conducted by means of *t*-tests with Bonferroni corrections for multiple comparisons. Lastly, for the stuttering group, we used Pearson correlation coefficients to explore whether there was a relationship between participants' stuttering frequency (defined as the average percent stuttered syllables across the speaking and reading

tasks of the SSI–4, see Table 1) and any of the dependent variables or the amount of N1 amplitude change in the speaking condition vs. the reading condition.

3. Results

Grand average LLAEPs for the different ROIs (Left ROI, Central ROI, Right ROI), conditions (*speaking*, *reading*, *seeing*), and groups (nonstuttering, stuttering) are shown in Fig. 2. Summarized group data (means and standard errors of the mean) for N1 and P2 amplitude and the distribution of individual subjects (boxplots with individual subject markers added) for the amount of within-subject N1 and P2 modulation in the *speaking* condition as compared with the *reading* condition are represented in Fig. 3.

3.1.N1 amplitude

N1 amplitude data showed statistically significant main effects of ROI, $F(2, 44) = 38.081$, $p < .001$, and Condition, $F(1.983, 41.647) = 7.210$, $p = .002$, but not Group ($p = .452$). The ROI effect was associated with descriptively larger N1 amplitudes in the Central ROI ($M = 10.097$ μV, $SD = 3.442$) than in the Left ROI ($M = 8.125$ μV, $SD = 2.542$) and the Right ROI ($M = 7.753$ μV, $SD = 2.467$). The Condition effect was associated with overall smaller N1 amplitudes in the speaking condition ($M = 7.729$ μV, $SD = 2.687$) as compared with the reading condition ($M = 9.117$ μV, $SD = 3.209$) and the seeing condition ($M = 9.128$ μV, $SD = 3.126$). However, these main effects were modified by statistically significant interactions of Condition × ROI, $F(3.585, 78.873) = 3.955$, $p = .007$, and Condition × Group, $F(1.893, 41.647) = 3.738$, $p = .034$, in the absence of an ROI × Group interaction ($p = .884$) or an ROI × Condition × Group interaction ($p = .120$). The Condition × ROI interaction occurred because, averaged across groups, N1 amplitude differences between the speaking condition and the reading and seeing conditions were more extensive for the Left ROI and the Central ROI than for the Right ROI.

Most important for the hypothesis under investigation is the Condition × Group interaction. As can be seen in Fig. 3A, the N1 amplitude of the nonstuttering group was smaller in the *speaking* condition ($M = 7.538$ μV, $SD = 1.962$) than in both the *reading* condition ($M = 10.072$ μV, $SD = 2.533$), $t(11) = -7.802$, $p < .001$, and the *seeing* condition ($M = 9.659$ μV, $SD = 2.745$), $t = (11) = -3.695$, $p = .003$. For the stuttering group, on the other hand, the N1 amplitude in the *speaking* condition ($M = 7.921$ μV, $SD = 3.342$) was not statistically significantly different from the N1 amplitude in either the *reading* condition ($M = 8.163$ μV, $SD = 3.624$, $p = .680$) or the *seeing* condition ($M = 8.598$ μV, $SD = 3.505$, $p = .414$). Unlike these within-group comparisons across conditions, between-group comparisons of N1 amplitude did not reveal statistically significant differences for any of the three conditions ($p > .150$).

When expressing each individual subject's extent of auditory modulation prior to *speaking* as a reduction in N1 amplitude relative to the *reading* condition, there was a complete separation of the interquartile-ranges of the stuttering and nonstuttering subject samples (Fig. 3C). In fact, as can be seen in the same figure, whereas all 12 nonstuttering speakers showed a reduction of the N1amplitude prior to speaking, 4 of the 12 stuttering speakers even showed an *increase* of the N1 amplitude prior to speaking. Topographic maps of both

groups' N1 response in the three primary conditions, and particularly the comparison *reading* minus *speaking*, also clearly illustrate this difference between stuttering and nonstuttering speakers in N1 amplitude modulation prior to speech onset (Fig. 4).

3.2.N1 latency

N1 latency data showed a statistically significant main effect of ROI, $F(2, 44) = 3.495$, $p = .039$, with overall longer latencies for the Left ROI ($M = 100.377$ ms, $SD = 8.308$) than for the Central ROI ($M = 98.450$ ms, $SD = 6.565$) and the Right ROI ($M = 99.047$ ms, $SD = 8.118$). The main effects of Condition and Group were not statistically significant ($p = .745$ and $p = .747$, respectively). There was a statistically significant ROI × Group interaction, $F(2, 44) = 3.722$, $p = .032$. For the nonstuttering group, the latency in the Left ROI ($M = 99.902$ ms, $SD = 7.992$) was longer than that in the Right ROI ($M = 97.514$ ms, $SD = 7.692$), $t(11) = 3.239$, $p = .007$. For the stuttering group, the latency in the Left ROI ($M = 100.852$ ms, $SD = 8.941$) was not statistically different ($p = .804$) from that in the Right ROI ($M = 100.580$ ms, $SD = 8.572$). In other words, N1 latencies of the stuttering group were more symmetric across the left and right hemispheres than those of the nonstuttering group. Of particular importance in the context of auditory modulation prior to speaking, however, there was no statistically significant Condition × Group interaction ($p = .203$). The Condition × ROI ($p = .151$) and Condition × Group × ROI ($p = .630$) interactions were also not statistically significant for the N1 latency.

