Human electrophysiological examination of buildup of the precedence effect

Andrew Dimitrijevic and David R. Stapells

School of Audiology and Speech Sciences, The University of British Columbia, Vancouver, British Columbia, Canada

Correspondence and requests for reprints to Andrew Dimitrijevic, School of Audiology and Speech Sciences, The University of British Columbia, 5804 Fairview Avenue, Vancouver, British Columbia, Canada V6T 1Z3
Tel: +1 604 827 5579; fax: +1 604 822 6569; e-mail: andrew@audiospeech.ubc.ca

Sponsorship: This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

Received 13 April 2006; accepted 19 April 2006

Event-related potential correlates of the buildup of precedence effect were examined. Buildup is a type of precedence effect illusion in which perception changes (from hearing two clicks to hearing one click) during a click train. Buildup occurs faster for right-leading than left-leading clicks. Continuous click trains that changed leading sides every 15 clicks were presented. Event-related potential N1 amplitudes became smaller with click train for right-leading only. N1 latency decreased with click trains. Mismatch negativity was seen after lead–lag sides were changed. When the perceived change differed in location (left-to-right), mismatch negativity peaked earlier than when the perceived change differed in location and number of clicks (right-to-left). Results suggest that buildup relates to: N1 refractoriness, event-related potential 'lead domination' and mismatch negativity differences.

Keywords: auditory, buildup, Clifton effect, event-related potential, lateralization, mismatch negativity, N1, precedence effect

Introduction
The precedence effect (PE) refers to phenomena that place emphasis or precedence to the first arriving stimulus for sound sources [1]. In sound-field studies, stimuli often consist of both left and right sounds delivered via speakers. Therefore, PE stimuli are characterized by having two sounds from two sources: the leading stimulus (e.g. left speaker) and a lagging stimulus (e.g. right speaker). One aspect of PE is the perceptual fusion of leading and lagging stimuli at small interspeaker time delays (ISD, 1–5 ms) that results in a single auditory image lateralized to the lead side [1]. Increasing the ISD results in the lagging side becoming audible and one hears two distinct sounds. The minimum time delay at which listeners hear ‘two events’ is referred to as the echo threshold. Clifton and colleagues [2,3] showed that trains of lead–lag pairs result in an elevation of echo threshold. Initially, one hears two distinct sounds (ISD is greater than echo threshold), but as the train proceeds, the lag stimulus ‘fades’ away resulting in the participant hearing only one click. This elevation of echo threshold is the buildup of PE. After buildup, if the lead and lag pairs are suddenly reversed, the PE breaks down (Clifton effect) and buildup proceeds with another train (with reversed lead–lag pairs). To our knowledge, there have been two human event-related potential (ERP) studies examining PE [4,5] but none examining the buildup of PE. Both these studies have shown evidence for auditory cortex involvement in PE and no brainstem responses demonstrating PE.

Most of our knowledge about the neurophysiology of PE comes from animal studies. The PE has been examined at most levels of the auditory system ranging from the auditory nerve up to the auditory cortex [6–8]. The general finding in these studies is a reduced response to the lagging stimulus and little change in response to the leading stimulus. Higher-order (cortical) brain structures are likely involved in PE and buildup of PE because there is: (i) a left–right asymmetry with buildup [9] and (ii) no evidence of buildup in the inferior colliculus [7].

In the current study, we reasoned that there would be noticeable differences in cortical N1 and MMN waveforms while participants are experiencing buildup of PE, as these ERP waves are believed to reflect sensory, precognitive aspects of auditory processing up to the level of the auditory cortex.

Materials and methods
Subjects and stimulus protocol
Thirteen (six men) participants (mean age: 26 years, self-reported right-handed) with no significant history of audiological or neurological deficits and with self-reported normal hearing participated in the study after giving written informed consent.

Click trains consisted of 15 pairs of 0.1-ms duration, 88 dB peak sound pressure level clicks presented at a rate of 1 Hz to both left and right speakers. The time delay between the
two speakers for the clicks was always 10 ms. At the end of the train, the lead and lag sides were reversed (Fig. 1).

