Automated auditory brainstem responses with CE-Chirp®
at different intensity levels

Potencial evocado auditivo de tronco encefálico automático com
o estímulo CE-Chirp® em diferentes intensidades

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ABSTRACT

Purpose: To study the results from the Automated Auditory Brainstem Response (AABR) using the CE-chirp® stimulus at 30 and 35 dBHL.

Methods: The AABR was conducted in 40 newborns with and without risk indicators for hearing loss using both clicks and CE-chirp® stimuli at 30 and 35 dBHL. The diagnostic ABR was also performed, as gold-standard procedure. “Pass/refer” results were analyzed, and validation values and response detection times were determined. Results: The “pass” results were more frequent with the CE-chirp® AABR, at both intensities tested. However, this difference was significant only for the left ear, at 30 dBHL. There was no significant difference between the two intensities for the “pass/fail” results obtained with CE-Chirp® and click stimuli. The mean response detection time was lower for the CE-chirp® stimulus at both intensities. This finding was significant at 35 dBHL for both ears, and at 30 dBHL for the right ear. Significant differences were found between intensities for the right ear. Conclusion: The CE-Chirp® stimulus showed good specificity and short response detection time at 30 dBHL. Further studies with hearing loss are needed to investigate the sensitivity of this stimulus at this intensity.

Keywords: Hearing tests; Infant, Newborn; Hearing; Hearing loss; Diagnosis

RESUMO

Objetivo: Estudar os resultados do Potencial Evocado Auditivo de Tronco Encefálico-Automático (PEATE-A) com estímulo CE-Chirp®, nas intensidades de 30 dBnNA e 35 dBnNA.

Métodos: O PEATE-A com o estímulo CE-Chirp®, na intensidade de 30 e 35 dBnNA, foi registrado em 40 recém-nascidos (RN) com e sem indicadores de risco para deficiência auditiva (IRDA) e comparado ao PEATE-A com estímulo clique, nas mesmas intensidades, e ao PEATE diagnóstico. Os resultados “passa/falha” foram descritos e medidas de validação e tempo de detecção de resposta no PEATE-A foram determinados.

Resultados: O resultado “passa” foi sempre mais frequente no PEATE-A com o CE-Chirp®, nas duas intensidades. No entanto, essa diferença foi significativa apenas para a orelha esquerda, em 30 dBnNA. Não houve diferença significativa entre as duas intensidades, para os resultados “passa/falha”, em ambas as orelhas, para o estímulo CE-Chirp® e estímulo clique. O tempo de detecção de resposta foi menor para o CE-Chirp® nas duas intensidades, sendo estatisticamente significativo para a intensidade de 35 dBnNA, nas duas orelhas e para 30 dBnNA na orelha direita. Foram observadas diferenças entre as intensidades na orelha direita.

Conclusão: O CE-Chirp®, em 30 dB, demonstrou boa especificidade e curto tempo de detecção de resposta. Pesquisas com perda auditiva são necessárias para estudar a sensibilidade do estímulo nessa intensidade.

Descritores: Testes auditivos; Recém-nascido; Audição; Perda auditiva; Diagnóstico

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INTRODUCTION

Among the automated procedures used to identify hearing loss at birth, the Automated Auditory Brainstem Response (AABR) is considered an efficient and sensitive technique, since it is less influenced by middle ear alterations and provides information from the hair cells up to the brainstem (1). It is the indicated procedure for the hearing screening of newborns with risk indicators for hearing loss (2,3).

It is known that mild hearing loss may hinder speech development, as well as individuals’ academic achievements (4). However, hearing screening devices, in general, use acoustic stimuli at intensity levels between 35 and 40 dBnHL, making it necessary to develop equipments that use lower intensity levels of stimulation in order to identify milder hearing losses. The screening algorithms must be improved to guarantee the adequate specificity at intensity levels of 35 or even 30 dBnHL, and the first step in this direction is to optimize the acoustic stimulus (5).

In this context, the chirp stimulus have been studied, and is considered clinically promising (6-7). It differentiates from the traditional click stimulus especially due to how it stimulates the cochlea. The click – which is a wide band stimulus – was produced to present all its frequency components simultaneously. Thus, considering the cochlear tonotopy, each region of the basilar membrane is sequentially stimulated, from base to apex. Therefore, the components of lower frequencies take more time to reach the apex of the cochlea, causing a temporal delay in the stimulation of part of the basilar membrane. Consequently, the neural fibers corresponding to basal regions of the cochlea are activated a few milliseconds before the activation of apical fibers. This time difference in the excitation of different neural fibers results in a decrease of the neural synchrony needed to evoke an auditory potential (8).