3.3.P2 amplitude

Similar to the N1 amplitude data, P2 amplitude also showed statistically significant main effects of Condition, $F(1.756, 38.634) = 6.851$, $p = .004$, and ROI, $F(1.877, 41.295) = 29.755$, $p < .001$, but not Group ($p = .558$). Both effects followed the same trend as those described for N1: across conditions, P2 amplitudes were smaller in the speaking condition ($M = 4.353$ μV, $SD = 2.944$) than in both the reading condition ($M = 6.423$ μV, $SD = 3.750$) and the seeing condition ($M = 5.863$ μV, $SD = 4.269$); across ROIs, P2 amplitudes were larger in the Central ROI ($M = 6.720$ μV, $SD = 4.047$) than in the Left ROI ($M = 4.881$ μV, $SD = 2.958$) and the Right ROI ($M = 5.037$ μV, $SD = 3.042$). These main effects were modified by a statistically significant Condition × ROI interaction, $F(4,88) = 3.086$, $p = .020$: here, averaged across groups, P2 amplitude differences between the speaking condition and the reading and seeing conditions were more extensive for the Central ROI than for the Left ROI and the Right ROI. Also consistent with the N1 data, the ROI × Group and Condition × ROI × Group interactions for P2 amplitude data were not statistically significant ($p = .610$ and $p = .278$, respectively). In this case of P2 amplitudes, however, there was no statistically significant Condition × Group interaction ($p = .234$, data included in Fig. 3B and 3D).

3.4.P2 latency

Measurements of P2 latency showed a statistically significant main effect of Condition, $F(1.636, 35.993) = 5.735$, $p = .010$, with shorter latencies in the speaking condition ($M = 181.214$ ms, $SD = 21.088$) than in the reading condition ($M = 188.799$ ms, $SD = 27.940$) and the seeing condition ($M = 201.867$ ms, $SD = 36.658$). In addition, there also was a

statistically significant main effect of ROI, $F(1.258, 27.671) = 6.128$, $p = .014$, with shorter latencies in the Central ROI ($M = 186.167$ ms, $SD = 23.719$) than in the Left ROI ($M = 194.811$ ms, $SD = 27.816$) and Right ROI ($M = 190.903$ ms, $SD = 22.593$). None of the interactions Condition × Group, ROI × Group, Condition × ROI, or Condition × ROI × Group interactions were statistically significant ($p > .089$ in all cases).

3.5.Rest condition

Fig. 5 illustrates the stuttering and nonstuttering groups' LLAEPs from the eyes-closed *rest* condition as recorded in all three ROIs. The main effect of ROI was statistically significant for both N1 amplitude, $F(2, 44) = 32.083$, $p < .001$, and P2 amplitude, $F(1.866, 41.052) = 26.654$, $p < .001$. In both cases, amplitudes were larger for the Central ROI than for the Left and Right ROIs. There were, however, no statistically significant effects on N1 or P2 amplitude for Group ($p > .390$) or ROI × Group ($p > .317$). For N1and P2 latencies, none of the main effects or interactions were statistically significant ($p > .078$ in all cases).

3.6.Correlational analyses

Pearson correlation coefficients revealed that there were no statistically significant relationships ($p > .159$ in all cases) between stuttering frequency and any of the dependent variables or between stuttering frequency and the amount of change in N1 amplitude in the *speaking* condition vs. the *reading* condition.

4. Discussion

Several research groups have previously suggested that stuttering may be associated with deficits in fundamental processes of sensorimotor integration underlying speech motor learning and speech motor control (Beal et al., 2010; Brown et al., 2005; Cai et al., 2012; Chang et al., 2011; Daliri et al., 2013; Hickok et al., 2011; Kell et al., 2009; Liotti et al., 2010; Max, 2004; Watkins et al., 2008). However, an answer to the question of which specific sensorimotor mechanisms are affected in this disorder of speech fluency has remained elusive.

Recent empirical and theoretical work on the neural control of movement has demonstrated that one important aspect of sensorimotor integration involves the prediction of a movement's sensory consequences (e.g., auditory feedback would be predicted during speech movement planning). Incorporating this information into our own theoretical framework for stuttering (Max, 2004), we have proposed that stuttering may be associated with difficulties in using such predictions to appropriately prime task-relevant sensory systems in advance of their subsequent role in online feedback monitoring and control. Here, we tested one type of sensory prediction directly by using probe tones and EEG recordings (focusing on the N1 and P2 components of the auditory evoked potential) to investigate adjustments in auditory processing during speech movement planning in stuttering vs. nonstuttering adults. In particular, we compared, for these two groups of speakers, the modulation of auditory evoked potentials in response to probe tones presented prior to speaking (i.e., during speech movement planning) and in control conditions without preparation for motor activity (i.e., silent reading and seeing nonlinguistic symbols). We

hypothesized that, if stuttering is associated with deficient modulation of auditory cortical regions prior to speech onset, the stuttering group would fail to show the typical pre-speech N1 amplitude attenuation that we have previously documented for normally fluent speakers (Max et al., 2008).

The primary finding of this study is fully in agreement with the proposed hypothesis: the nonstuttering group showed the expected reduction in auditory N1 amplitude during speech movement planning relative to their own auditory N1 amplitude in the control conditions, but the age-, handedness-, and sex-matched stuttering group failed to show this modulation of N1 amplitude prior to speech initiation as compared with the control conditions. At the individual subject level, the majority of stuttering subjects showed an amount of auditory modulation that was smaller than that observed for any of the nonstuttering subjects, and there was no overlap between the inter-quartile ranges of both groups for this measure of modulation. Topographic maps based on data reflecting the difference in auditory response between the *reading* and *speaking* conditions also clearly confirmed the substantial between-group difference in auditory modulation prior to speech onset.