Electroencephalography recordings and analysis
Cortical ERPs were recorded from 32 channels (impedance <10 kΩ), including standard 10–20 placements, and referenced to the nose. Electro-oculograms were recorded using two bipolar electrodes above and below the right eye and two bipolar electrodes on left and right outer canthi. Recordings were performed using a nose reference and then re-referenced to an average reference. The signals were amplified and bandpass filtered (0.1 and 30 Hz). Epochs were extracted using a −100 to 500 ms window. Ocular artifact correction was performed in each participant using a singular value decomposition-based spatial filter [10,11].

The volunteers participated in two conditions: an active recording in which participants were asked to press a button when click fusion occurred (i.e. perceiving the change from two clicks to one click) and a passive recording in which participants were asked not to attend to the stimuli and watched a closed-captioned movie. Passive and active recordings were performed twice and averaged separately. Each session consisted of 30 trains per side. Responses to the first three clicks in each train for left-leading and right-leading stimuli were averaged separately. Similarly, responses to the last three stimuli were averaged together. Having averages based on the first and last three stimuli allowed us to separately group the responses that were pre- and post-buildup stages. Averages were based on 180 trials. ERP waveforms were quantified by each participant’s N1 amplitudes (baseline to peak) and latencies, in which N1 was taken to be the most negative peak occurring between 80 and 140 ms.

MMNs were analyzed by comparing the difference waves (deviant minus standard) in which standard waves were the averaged response of the last three clicks of the train and the deviant waves were the averaged response of the first three clicks of the train. This was performed separately for each participant for left-leading to right-leading (left-to-right) and for right-leading to left-leading (right-to-left). The MMN latency and amplitude were measured from the most negative peak in the 100–300 ms window.

The buildup effect was determined by comparing the amplitude/latency of the averaged response of the first three responses to the last three responses of the train. Results were analyzed using two-way repeated-measures analyses of variance (ANOVA). For the buildup effect in the midline electrode (Cz), a two-way ANOVA [side (left and right-leading stimulus) × click train (i.e. averaged first three responses) and averaged last three responses] was performed for N1 amplitude and latency. Hemispheric effects were determined by comparing the amplitude/latency of C3 and C4 electrodes in a two-way ANOVA [electrode (C3 and C4) × click train]. Differences in MMN between conditions or sides of reversals were performed by comparing peak amplitude and latency differences. For the Cz electrode, a t-test was used to compare peak amplitude/latency with reversal side (i.e. left-to-right and right-to-left). Hemispheric electrodes were analyzed using a two-way ANOVA [reversal side × electrode (C3 and C4)]. All post-hoc tests were performed using a Newman–Keuls test.

Results

Behavioural results

Participants reported that the buildup of PE occurred faster for the right-leading clicks versus the left-leading clicks. It took approximately six clicks on the left-leading side for buildup to occur, whereas only one or two clicks were required for buildup to occur with right-leading clicks. These results relate well to previously published reports of buildup asymmetry to left-leading versus right-leading clicks [9].

Event-related potentials results

Figure 2 shows the grand mean ERP waveforms for left-leading and right-leading active and passive conditions. Table 1 shows mean N1 amplitude/latencies.

Active condition

Midline electrode effects

Cz showed a significant N1 amplitude interaction between click train and leading side. Post-hoc analysis showed that only the right-leading side resulted in decreased N1 amplitude (P=0.005) for the last three clicks. A main effect of click train was seen resulting in earlier N1 latencies [F(1,12)=6.2; P=0.029] for the last three clicks.

