Auditory evoked cortical responses to frequency glides in subjects with retrocochlear hearing impairment

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SUMMARY Auditory cortical responses evoked by stimulation with frequency glides of a continuous tone have been recorded from 44 subjects with intracranial tumours affecting auditory function. Response latencies obtained when stimulating the ear on the side of the tumour were different from the non-tumour ear as well as from groups with cochlear impairment and normal hearing. Tumours caused a reduction of a specific sensitivity to the frequency glide stimulation, affecting further processing of the dynamic change in tone frequency. The test appears to have diagnostic potential.

In evaluating auditory function, stimuli usually have been acoustically simple, such as pure tones or clicks, or very complex, such as human speech. With the purpose of trying to bridge this gap, dynamic stimuli consisting of brief frequency glides of specified duration and magnitude in a continuous pure tone were studied to obtain increased knowledge of auditory function and effects of various disorders of the auditory system. In previous reports, we have presented studies where such stimuli were used to evoke auditory cortical responses from subjects with normal hearing¹ as well as with inner ear hearing loss.²

In addition to the extensive studies on these limited groups of subjects, evoked auditory responses to frequency glides have been recorded in our clinic on all patients which have been seen for evaluation of unilateral sensorineural hearing loss. For many of those patients, no final diagnosis as to the site of lesion has been reached. However, one subgroup proved to be a general exception to this rule, namely those with intracranial tumours that affected auditory nerve function. Over a period of six years, auditory cortical responses evoked by frequency glides have been recorded from 44 such patients. The results from these examinations were different from what had previously been found on other groups and will be presented in this report.

Subjects

Forty-four subjects with retrocochlear lesions were examined. Of these, 28 had acoustic neuromas, three had meningiomas and two had cholesteatomas in the cerebellopontine angle, that were all later surgically verified. One had a microglioma affecting the cerebellum and brainstem bilaterally, verified post mortem. In the remaining 10 subjects, the diagnosis was based on neuroradiologic findings (computed tomography and metagrapy), the clinical diagnosis being either cerebellopontine angle tumour or intra-canalicular acoustic tumour.

The subjects' ages varied from 15 to 73 years with a mean of 54 and a median of 58 years. Twenty-three of the subjects were men and 21 women. Of the 43 cases of unilateral tumour, 21 had involvement of the right and 22 of the left side. Hearing loss at 1 kHz varied over the range 5–120 dB HL with a mean of 53 dB on the tumour side. On the non-tumour side the range of hearing threshold levels at 1 kHz was −5 to 55 dB with a mean of 9 dB. All except five were within normal range (that is ≤ 20 dB). Table 1 shows the distributions of hearing threshold levels in four classes for 1 and 4 kHz. Also the distribution of speech discrimination scores is presented.

Methods

What is specific in this test is the dynamic stimulus, which is based on a continuous pure tone, the base frequency of which, f₀, is usually 1 kHz (fig 1). On three subjects, whose hearing thresholds were too poor at this frequency (110 dB HL or more), 500 Hz was used instead. The actual stimulus is the frequency glide of this tone with a magnitude Δf of either 50 or 200 Hz, that is 5 or 20%, and duration 20 ms. After 0.5 s the tone frequently returns slowly from f₀ + Δf to f₀. The interval between successive stimuli, ISI, was varied randomly from 2 s and up with a mean of 4 s. On eight of the
subjects, a different dynamic stimulus, glides in amplitude or sound pressure of a continuous tone, was used in addition to the frequency glides. The change in sound level that was used was either 5 or 20 dB, and the base sound level was always the same as that used for the frequency glides.

The tone was presented monaurally by means of a TDH39 earphone on a sound level in the most comfortable range. On normal ears, 60 dB HL (above normal threshold of hearing) was used. On ears with retrocochlear hearing loss, levels between 60 and 110 dB HL were used with a mean of 89 dB. Masking of the contralateral ear by means of narrow-band noise was used when the stimulus level exceeded 60 dB HL.

The auditory cortical response was recorded by means of Ag/AgCl-electrodes attached to the vertex (Cz) and the left mastoid with a ground electrode on the right mastoid. The recording pass-band was 0.1–12 Hz. The time delay caused by the lowpass filter had been corrected for in the determination of response latency. Fifty 500 ms sweeps were summed in a computer to obtain an averaged response. When time permitted, replications were made. The subject sat in a chair in a sound-insulated room, reading a magazine of his own choice, with the purpose of keeping his state of arousal as constant as possible. A detailed description of method and equipment has been presented earlier.