A second finding directly related to the phenomenon of auditory modulation indicates that both groups showed smaller P2 amplitudes during speech movement planning as compared with the no-speaking control conditions. Descriptively (based on group mean amplitudes), this P2 amplitude reduction prior to speech onset even appeared to be greater in the stuttering group than in the nonstuttering group. However, the condition by group interaction did not reach or approach statistical significance, and the corresponding box plots in Fig. 3 (panel D) make it clear that the range of P2 amplitude reductions across individual subjects was highly similar for the stuttering and nonstuttering groups. It should be noted also that the interpretation of descriptive data regarding such later components of the auditory evoked potential (P2 and later) is further complicated by two additional observations. First, a comparison of the box plots for the control subjects' amplitude modulation data reveals that the across-subjects range for P2 modulation (Fig. 3D) is more than twice as large as that for N1 modulation (Fig. 3C). Hence, the individual subject data for P2 are associated with substantially more variability. Second, the group grand average auditory evoked potentials (Fig. 2) show that the stuttering subjects' *speaking* condition, as compared with their non-speech control conditions, is not associated with a specific reduction in the P2 component but with a generally less positive/more negative potential from approximately 150 ms after stimulus onset until the end of the extracted epochs (400 ms after stimulus onset). Based on the data available to date, however, this generally downward-shifted potential appears due to random inter-subject variability, rather than systematic between-group differences, given that (a) our initial study on pre-speech auditory modulation found a similar effect in nonstuttering speakers (Max et al., 2008), and (b) a separate new study with *speaking*, *reading*, and *listening* conditions found this effect in neither stuttering nor nonstuttering subjects (Daliri & Max, 2014).

As a third finding—informative about stuttering individuals' auditory processing in general but not directly related to pre-speech sensory modulation—our analyses revealed that the nonstuttering group showed a small but statistically significant N1 latency difference between the Left and Right ROIs (2.4 ms longer on the left) across the *speaking*, *reading*,

and *seeing* conditions, whereas such a lateralization difference was absent in the stuttering group. In the eyes-closed *rest* condition, the two groups did not differ in any measures of N1 or P2 amplitude or latency.

Together with these novel findings, two potential caveats are worth noting. First, it could be argued that the descriptive data in Fig. 3A are compatible with the alternative interpretation that, whereas the control group showed a reduced N1 amplitude in the *speaking* condition vs. the *reading* and *seeing* conditions, the stuttering group showed a reduced N1 amplitude in all three conditions (as opposed to a lack of modulation in the *speaking* condition relative to the other two conditions). However, this interpretation is problematic for several reasons. Besides the fact that the modulation of an auditory response can only be defined relative to an unmodulated reference response (which is not available when taking the alternative position), the alternative interpretation would require that the stuttering and nonstuttering groups show a similar auditory response in the *speaking* task (inhibited in both groups) but a different auditory response in the *reading* and *seeing* tasks (not inhibited in the nonstuttering group, inhibited in the stuttering group). Although Fig. 3A is descriptively consistent with such a pattern of results, the inferential statistical results from post-hoc between-groups comparisons provided no support for this interpretation. Moreover, between-subjects comparisons of EEG data reflect not only real neurophysiological differences between the subject groups, but also normal anatomical inter-subject variation in the effects of skin and bone on the extracranially recorded electrical fields (Nunez & Srinivasan, 2006). For example, if one focuses only on descriptive data, it can be seen in Fig. 5A and Fig. 5C that our stuttering group showed smaller N1 amplitudes even in the separate, eyes-closed *rest* condition. For this reason, within-subjects comparisons and group-by-condition interactions provide less ambiguous data and are therefore generally recommended for evoked potential studies (Coulson, 2007; Luck, 2014).

As a second potential caveat, it should be acknowledged that we found no statistically significant linear correlations between stuttering subjects' extent of auditory modulation and clinical measurements of their stuttering frequency. Although discovering such correlations would certainly be informative, the potential relationship between electrophysiological auditory measures obtained during an experimental task and stuttering frequency measures obtained from conversational and oral reading speech samples is likely not straight forward. For a discussion of at least some of the complexities involved in attempts to link such disparate measures, we refer to our perspective described in Daliri et al. (2014).

Implications and conclusions

In summary, the overall conclusion that can be drawn from the present study is that stuttering speakers failed to show the typical pre-speech attenuation of auditory N1 responses to probe tones as documented for nonstuttering speakers both here and in Max et al. (2008). This conclusion based on data in the auditory domain is compatible with McClean's (1996) previous finding, in the somatosensory domain, that stuttering speakers show limited attenuation of lip muscle reflexes evoked prior to the onset of speech. Individual subject data from our own study show that the pre-speech auditory modulation of 10 out of 12 stuttering subjects (83%) was more limited than that observed at the 75th

percentile of the nonstuttering group. In McClean's (1996) study, 10 out of 14 stuttering subjects (71%) failed to show significant modulation of the lip reflex prior to speech initiation. Hence, combined, these studies strongly suggest that stuttering is associated with deficiencies in predictively modulating relevant sensory systems for their crucial contributions to speech sensorimotor control. In the context of contemporary theoretical perspectives on the neural control of voluntary movements, those contributions of the auditory and somatosensory systems are likely to involve not only the online monitoring of actual feedback but also the fine-tuning of planned motor commands based on the movements' *predicted* sensory consequences (see Max, 2004). Disruptions in either of these two important functions (correcting movement planning and implementing error monitoring) may directly lead to the repetitive articulatory movements or sustained vocal tract postures that are identified as the primary characteristic of stuttering (Max, 2004).