![Fig. 1](image-url) Schematic of click train stimuli. Binaural click trains always consisted of 15 pairs of clicks (only first three and last three per side are shown). The interspeaker time delay (ISD) was always 10 ms (thin dotted line). The thick dashed line represents the reversal of lead and lag stimuli.
Hemispheric electrode effects
In the right-leading condition, N1 amplitude reductions were seen at C3 and C4 \( F(1,12)=10.1; P=0.006 \) as well as reductions in N1 latency \( F(1,12)=15.0; P=0.002 \) for the last three clicks. In the left-leading condition, no significant changes in N1 amplitude were observed, whereas N1 latency became shorter later in the click train \( F(1,12)=9.2; P<0.001 \).

Passive condition
Midline electrode effects
Cz showed no significant changes in latency or amplitude with click train position for either leading side.

Hemispheric electrode effects
In the right-leading condition, N1 amplitude decreased with click train \( F(1,12)=8.0; P=0.015 \). An interaction between click train and hemispheric electrode showed that N1 latency decreased for the later clicks at C3 (i.e. contralateral to leading click) \( F(1,12)=6.8; P=0.023 \). Left-leading clicks did not show significant changes in amplitude or latency with click train position.

Mismatch negativity
Figure 3 shows the difference waveforms arising from switches (left-to-right and right-to-left). Waveforms are shown in an MMN format in which responses to stimuli at the end of the train were treated as standards and responses at the beginning of the train are treated as deviants. Two possible standard–deviant combinations exist: switches left-to-right and switches right-to-left.

Active condition – direction of reversal
MMN amplitudes evoked by the different switches did not differ at Cz. A significant interaction between reversal side and hemispheric electrode was observed \( F(1,12)=4.9; P=0.047 \). Post-hoc analysis showed a nonsignificant trend for C3 left-to-right amplitude to be greater than right-to-left \( (P=0.061) \). The MMN latencies at Cz for left-to-right and right-to-left switches did not show a significant difference. A significant interaction between reversal side and hemispheric electrode was observed \( F(1,12)=7.2; P=0.020 \). Post-hoc analysis showed that at C3, the MMN was later in the right-to-left versus left-to-right condition \( (P=0.034) \) and similarly, the MMN at C4 was later in the right-to-left versus left-to-right condition \( (P<0.001) \). Additionally, a
hemispheric asymmetry was noted in which the deviant in the EEG channel contralateral to lead stimulus resulted in an earlier MMN (left-to-right C3 occurred later than C4; $P=0.027$).

### Passive condition – direction of reversal

Cz MMN amplitude or latency did not differ according to reversal side. C3 and C4, left-to-right MMNs were, however, shorter than right-to-left MMNs [$F(1,12)=10.3; P=0.008$].

### Discussion

The results of this study show that buildup of PE was reflected in changes in the cortical ERP waveforms reflecting precognitive sensory processing. N1 amplitude reductions with click train position were seen only in the right-leading condition. N1 latency decreased in both left-leading and right-leading conditions. MMNs occurred later with right-to-left compared to left-to-right switches.

Reductions in N1 amplitude with repeating stimuli have often been associated with refractoriness [12–18]. Refractoriness may have been responsible for reductions in right-leading responses because buildup of the PE occurred right away and perceptually remained unchanged throughout the duration of the click train. If the same neuronal generators are being stimulated repeatedly, then refractoriness may explain why N1 decreases were seen in the right-leading condition. In the left-leading condition, perception is slowly changing and the N1 generators may thus not be repeatedly activated; they therefore show less refractoriness. N1 refractoriness does not appear to be a global stimulus phenomenon because deviant stimuli result in restoration of baseline amplitude [18].