On the other hand, the chirp stimulus was produced with the aim to compensate temporal dispersion by promoting a delay in its high frequencies, until the lower frequencies are close to the apex of the cochlea. The result is a maximum synchronous displacement, and neural discharges produced by the stimulation of all regions on the basilar membrane (9). That is, different from the click stimulus, the high frequency components of the chirp are presented after its low frequency components, and not simultaneously.

Studies with diagnostic procedures have shown that the amplitude of wave V is greater for the chirp stimulus, when compared to the click (5,6,8). Moreover, it has been observed that the chirp promotes a decrease in screening time, since it improves the signal-to-noise ratio of the responses, especially at lower intensities, making it more efficient (5,6,10). These findings have shown that the wide-band chirp stimulus may contribute to automated neonatal hearing screening procedures, thus suggesting that its use, combined with appropriate statistical tests for response detection, might improve the efficiency of the AABR (9).

The specificity values for click stimulus at 35 dBnHL have varied from 70.6% to 99.5% in hearing screening studies (11-15). For the intensity of 30 dBnHL, the stimulus have presented specificity of 97.23% when a detection method in the frequency domain was used along with q-sample tests (16).

The mean screening time usually taken when the AABR is performed at 35 dBnHL is 15 minutes, including patient’s preparation (13-15,17,18). Studies using new algorithms have found response detections times, for this same intensity level, between 25 seconds and 5 minutes (16,19-21) and, for 30 dBnHL, 32.9 seconds (10).

Recent studies with automated procedures of hearing screening, using the beraphone equipment and the chirp stimulus, have shown good specificity and sensitivity – of 97% and 100%, respectively (9,10). The mean screening time have been observed around 11.4 minutes, considering the time taken in preparation (10), and 28 seconds, without considering it (9).

The increase promoted in the amplitude of wave V by the chirp, associated to automated detection methods that use efficient statistical tests, provide better automated response detection. Thus, it is possible to record evoked potentials in automated procedures, even at lower intensities (20-40 dB) (6,22). As a result, mild hearing losses may be identified at birth.

Studying the efficacy of neonatal hearing screening (NHS) procedures carried out at weaker levels of stimulation is very important to guide the possibility of changing the protocol and using it universally in a reliable manner. Hence, this study had the aim to study the results from AABR using CE-chirp® stimulus at 30 and 35 dBnHL.

METHODS

Participants were 40 newborn infants (NB), 17 male and 23 female, who were born at a philanthropic maternity hospital in the state of São Paulo, Brazil. Nine of the NB presented risk indicators for hearing loss (heredity, consanguinity, and congenital infection). Inclusion criteria in the study were: at least 37 weeks gestational age at birth, more than 24 hours of life, absence of suspected neurological alterations or suggested syndromes, absence of agenesis of the external ear or ear canal.

The study was approved by the Research Ethics Committee of the Pontifícia Universidade Católica de São Paulo (PUC), under protocol number 118/2011. The parents or legal guardians of all subjects included in the study signed the Free and Informed Consent.

Subjects’ medical files were consulted, and the following electrophysiological procedures were conducted: AABR with click and CE-chirp® stimuli, at 30 and 35 dBnHL, and diagnostic ABR. The diagnostic ABR was used as gold standard to ensure and verify the sensitivity and specificity of the responses obtained in the AABR.

The diagnostic ABR was conducted using the Eclipse Black Box – software EP25, from Interacoustics® MedPC.
The ipsilateral recording used click stimulus (ABR-click) by air conduction (AC) and also by bone conduction (BC), when the AC was altered. The presence of wave V at 20 dBnHL was considered the normal standard for both AC and BC. The click stimulus had duration of 100 µs, presented at a repetition rate of 27.7 Hz, condensation (AC) and rarefaction (BC) polarity, with filter of 100-3000 Hz and a 12-millisecond window.

Wave V was considered as the positive peak occurring between 5 and 12 ms after stimulus presentation and preceding the most negative deflection. When wave V was not identified at 80, 40, or 20 dB, intensity was increased at 10 dB steps, until the wave was identifiable again. The maximum intensity considered was 100 dBnHL for AC, and the intensity considered normal in BC ABR was 50 dB. The lower intensity at which wave V could be observed and reproduced was considered the Minimum Response Level (MRL).

The AABR was conducted using the Titan equipment, software ABRIS 440, from Interacoustics®, linked to a computer. This software has an automated response detection method that uses the q-sample test and Bayesian weighting. Stimuli were presented at a repetition rate of 90 Hz, with alternate polarity. Both the click and the CE-chirp® stimuli presented the same frequency spectrum (350 Hz; 11,300 Hz). The maximum time established to determine the presence/absence of responses in the AABR was 180 seconds.