This suggestion does raise the question why our stuttering subjects were able to produce the target utterances for the present experiment without perceptually noticeable dysfluencies despite the demonstration of atypical pre-speech auditory modulation in this situation. Although any answer to this question is merely speculative at this time, the apparent discrepancy may be related specifically to the fact that all target utterances consisted of monosyllabic CVC words that contained no consonant clusters and that were produced in isolation. It is well documented that both shorter words and words produced in isolation are less likely to result in stuttering than longer words and connected speech (Brown, 1938; Brown & Moren, 1942; Wingate, 1967; Wingate, 2002). Such short and isolated words may be only minimally taxing in terms of the CNS' reliance on auditory feedback. That is, if the production of such words depends almost entirely on feedforward, rather than feedback, control mechanisms (see Kim & Max, 2014), then the production of this type of utterances may not be directly impacted by limitations in modulating the auditory system prior to speech onset. We acknowledge, however, that the functional relevance of this pre-speech auditory modulation phenomenon itself remains to be determined in future studies. Specifically, a primary question that remains to be addressed is whether the phenomenon reflects increases vs. decreases in the weighting of feedback control mechanisms during speech production. If the decreased N1 amplitude actually corresponds to an overall attenuated auditory responsiveness (as opposed to a "fine-tuning" or "priming" of this sensory system for *enhanced* auditory monitoring), then it cannot be excluded that the stuttering speakers' lack of modulation may reflect a compensatory mechanism that seeks to benefit from the availability of sensory feedback for online movement corrections (Max, 2004).

Similarly, explanations of the specific neural mechanisms leading to the observed absence of pre-speech auditory modulation in individuals who stutter will require further experimental and theoretical work, but at least two hypotheses can be formulated to guide this line of inquiry. First, given that (a) modulation of the earlier N1 component but not the later P2 component of the auditory evoked potential differentiated between stuttering and nonstuttering subjects and (b) atypical modulation in stuttering subjects has also been observed outside of the auditory domain (McClean, 1996), stuttering may be associated with a delay in sending the modulation signals themselves. That is, slower motor preparation in

stuttering individuals may cause the modulating neural signals to reach sensory cortex at a later point in time, closer to speech onset. In our study, each auditory stimulus was delivered 400 ms after initial presentation of the target word. Thus, on average, the evoked N1 and P2 components occurred approximately 500 ms and 600 ms, respectively, into the movement planning phase. The first explanatory hypothesis suggests that stuttering speakers' auditory modulation signals (associated with motor preparation) may have reached auditory cortex more than 500 ms after initial presentation of the target word. In contrast, a second hypothesis is that the deficient auditory modulation in stuttering subjects stems not from a functionally delayed motor system but from structural white matter abnormalities between speech (pre-) motor regions and the neural generators of the N1 component. We propose that these alternative (but certainly not exhaustive) hypotheses can be tested directly by varying the time of delivery of the auditory stimuli (e.g., 400, 500, 600 ms after presentation of the word), and examining whether stuttering subjects do show N1 modulation when the auditory stimuli are presented later into the movement planning phase. The first hypothesis predicts that stuttering speakers may show typical N1 modulation at time points closer to movement onset whereas the second hypothesis predicts that N1 modulation will remain limited in stuttering speakers regardless of the time of stimulus delivery.

It is worth noting here that the first of these hypotheses may be more consistent with the results of Beal et al. (2010, 2011) and Liotti et al. (2010) who found no differences between stuttering and nonstuttering speakers in the modulation of auditory cortex activity in response to one's *own auditory feedback after speech onset* as compared with played-back, pre-recorded speech (a paradigm developed by Houde, Nagarajan, Sekihara, & Merzenich, 2002). Given that the experimental procedures differ substantially, however, we speculate that the latter paradigm is likely to address neural processes that are distinct from those addressed by our own paradigm. In the future, more comprehensive studies should be designed to explore the relationship and potential overlap, if any, between the sensorimotor interactions responsible for each of these two forms of auditory modulation.

In conclusion, this study investigated pre-speech auditory modulation in stuttering and nonstuttering adults. Auditory modulation was examined by comparing N1 and P2 amplitude and latency measures in long-latency auditory evoked potentials elicited with pure tones during the delay phase of a delayed-response speaking condition as compared with no-speaking control conditions. During this speech movement planning phase, only the nonstuttering subjects showed a statistically significant reduction in the amplitude of the N1 component. For the stuttering subjects, N1 amplitude did not different between the speech and control conditions. Consequently, these electrophysiological data suggest that stuttering is associated with deficiencies in modulating the cortical auditory system, and potentially relevant sensory systems in general, prior to speech initiation.

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Highlights

1. We examined modulation of the auditory system during speech movement planning.
2. Nonstuttering adults showed pre-speech attenuation of the N1 response to pure tones.
3. Stuttering adults did not modulate N1 amplitude, indicating sensorimotor deficiencies.