In addition to the dynamic stimulation, 34 of the subjects were also tested by stimulation with ordinary 1 kHz tone pulses (duration 200 ms, rise/fall-time 40 ms) presented on high sound level—the average 80 dB HL on the non-tumour side and 100 dB on the tumour side. The patients were also tested by a number of other audiometric tests, such as speech discrimination and auditory fatigue tests. Since 1979, recording of auditory brainstem responses have been included.

The latency of the N1- or N100-component, that is the vertex-negative peak in the latency range 100–200 ms after stimulus onset, is the characteristic of the response that shows the least variability and is therefore used as the quantitative descriptor of the response.

Statistical analysis was based on Student's t test. Although the statistical distribution function of evoked response latencies may be assumed to be non-normal, the results obtained previously on normal-hearing and cochlear hearing loss groups show coefficients of skewness that do not differ significantly from zero. This in turn implies that in significance tests of fairly small samples the stipulation of

Table 1 Distribution of pure tone hearing threshold levels (HTL) at 1 and 4 kHz and speech discrimination scores. HTL of 20 dB and better is normal range in age group 18–30 years

<table>
<thead>
<tr>
<th>Frequency (kHz)</th>
<th>Tumour side</th>
<th>Non-tumour side</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 kHz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTL ≤ 20 dB (normal range)</td>
<td>10 ears (22%)</td>
<td>38 ears (88%)</td>
</tr>
<tr>
<td>&gt;20 ≤ 50 dB</td>
<td>11 (24%)</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>&gt;50 ≤ 80 dB</td>
<td>18 (40%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>&gt;80 ≤ 120 dB</td>
<td>6 (13%)</td>
<td></td>
</tr>
<tr>
<td>4 kHz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTL ≤ 20 dB (normal range)</td>
<td>3 ears (7%)</td>
<td>23 ears (53%)</td>
</tr>
<tr>
<td>&gt;20 ≤ 50 dB</td>
<td>8 (18%)</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>&gt;50 ≤ 80 dB</td>
<td>17 (38%)</td>
<td>11 (26%)</td>
</tr>
<tr>
<td>&gt;80 ≤ 120 dB</td>
<td>8 (18%)</td>
<td></td>
</tr>
<tr>
<td>&gt;120 dB (max output of audiometer)</td>
<td>9 (20%)</td>
<td></td>
</tr>
<tr>
<td>Speech discrimination scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥92% (no significant loss)</td>
<td>6 ears (13%)</td>
<td>37 ears (86%)</td>
</tr>
<tr>
<td>≥70 ≤ 90%</td>
<td>9 (20%)</td>
<td>6 (14%)</td>
</tr>
<tr>
<td>&lt;70%</td>
<td>30 (67%)</td>
<td></td>
</tr>
</tbody>
</table>

Fig 1 Illustration of the frequency glide stimulus of magnitude Δf. The base frequency of the continuous tone is f₀, and ISI is the interstimulus interval.
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normality for using the t test may be regarded as almost fulfilled.2

Results

N1-latencies of evoked responses when stimulating the tumour side and the non-tumour side are shown for frequency glides of 50 Hz (5%) in fig 2 and of 200 Hz (20%) in fig 3 with results for left and right stimulated ear shown by different symbols. Where replications were made, only results from the first run are shown. In the tumour side data, shown on the left side of the figures, a dashed line indicates a limit which is the mean value plus two standard deviations as obtained in the group of subjects with cochlear lesions previously investigated.3 Similarly, on the non-tumour side, the limit indicated is the mean latency plus two standard deviations as recorded in the group of subjects with normal hearing.1

Symbols with upward-pointing arrows in the figures indicate that no response could be identified in the recordings. Counting tested ears, 36 out of 45 (80%) on the tumour side produced latencies outside the indicated limit for 50 Hz glide stimulation and 33 out of 45 ears (73%) for 200 Hz glides. On the non-tumour side only eight ears out of 43 (19%) were associated with latencies outside the limit for 50 Hz glides and two out of 43 (5%) for 200 Hz glides.