The two procedures were performed in both ears. There was no specific order for the procedures or for the two intensity levels used. All electrophysiological procedures occurred preferentially close to the hospital discharge, in a room assigned by the hospital, with no acoustic treatment. The infants were comfortably accommodated in the maternity cribs or in their mothers’ laps, and were in natural sleep.

**Data analysis**

The results (pass/fail) from the AABR performed at 30 and 35 dBnHL with click and CE-chirp® stimuli were descriptively and comparatively analyzed. The comparison between procedures was carried out using the McNemar test (Fisher and Van Belle, 1993). The comparison between ears, for both stimuli and both intensities, used the Fisher’s exact test (Fisher and Van Belle, 1993). The measures of diagnostic abilities – Youden’s index and Kappa coefficient – were determined considering the gold standard. Intensities and stimuli were separately compared, by ear. The hypotheses testing considered a significant level of 0.05.

**RESULTS**

The results from the diagnostic ABR, considered gold standard, were normal for all infants, in both ears, that is, all subjects presented AC and BC thresholds within the normal standard limits adopted for this study (20 dBnHL).

The NB had a mean of 32.24 (24.48-40) hours of life and 39.45 (38.33-40.57) gestational age when the screening was performed.

The results from the AABR using CE-chirp® stimulus at 30 and 35 dBnHL were analyzed for the right and left ears. The percentages of “fail” results, at both intensity levels, were low. There were no cases of “fail” at 35 dBnHL and “pass” at 30 dBnHL. The values obtained in the Kappa coefficient indicated strong agreement between the results obtained at 30 and 35 dBnHL, and there were no differences between the results distributions, at both intensity levels, for either ear (Table 1).

The specificity, accuracy and negative predictive (NPV) values for the click and CE-chirp® stimuli at 30 and 35 dBnHL are presented, for both ears, in Table 2.

For the right ear, the proportion of infants that “passed” the AABR with CE-chirp® stimulus at 30 dBnHL was higher than for the test performed with clicks at the same intensity level. However, the p-value obtained showed there was no significant difference between stimuli for the subjects that “passed” at 30 dBnHL. For the left ear, on the other hand, the percentage of “pass” results was significantly different between stimuli (higher for the CE-chirp®, when compared to the clicks). The comparison between results obtained with CE-chirp® and click stimuli in the AABR, at 30 dBnHL, is described in Table 3, for both ears.

### Table 1. Results (pass/fail) distribution for the AABR performed with CE-chirp® stimulus at 30 and 35 dBnHL, for right and left ears (n=40)

<table>
<thead>
<tr>
<th>CE-chirp® 30 dB</th>
<th>Right ear</th>
<th></th>
<th>Left ear</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pass</td>
<td>Fail</td>
<td>Total</td>
</tr>
<tr>
<td>Pass</td>
<td>38</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>95.0%</td>
<td>0.0%</td>
<td>95.0%</td>
</tr>
<tr>
<td>Fail</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>2.5%</td>
<td>2.5%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>97.5%</td>
<td>2.5%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

McNemar test: p<0.999 and Kappa=0.66 (standard error=0.32) for the right ear; McNemar test: p<0.999 and Kappa=0.79 (standard error=0.21) for the left ear
At 35 dBnHL, no significant differences were found between stimuli for the percentages of NB that “passed” the AABR, for both right (p>0.999) and left (p=0.125) ears. There was strong agreement between the results obtained with both stimuli for the right ear (Kappa=0.66) and moderate agreement for the left ear (Kappa=0.46). However, the number of “fail” results was higher for the AABR with click stimulus. There were no cases of “fail” with the CE-chirp® and “pass” with the clicks (Table 4).

Based on the results presented in Tables 3 and 4, no significant differences were observed between the results (pass/fail) obtained for right and left ears in the AABR with CE-chirp® stimulus, at 30 and 35 dBnHL (p=0.999). In addition, there were also no differences between ears for the AABR with click stimulus, both at 30 dBnHL (p=0.180) and 35 dBnHL (p=0.125). A higher number of “fail” results were obtained in the left ear at 30 dBnHL, for both stimuli, although these results were not significant.