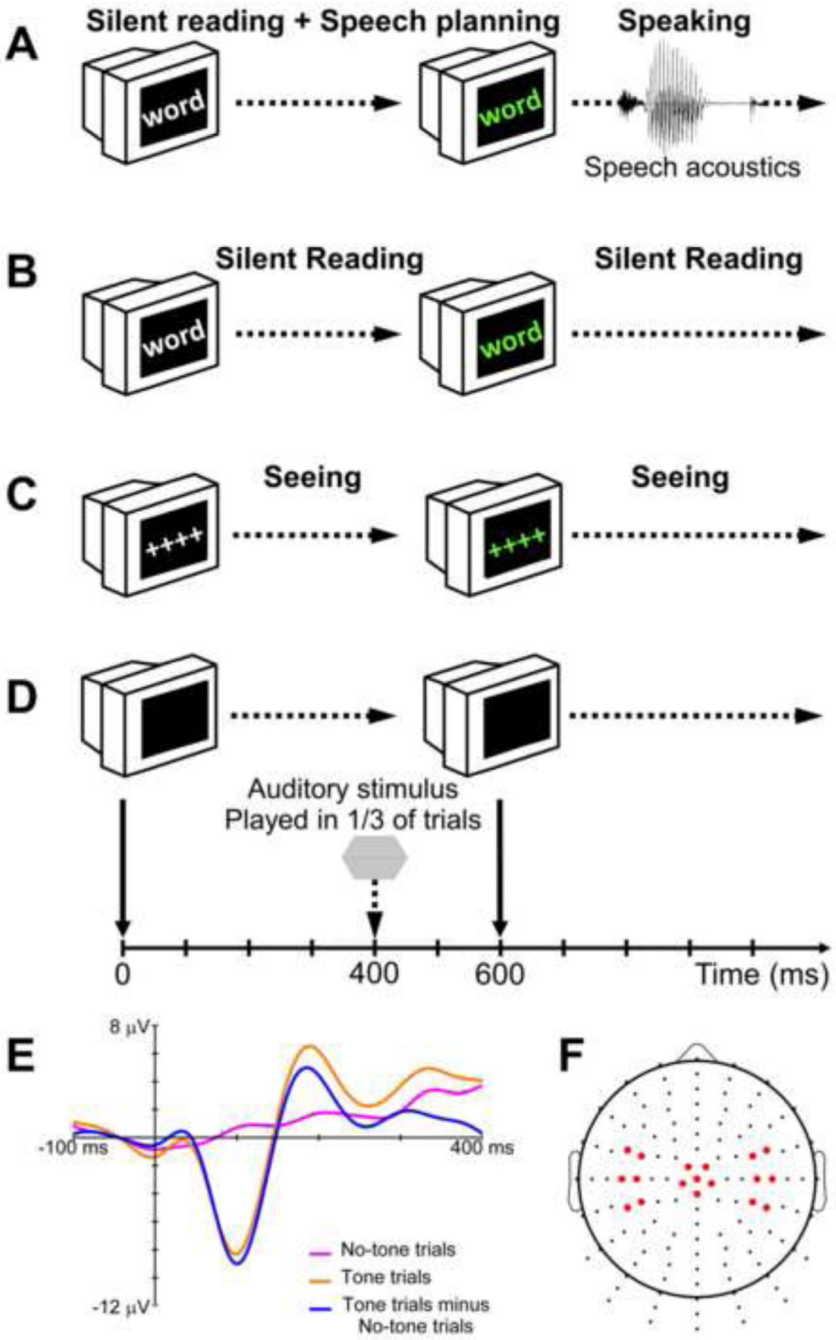

Fig. 1.

Experimental procedures for *speaking* (A), *reading* (B), and *seeing* (C) conditions. In 1/3 of the trials (tone trials) for each condition, an auditory stimulus (1 kHz, 50 ms duration, 75 dB SPL) was presented (D). In the remaining trials (no-tone trials), no auditory stimulus was presented. To best estimate the auditory cortex response to the stimulus, each subject's averaged signal for no-tone trials was subtracted from that for tone trials (E). Subtracted signals were obtained for each of three ROIs, with each ROI's signal representing the average of 6 electrodes.