A comparison of latencies obtained in response to stimuli presented to left and right ears, respectively, shows no side difference on the non-tumour side. Nor was any left/right difference seen on the tumour side for tone pulse and 50 Hz glide stimulation. However, right ears produce latencies for 200 Hz glides that are shorter than those from left ears, but the difference is statistically barely significant (0-05 < p < 0-1, Wilcoxon rank test for unmatched pairs, two-tailed test).

Table 2 shows the incidence of response latencies falling outside the limits for both, one, or none of the two stimulus magnitudes. The difference between the present group of subjects with retrocochlear hearing impairment and the group having cochlear hearing loss is clearly evident for the tumour side, while the results on the non-tumour side do not differ significantly from the data from the normal-hearing group. The latency differences between tumour and non-tumour sides are statistically highly significant (p < 0-001).

A calculation of the ratio between response latencies for the tumour side over the non-tumour side, for those subjects where responses could be identified, gave a mean ratio of 1-29 for 50 Hz glides (SD = 0-19, n = 17 ears) and of 1-30 for 200 Hz glides (SD = 0-30, n = 35 ears).

Fig 4 shows the latencies obtained with stimulation with conventional tone pulses. The dashed lines mark the mean values and the vertical bars ± one standard deviation. On the tumour side the mean latency was 134 ± 19·4 ms and on the non-tumour side 121 ± 7·2 ms. Thus, in spite of an average 20 dB higher stimulus level in the tumour ear, the response latency obtained

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Fig 2  N1-latencies recorded in response to 50 Hz (5%) glides on tumour and non-tumour sides. Right ear stimulation is shown by open circles and left ear by filled triangles. Symbols with arrows indicate that no response could be identified in the recording. When more than one recording has been made on a subject, the result from the first one is shown. Mean value plus 2 SD for a group with cochlear lesions (left half) and a group with normal hearing (right half) are shown by dashed lines.

Fig 3  N1-latencies in response to 200 Hz (20%) glides. Symbols and other conditions as in fig 2.
Tone pulse stimulation the two cases that 8-6ms, n= his to the other that of lesions cochlear levels sound on obtained mean ratios for smaller significantly between ratio of percent < (p = 0.005). The latency ratio between tumour and non-tumour side was on the average 1.12 with SD = 0.12. This mean ratio is significantly smaller (p < 0.005) than that obtained for frequency glide stimulation, however, where the mean ratios were 1.29 and 1.30. The mean latency obtained on the tumour side was significantly longer (p < 0.005) than that of a group of subjects with cochlear lesions tested with tone pulses on similar sound levels (mean 123 ms, SD ± 8.3 ms, n = 23), while the non-tumour side data did not differ from that of a normal-hearing group (mean 119 ms, SD ± 8.6 ms, n = 17).

Figs 5–7 show recordings from three individual cases that illustrate the general findings well. Case 25 (fig 5) had a small acoustic neuroma on his right side. Tone pulse stimulation gave identical N1-latencies on the two ears. With 50 Hz frequency glides presented to his tumour ear no response could be seen, while on the other ear a normal response was present. With 200 Hz glides a significantly delayed response was found on the right (tumour) side. Also case 29 (fig 6) had a small acoustic neuroma, on her left side. Tone pulse responses had nearly identical N1-latencies while both frequency glide stimuli gave rise to 30–40 ms longer latencies on the tumour side. Case 10 (fig 7) had cerebellopontine angle cholesteatoma with essentially normal hearing thresholds both before and after operation. However, preoperative speech discrimination was only 60% on the affected ear. Postoperatively it increased to 96%, that is within normal range. On the tumour side, responses to frequency
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Fig 6 Case 29 had a small acoustic neuroma on her left side. Response latencies to frequency glides are 30–40 ms longer on the tumour side.

glides were significantly delayed in the preoperative measurement but were clearly within normal range postoperatively. Responses to tone pulse stimulation gave rise to N1-latencies within normal range both pre- and postoperatively.

N1-latencies in response to amplitude glides as recorded from eight of the subjects had a mean value of 158 ms on the tumour side and 134 ms on the non-tumour side for five dB glides. This difference is, however, not statistically significant. For 20 dB glides the mean latencies were 128 and 109 ms, respectively, which difference is significant (p < 0.1). However, on these particular subjects, N1-latencies to frequency glides gave highly significant differences between tumour and non-tumour side (p < 0.001). Also N1-latencies in responses to tone pulses showed a significant side difference (p < 0.05).