Regarding the response detection time, the stimuli were compared for the same intensity level, and the intensity levels were compared for the same stimulus. The comparison of time distributions between stimuli showed that the time obtained for the AABR with CE-chirp® was shorter than for the AABR with clicks, at 35 dBnHL, in the right (p<0.001) and left (p<0.001) ears. The same result was obtained at 30 dBnHL in the right ear (p<0.001). The time obtained for the AABR with CE-chirp® tended to be shorter than with click stimulus, at both intensity levels and in both ears. It was also observed that the mean response detection time values were higher at 30 dBnHL, except for the AABR with clicks.

### Table 2. Descriptive statistic values for specificity, negative predictive value (NPV) and accuracy of the click and CE-chirp® stimuli at 30 and 35 dBnHL, for right and left ears

<table>
<thead>
<tr>
<th>CE-Chirp® 30 dB</th>
<th>CE-Chirp® 35 dB</th>
<th>Click 30 dB</th>
<th>Click 35 dB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RE (%)</td>
<td>LE (%)</td>
<td>RE (%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>95</td>
<td>92.5</td>
<td>97.5</td>
</tr>
<tr>
<td>NPV</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Accuracy</td>
<td>95</td>
<td>92.5</td>
<td>97.5</td>
</tr>
</tbody>
</table>

Note: RE = right ear; LE = left ear

### Table 3. Results (pass/fail) distribution for the AABR performed with CE-chirp® and click stimuli at 30 dBnHL, for right and left ears

<table>
<thead>
<tr>
<th>Click 30 dB</th>
<th>Right ear</th>
<th>CE-chirp® 30 dB</th>
<th>Total</th>
<th>Left ear</th>
<th>CE-chirp® 30 dB</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pass</td>
<td>35</td>
<td>0</td>
<td>35</td>
<td>30</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>Fail</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>2</td>
<td>40</td>
<td>37</td>
<td>3</td>
<td>40</td>
</tr>
</tbody>
</table>

McNemar test: p=0.250 and Kappa=0.54 (standard error=0.23) for the right ear; McNemar test: p=0.016 and Kappa=0.39 (standard error=0.17) for the left ear

### Table 4. Results (pass/fail) distribution for the AABR performed with CE-chirp® and click stimuli at 35 dBnHL, for right and left ears

<table>
<thead>
<tr>
<th>Click 30 dB</th>
<th>Right ear</th>
<th>CE-chirp® 30 dB</th>
<th>Total</th>
<th>Left ear</th>
<th>CE-chirp® 30 dB</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pass</td>
<td>38</td>
<td>0</td>
<td>38</td>
<td>34</td>
<td>0</td>
<td>34</td>
</tr>
<tr>
<td>Fail</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>2</td>
<td>40</td>
<td>38</td>
<td>2</td>
<td>40</td>
</tr>
</tbody>
</table>

McNemar test: p=0.999 and Kappa=0.68 (standard error=0.32) for the right ear; McNemar test: p=0.125 and Kappa=0.46 (standard error=0.22) for the left ear
in the left ear. Significant differences were observed in the comparison between intensity levels for the same stimulus, only in the right ear (p<0.001) (Table 5).

**DISCUSSION**

This study analyzed the results obtained in AABR at a low intensity level (30 dBnHL), and studied measures of the diagnostic ability of the CE-chirp® stimulus in automated procedures of NHS.

Results showed that the new stimulus was more efficient, when compared to the click stimulus, because it presented shorter response detection time. Studies that compared the use of these stimuli in diagnostic procedures with hearing adults have also observed decrease in the screening time, mainly due to the increase in the amplitude of wave V, caused by the simultaneous and, thus, synchronic activation of the auditory fibers.

A research that used the click stimulus and the q-sample test found a mean response time of 28.3 (14-105) seconds at 35 dBnHL, which was shorter than the findings in this study. However, this result was longer than the mean response time found in this study for the CE-chirp® stimulus, which suggests that the CE-chirp® presents shorter detection time than the click stimulus. A recent study that used an optimized chirp (CE-chirp™) at 35 dBnHL found a mean time of 28 seconds, with minimum and maximum times of 15 and 22 seconds, respectively.

At the intensity of 30 dBnHL, the research previously mentioned found a mean response detection time of 32.9 seconds, which was shorter than the findings in this study. The higher number of participants in the previous study may have influenced the mean response detection time, in the presence of outliers.

The comparison between intensity levels for both stimuli (Tables 3 and 4) showed a result that was not expected, maybe due, for example, to changes in the state of consciousness of the NB, or to an increase in the residual noise between one recording and the next. On the other hand, the mean time may have been increased by the presence of outliers at 35 dBnHL, since the median obtained at 35 dBnHL (56 seconds) was lower when compared to the obtained at 30 dBnHL (59.5 seconds).