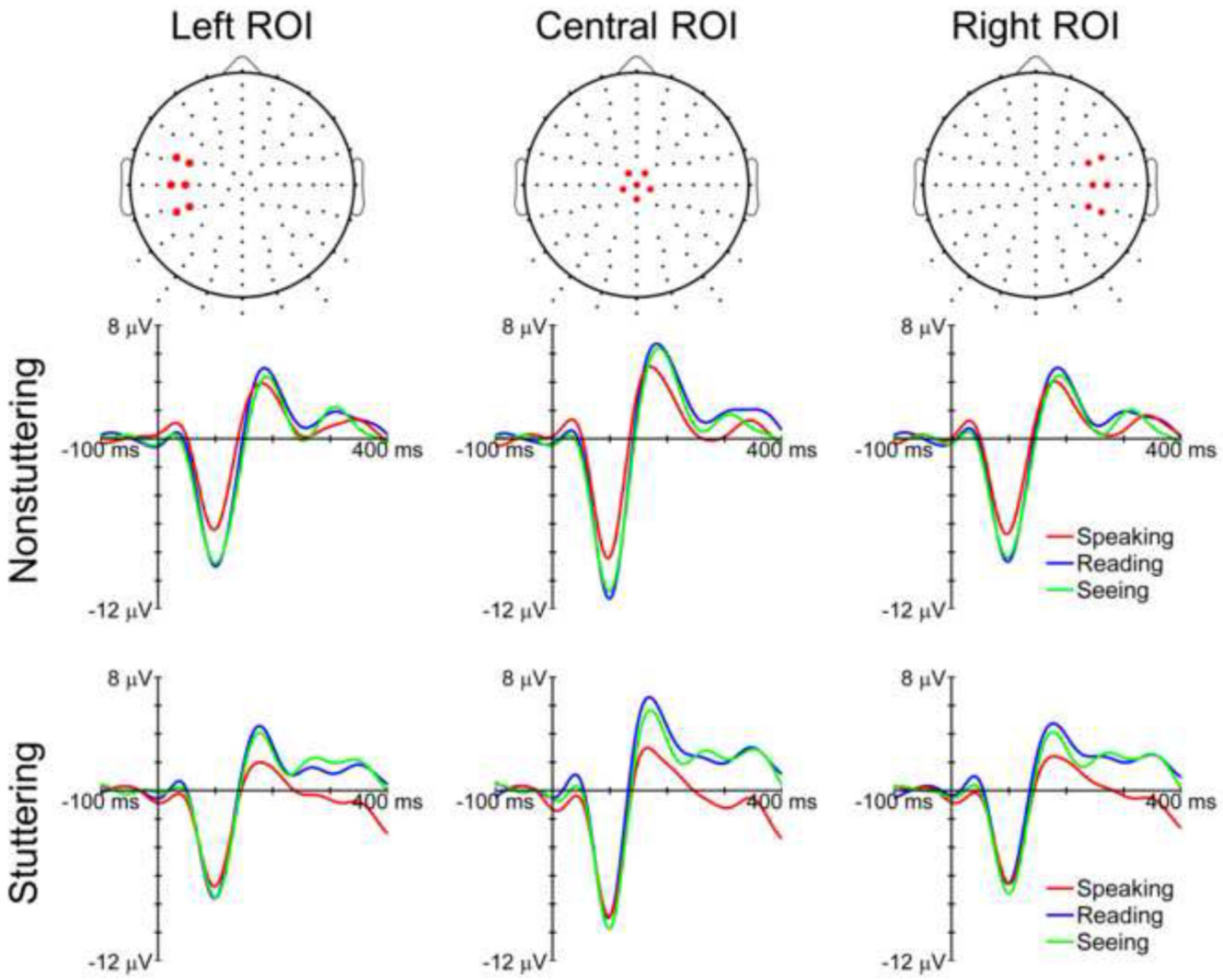

Fig. 2.

Grand average LLAEPs from the Left ROI (left column), Central ROI (middle column), and Right ROI (right column) for individuals who stutter (bottom row) and individuals who do not stutter (middle row) during speech movement planning (red), silent reading (blue), and seeing nonlinguistic symbols (green). Individual electrode channels contributing to each ROI are colored red in the scalp representations (top row). Only the nonstuttering group showed a distinct attenuation of N1 amplitude prior to speaking as compared with both silent reading and seeing.