Auditory fatigue was tested by means of a tone decay test on 38 of the 44 subjects. Of these, 18 were found to have no or insignificant threshold tone decay when testing the ear on the tumour side (at most 5 dB at 1 kHz and/or 30 dB at 2 kHz), while 12 had clearly abnormal results (30 dB or more at 1 kHz and/or 45 dB or more at 2 kHz). Table 3 shows some data for these two subgroups. The only apparent difference is in response identification for 50 Hz glides, where fewer of the subjects with significant decay produced responses. However, using the Wilcoxon rank test for two independent samples, no statistically significant difference between the two subgroups was found.

On the eight subjects on whom were recorded evoked responses to amplitude glides in addition to the frequency glides, the results showed no significant N1-latency difference between tumour and non-tumour sides for five dB glides. For 20 dB glides stimulation on the tumour side produced response latencies that were barely significantly longer than when stimulating the non-tumour side. However, when the frequency glides were used on these particular subjects, highly significant side effects were recorded.

Auditory brainstem responses were recorded from 22 of the 44 subjects. On 12 of these (55%), an

![Graph of Case 29](image)

![Graph of Case 10](image)

Fig 7 Pre- and postoperative recordings of responses to frequency glides from a subject with left-sided cerebellopontine angle cholesteatoma. On the tumour side, preoperative responses are significantly delayed, while postoperatively they are found within normal range.
abnormal response was identified from the tumour side. On the remaining 10 (45%), the response was either considered absent or interpretation very uncertain.

<table>
<thead>
<tr>
<th>Number of subjects</th>
<th>18</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects with no identifiable response to 50 Hz glides</td>
<td>8 = 44%</td>
<td>8 = 67%</td>
</tr>
<tr>
<td>Number of subjects with no identifiable response to 200 Hz glides</td>
<td>4 = 22%</td>
<td>3 = 25%</td>
</tr>
<tr>
<td>N1-latency for 50 Hz glides</td>
<td>M 177.6 ms</td>
<td>172.5 ms</td>
</tr>
<tr>
<td>N1-latency for 200 Hz glides</td>
<td>M 157.7 ms</td>
<td>145.7 ms</td>
</tr>
<tr>
<td>N1-latency for tone pulses</td>
<td>M 130.7 ms</td>
<td>132.0 ms</td>
</tr>
<tr>
<td>No decay</td>
<td>Abnormal decay</td>
<td></td>
</tr>
<tr>
<td>SD 24.5 ms</td>
<td>SD 30.9 ms</td>
<td></td>
</tr>
<tr>
<td>SD 13.7 ms</td>
<td>SD 28.6 ms</td>
<td></td>
</tr>
<tr>
<td>SD 12.1 ms</td>
<td>SD 12.2 ms</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Comparison of N1-latencies in two subgroups according to degree of hearing threshold tone decay. M = mean value, SD = standard deviation

Discussion

Several possible factors may be involved in the abnormal evoked responses recorded on the tumour side of subjects with retrocochlear hearing impairment: (1) general reduction of neural conduction velocity caused by the tumour, similar to that usually found in auditory brainstem responses and in facial reflex examinations of subjects with acoustic neuroma (2) reduced excitation on the tumour side due to abnormal fatigue when the ear is exposed to continuous tone stimulation (3) reduced specific sensitivity to this particular stimulus, the frequency glide.

If the tumour gave rise to a general reduction of neural conduction time as the main cause of the increased N1-latency in response to frequency glides, one would expect a similar degree of increased latency in responses to tone pulse stimulation. Such a finding was actually described by Shimizu in a study of four cases with acoustic neuromas. However, Townsend and Cody studying six subjects with the same diagnosis could not confirm this finding.

In the present study, the loud tone pulses and the 200 Hz glides produce approximately equivalent latencies, around 120 ms, when stimulating the non-tumour side. On the tumour side, the sound levels of the tone pulses and the tone with frequency glides were chosen to give approximately the same loudness as those used on the non-tumour side. Also, the same rules for the use of contralateral masking were applied. Thus, if the main reason for increased latencies in response to frequency glides to the tumour side were a general reduction in neural conduction velocity, one would expect approximately the same latency increase for stimulation with the loud tone pulses and with the frequency glides of 200 Hz. This was however not found; the side difference for the frequency glides was much larger than for the tone pulses.