The greater variation found among subjects for the click stimulus, regarding the response detection time, might suggest that this stimulus is more influenced by variables such as residual noise, small muscular movements, and the presence of vernix. This variation is not favorable to automated NHS procedures, because it may increase the screening time and the number of “fail” and false-positive results.

Results also showed that the response detection time was always longer for the left ear, regardless of the stimulus used. However, there are no reports in literature that show significant differences between ears. In this study, the state of the external/middle ear was not controlled, and hence the presence of vernix in the left ear may have possibly influenced these results. It is known that conductive alterations of any nature lead to a decrease in the incident sound energy, as well as to an increase in the sound conduction time, thus influencing the response detection time.

It is important to emphasize that the insertion and removal of the earphone between procedures, when they are performed consecutively, may change the state of the ear canal, influencing the passing of sounds. Since the procedures were randomly performed, this may also have influenced the occurrence of “fail” results in the AABR screening while the diagnostic ABR presented responses at 30 dBnHL.

The new stimulus was also more efficient regarding the measures of diagnostic ability. A research that used the CE-chirp® in NHS at 35 dBnHL found a 97% specificity, which was similar to the results in this study (which found specificity of 97.5% for the right ear and 95% for the left ear). However, the authors of the previous study used an automated procedure as gold standard, instead of a diagnostic procedure, which does not rule out the presence of real-positive results among...
these false-positives. Thus, a direct comparison between the two studies may be conducted with caution. Another study\(^6\) that used the CE-chirp\(^\text{®}\) in the NHS protocol showed a 97.9% specificity. Other studies\(^{14,16}\) that have used the ABR as gold standard, conducted with equipment that use different detection methods among them, have found specificity of 100%\(^{16}\) and 75%\(^{14}\) for the click stimulus. The specificity values found in the present research for the click stimulus were different from these values.

A higher specificity was observed at 30 dBnHL for the CE-chirp\(^\text{®}\), when compared to the click stimulus, in both ears. The specificity found in another Brazilian study\(^7\), for the click stimulus, using the same response detection method used in this research, was of 97.23% (11 false-positive ears). A study conducted in the 90’s\(^{21}\) found 100% sensitivity and 98% specificity in the screening conducted with diagnostic ABR at 30 dBnHL and click stimulus.

Regarding the comparison of “pass” and “fail” results between the CE-chirp\(^\text{®}\) and the click stimuli at 30 and 35 dBnHL (Tables 3 and 4), if it is assumed that the “fail” results were caused by the presence of vernix, it may be that the chirp behaves differently from the click with this type of conductive alterations, especially at weak intensities.

The facts that no significant differences were found between intensities for the CE-chirp\(^\text{®}\) and that the specificities were very close contribute to an increase in the reliability and efficiency in using the intensity of 30 dBnHL in automated procedures. Several studies\(^7,8\) aiming at audiological diagnosis have shown that the ABR conducted at 30 dBnHL using chirp stimulus produces good amplitudes of the wave V, and may thus be used in NHS.

The differences found between stimuli for the response detection time at both intensity levels (although not much expressive at 30 dBnHL in the left ear) corroborate the literature and emphasize that the chirp stimulus, due to the ability to stimulate all regions of the basilar membrane at the same time, increases neural synchrony and the amplitude of the response, improves response detection, and reduces screening time\(^6,7\). The differences found between intensity levels for the CE-chirp\(^\text{®}\) stimulus were also expected, since the stronger the sound energy, the greater the amplitude of response and the shorter the time taken for the statistic test to “establish” the presence of response.

The fact that the CE-chirp\(^\text{®}\) presented similar specificity values at 30 and 35 dBnHL suggest that the stimulus may be used in hearing screening at 30 dBnHL in order to identify mild hearing losses. Also, the new stimulus may reduce the numbers of retests, false-positive results, and referrals for audiological diagnosis. Consequently, it might reduce parents’ anxiety and the costs with NHS.

In this study, none of the subjects presented conductive or sensorineural hearing loss in the ABR, and therefore there were no false-negative results. Thus, it was not possible to study the sensitivity of the stimuli for both intensity levels.

Further sensitivity and specificity studies may be carried out with greater samples and hearing losses of varied degrees and configurations, as well as studies including infants with and without middle ear alterations, in order to analyze and compare the behavior of the new stimulus in such conditions.

**CONCLUSION**

In this study, the AABR using the CE-chirp\(^\text{®}\) stimulus presented higher specificity and fewer false-positive results, as well as shorter response detection time, than the same test performed using the click stimulus, both at 30 and 35 dBnHL.

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