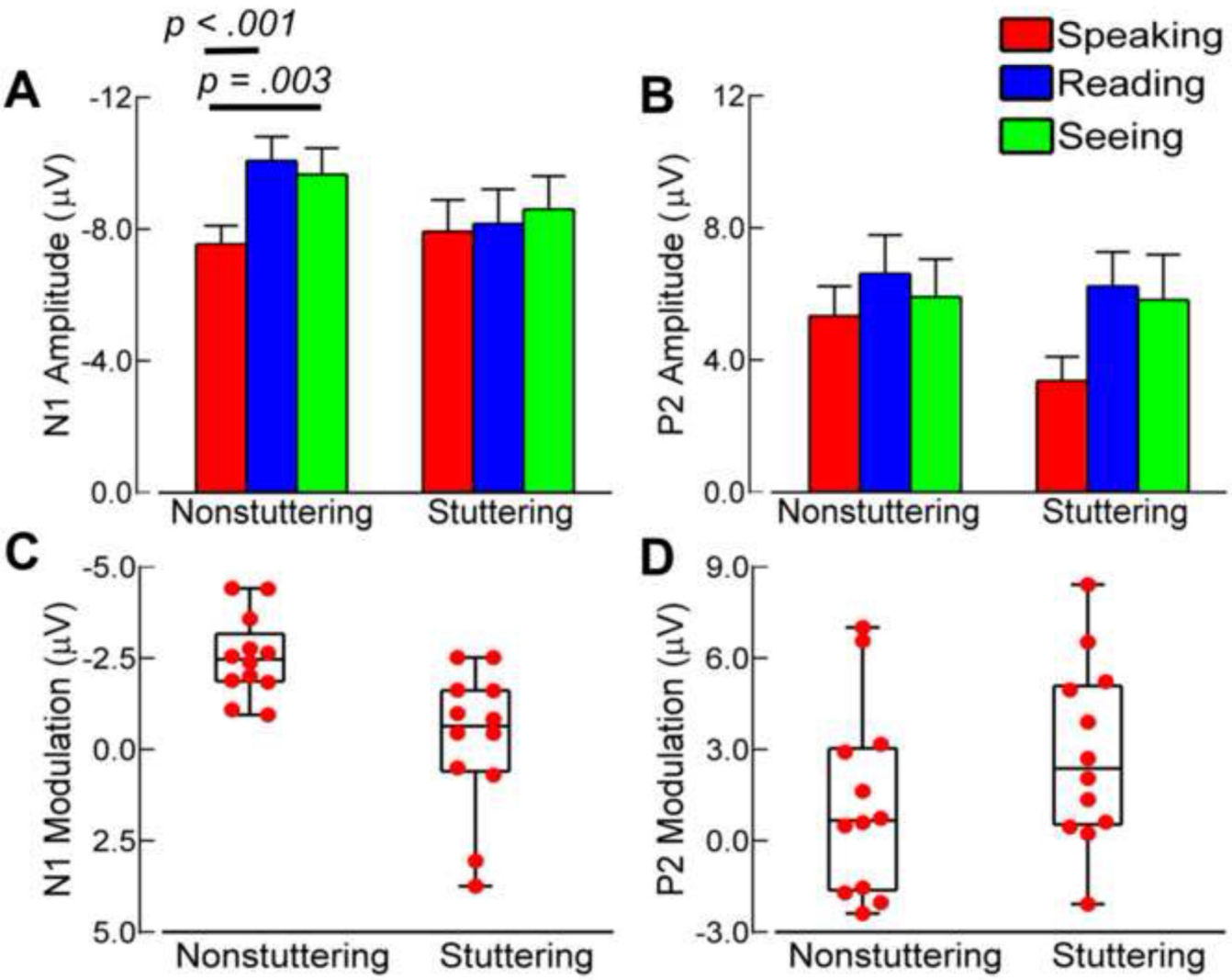

Fig. 3.

Stuttering and nonstuttering group means and standard errors (error bars) of the mean for N1 amplitude (A) and P2 amplitude (B) during speech movement planning, silent reading, and seeing nonlinguistic symbols. Subject distributions in terms of the amount of response modulation (amplitude decrease in the speaking condition vs. the reading condition) are shown as box plots with overlaid individual subject data (red markers) for the N1 (C) and P2 (D) components of the auditory evoked potential. There was a statistically significant Group × Condition interaction for N1 amplitude: the nonstuttering group showed a reduction in N1 amplitude prior to speaking, whereas the stuttering group's N1 amplitude remained unchanged across conditions. The Group × Condition interaction for P2 was not statistically significant. Data in all panels have been averaged across Left, Central, and Right ROIs.

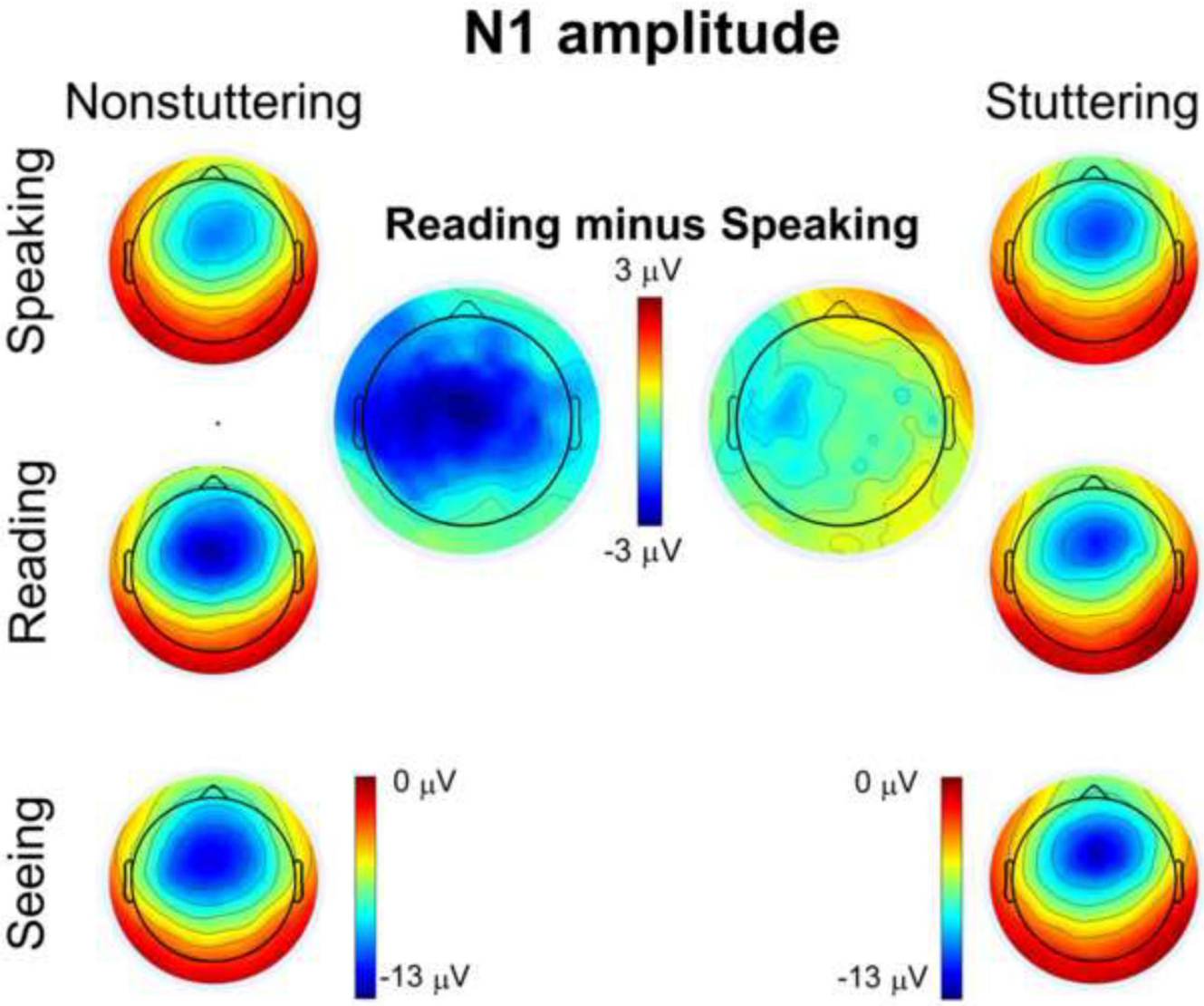

Fig. 4.