It is well known that cases with acoustic neuromas often display abnormal auditory fatigue, and the continuous tone used in the frequency glide stimulation could of course give rise to such fatigue and be part or all of the reason for the prolonged latencies. Thus, one would expect response latencies from subjects with abnormal auditory fatigue to be considerably longer than those recorded on subjects lacking auditory fatigue. This was however not found; the results showed that no significant difference could be proven between these two groups of subjects. This finding leads us to the conclusion that abnormal fatigue on the tumour side is not a likely explanation for the results.

This conclusion receives further support by the results from the eight subjects on whom amplitude glides of a continuous tone also were used as stimulus to evoke cortical responses. Using amplitude glides no significant side differences were found, while the frequency glides on these particular subjects gave highly significant side differences. If abnormal fatigue was the main reason for prolonged latencies on the tumour side, one would expect amplitude and frequency glides of a continuous tone to be equivalent in this respect, which was not found to be the case.

These results suggest that the tumour causes a reduction of a specific sensitivity to the frequency glide stimulation. This does not imply that the auditory nerve contains fibres that respond to the changing frequency as such, in the way that has been shown to exist in higher levels of the auditory pathways. It seems more reasonable to interpret this finding as a sign of the tumour affecting the complex neural message in the auditory nerve in a way that the subsequent processing of the dynamic change in tone frequency is altered.

Another interesting issue is what functional auditory effects this prolongation of N1-latency for frequency glide stimulation may indicate. An analysis of the speech discrimination scores of the tumour ears as determined by conventional clinical testing with phonetically balanced lists of monosyllabic test words showed a large variation, from 0 to 100%, and with a tendency to bimodal distribution. Dividing the tumour group into two subgroups according to speech discrimination scores less or more than 50%, 26 ears fell into the poorer group and 19 into the better. N1-latencies to frequency glides were significantly different in the two subgroups (Wilcoxon rank test for two independent samples; p < 0.01 for 50 Hz glides, p < 0.05 for 200 Hz glides). Furthermore, linear regression analysis showed a significant correlation between speech discrimination scores and N1-latencies in response to 200 Hz glides (r = −0.54, p <
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0.02) in the better subgroup. For 50 Hz glides, the correlation coefficient attained a value of –0.45, which is just outside the 0.05 limit of significance. For the subgroup with speech discrimination <50% no significant correlation was found. These results indicate that in the better category the cortical response to frequency glides shows some functional relationship with speech discrimination. For the subjects with poor speech discrimination, the lack of correlation may be explained by other factors than those involved in the frequency glide reactions being mainly responsible for the poor transmission of the speech signal message.

According to our experience, the recording of cortical responses using frequency glide stimulation is a very simple procedure that adds significantly to the power of the test battery used for examining patients with unilateral sensorineural hearing disturbances. Certainly, the recording of auditory brainstem responses (ABR) has gained a reputation as a very accurate method for top diagnosis of auditory disorders.14–15 In the present group of subjects, ABR recording was performed on 22 subjects. Since several of these subjects had severe hearing loss in the high frequency range, which is primarily stimulated with the high level click stimuli normally used for ABR, the absence of a response could be due to this fact as such without necessarily indicating a retrocochlear disorder. In general, the hearing threshold at 1 kHz or 500 Hz is considerably better than at higher frequencies on these patients. This provides a reliable basis for recording auditory cortical responses to frequency glides and investigating patients with even severe high-frequency peripheral hearing losses involving the basal turn, as well as more apical portions, of the cochlea. In our earlier study of cortical responses evoked by frequency glides of a 1 kHz tone, we found that subjects with cochlear lesions yielded clear responses with latencies that did not differ significantly from those of subjects with normal hearing for glides of 50 Hz and larger.2 We thus interpret a finding of significantly prolonged latencies or absence of a response after stimulating an ear with sensorineural hearing loss as an indication of retrocochlear location of the lesion.

Results from a preliminary study on subjects, who have been exposed to industrial solvents for more than nine years, also showed prolonged latencies in the auditory cortical response frequency glides in four out of five subjects examined.16 This indicates that central auditory lesions, as well as auditory nerve disorders, may give rise to prolonged auditory cortical response latencies.

The important contributions for this study by L Jerlvall, C Kinnefors and E Strand are gratefully acknowledged. Financial support was received from the Swedish National Board for Technical Development.

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S D Arlinger

*J Neurol Neurosurg Psychiatry* 1983 46: 917-923
doi: 10.1136/jnnp.46.10.917

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