Typically, refractoriness results in amplitude reductions with minimal changes in latency [13]. We observed no N1 latency change at Cz with click train position but did observe a decrease in N1 latency at C3 and C4. Therefore, another mechanism, in addition to refractoriness, is likely involved in these results. The greatest N1 amplitude change

---

**Table 1** N1 mean (standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>Amplitude (µV)</th>
<th>Latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C3</td>
<td>Cz</td>
</tr>
<tr>
<td><strong>Active</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right leading – first 3</td>
<td>−1.34 (0.76)</td>
<td>−1.38 (0.68)</td>
</tr>
<tr>
<td>Right leading – last 3</td>
<td>−0.74 (0.45)</td>
<td>−0.83 (0.73)</td>
</tr>
<tr>
<td>Left leading – first 3</td>
<td>−0.78 (0.72)</td>
<td>−0.90 (0.83)</td>
</tr>
<tr>
<td>Left leading – last 3</td>
<td>−0.68 (0.49)</td>
<td>−0.94 (0.71)</td>
</tr>
<tr>
<td><strong>Passive</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right leading – first 3</td>
<td>−0.83 (0.50)</td>
<td>−1.10 (0.74)</td>
</tr>
<tr>
<td>Right leading – last 3</td>
<td>−0.65 (0.60)</td>
<td>−0.81 (0.61)</td>
</tr>
<tr>
<td>Left leading – first 3</td>
<td>−0.64 (0.62)</td>
<td>−0.92 (0.78)</td>
</tr>
<tr>
<td>Left leading – last 3</td>
<td>−0.47 (0.43)</td>
<td>−0.83 (0.59)</td>
</tr>
</tbody>
</table>

![Mismatch negativity (MMN) responses elicited by lead–lag reversals. Standards were considered the last three stimuli at the end of the click train and deviants were the first three stimuli after the lead–lag reversal. Top and bottom show the MMNs in active and passive condition, respectively. The exclamation point on either side of the head schematic shows where the participants are perceiving stimuli.](image-url)
was seen in the active right-leading buildup condition. The initial N1 amplitude to the first three clicks was larger in the right-leading than the left-leading condition. Thus, the observed large N1 amplitude reductions were likely not due to refractoriness but due to the MMN arising from the reversal of the previous stimulus. This large negativity could then stabilize over the course of the click train thereby giving the impression of refractoriness. The N1 buildup effects were larger in the active condition, which may be the result of a larger MMN occurring in the active condition.

The current paradigm cannot resolve the role of refractoriness in these results. Nevertheless, this difference would not have occurred if there was no difference between left-sided and right-sided buildup (i.e. buildup occurs faster for right-leading stimuli), thus these results reflect PE and buildup (and resulting perception).

Reduced N1 amplitudes and earlier latencies with PE relate well to animal studies suggesting a trend towards lead dominance and/or less lag influence as a function of click position [4,8,7]. N1 shifts towards earlier latencies can be interpreted as the responses initially containing a ‘lag influence’ in the beginning of the train with the contribution of the lagging stimulus subsequently decreasing. Consequently, the ERP waveforms become more dominated by the lead (manifested as a latency shift). This latency shift would not be observed in the right-leading condition because buildup occurred faster than in the left-leading condition.

The perceptual changes associated with buildup resulted in differing MMNs. This suggests that an early, precognitive, stage of processing can override physical characteristics of incoming stimuli. The MMNs in this study are similar to previous MMN reports for spatial deviants [19–21]. The different MMNs that we observed suggest that changes primarily in location (left-to-right switch) are mediated by different brain processes than changes in both location and number of perceived stimuli (right-to-left switch). The different MMNs most likely do not reflect inherent left–right asymmetries with deviance detection [19–21]. Similar to other MMN studies [22,23], our MMNs were smaller when participants were not attending to the stimuli as well as larger in electrode sites that are contralateral to spatial deviants [24].

Conclusion

The results of the current study showed that buildup of PE is associated with changes in ERP waveforms. These changes are reminiscent of animal studies in which PE is associated with lead dominance and decreased lag influence. The MMN seen with sudden lead–lag reversals differed for left-leading and right-leading sides, providing further evidence that buildup is correlated with changes in ERP waveforms.

Acknowledgements

This project was supported by a grant (DRS) and a Postdoctoral Fellowship (AD) from the Natural Sciences and Engineering Research Council of Canada. The authors thank Curtis Ponton for his assistance with the methods relating to reducing ocular artifacts.

References