Nonstuttering (left column) and stuttering (right column) subjects' topographic maps for N1 amplitude (maps created at the latency of each individual subject's N1 peak amplitude) in the *speaking*, *reading*, and *seeing* conditions. Additional topographic maps shown in the center were created by subtracting the N1 response in the speaking condition from that in the reading condition. The subtraction graphs clearly show a strong pre-speech modulation of the auditory response in the nonstuttering group but not in the stuttering group.

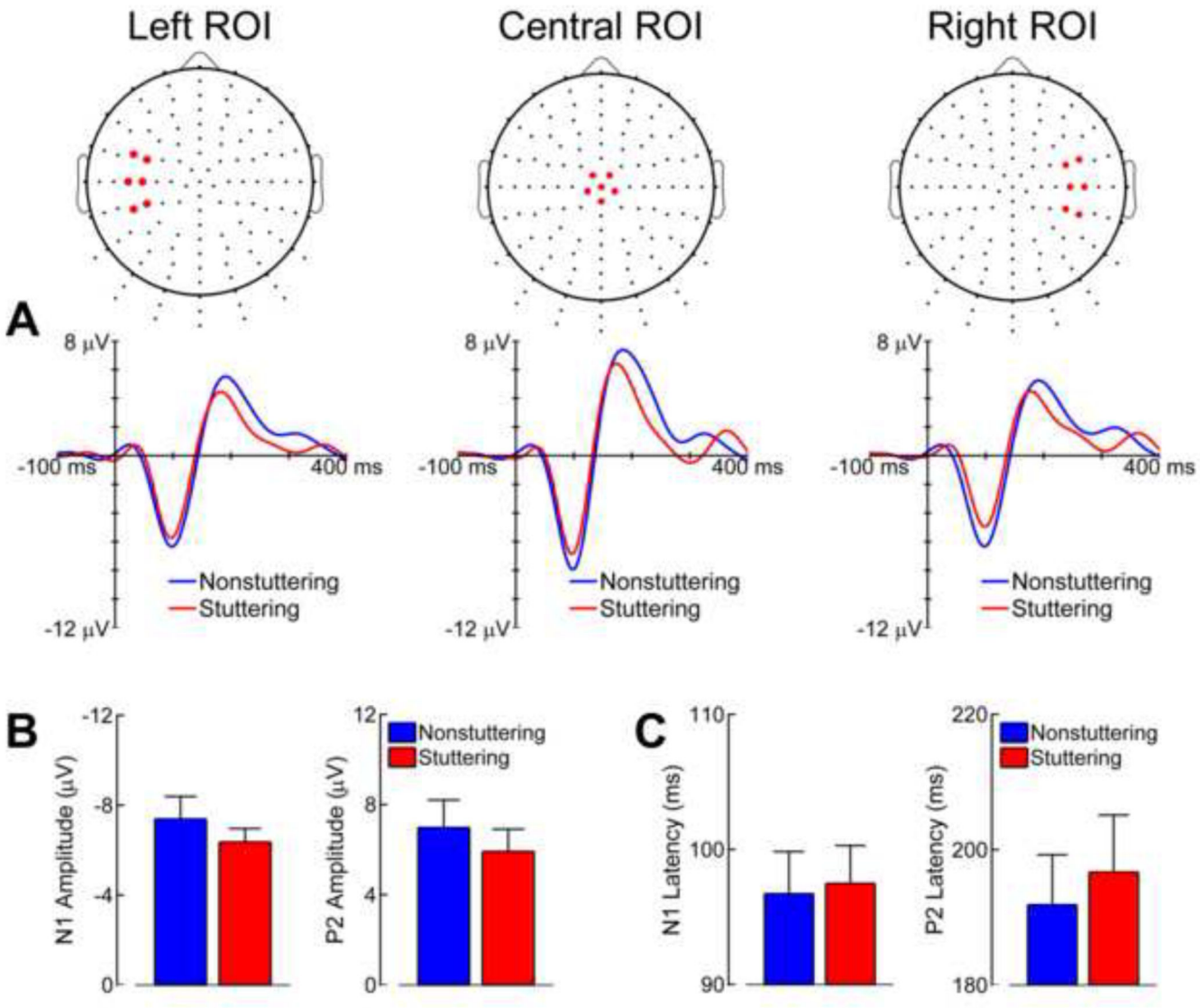

Fig. 5.

Eyes-closed rest condition LLAEPs from three ROIs for stuttering (red) and nonstuttering (blue) subjects (A). There was no statistically significant Group main effect for N1 or P2 amplitudes (B) or for N1 or P2 latencies (C). Error bars indicate standard errors.

Table 1

Individual participant information for the stuttering group (SSI score = Stuttering Severity Instrument 4th ed. overall score; Stuttering frequency (%SS) = percent stuttered syllables averaged across the SSI speaking and reading tasks).

Stuttering participant	Age (years)	Sex	Handedness	SSI score	SSI severity	Stuttering frequency (%SS)
1	18	male	right	22	mild	5.5
2	19	male	right	15	very mild	2.8
3	20	male	right	30	moderate	9.4
4	21	male	right	12	very mild	1.8
5	25	male	right	14	very mild	2.8
6	27	female	right	13	very mild	2.4
7	28	male	right	28	moderate	10.3
8	29	male	right	36	severe	21.1
10	30	male	right	26	moderate	15.3
9	31	male	right	25	moderate	9.3
11	33	male	right	19	mild	3.7
12	46	male	right	23	mild	5.4