Cortical activity in tinnitus patients and its modification by phonostimulation

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OBJECTIVE: The goal of this study was to observe spontaneous cortical activity and cortical activity modulated by tinnitus-matched sound in tinnitus patients and healthy subjects with no otoneurologic symptoms.

METHOD: Data were prospectively collected from 50 tinnitus patients and 25 healthy subjects. Cortical activity was recorded in all subjects with eyes closed and open and during photostimulation, hyperventilation and acoustic stimulation using 19-channel quantitative electroencephalography. The sound applied in the tinnitus patients was individually matched with the ability to mask or equal the tinnitus. The maximal and mean amplitude of the delta, theta, alpha and beta waves and the type and amount of the pathologic EEG patterns were noted during each recording. Differences in cortical localization and the influence of sound stimuli on spontaneous cortical activity were evaluated between the groups.

RESULTS: The tinnitus group exhibited decreased delta activity and increased alpha and beta activity. Hyperventilation increased the intensity of the differences. The tinnitus patients had more sharp-slow waves and increased slow wave amplitude. Sound stimuli modified the EEG recordings; the delta and beta wave amplitudes were increased, whereas the alpha-1 wave amplitude was decreased. Acoustic stimulation only slightly affected the temporal region.

CONCLUSION: Cortical activity in the tinnitus patients clearly differed from that in healthy subjects, i.e., tinnitus is not a “phantom” sign. The changes in cortical activity included decreased delta wave amplitudes, increased alpha-1, beta-1 and beta-h wave amplitudes and pathologic patterns. Cortical activity modifications occurred predominantly in the temporal region. Acoustic stimulation affected spontaneous cortical activity only in tinnitus patients, and although the applied sound was individually matched, the pathologic changes were only slightly improved.

KEYWORDS: Tinnitus; Cortical Activity; Neurotology.

INTRODUCTION

Tinnitus can originate anywhere along the audiologic pathway. In some cases, the source has remained unknown, which has led to the hypothesis that tinnitus is a phantom perception that is analogous to phantom pain (1,2). The role of cortical control is interesting from both scientific and therapeutical points of view. Changes in cortical activity can both elicit and suppress tinnitus. Thalamocortical dysrhythmia due to increased theta and gamma activity could be responsible for tinnitus (3). When coexisting with hearing loss, tinnitus might be the result of neuronal hyperactivity provoked by reduced peripheral input (4). This hyperexcitability is suspected to be located in parts of the auditory cortex that represent intact hearing frequencies (5). The left temporal gyrus is overactivated, independent of tinnitus laterality (6). Suppression of tinnitus was positively correlated with activation of the left and right temporal gyrus and the parahippocampal-hippocampal interface (6). In addition, increased spontaneous alpha power in the auditory cortex occurred in suppressed states. (7). Sound stimuli are believed to modulate the centrally generated sensations that result in tinnitus inhibition (2). Where tinnitus and sound interact, however, is not known. The effects of sound might be psychogenic, and long-term sound application could be harmful.
Table 1 - Global differences in EEGs between the healthy subjects and tinnitus patients.

| Condition          | Number of tests performed | Number of significant tests | Significance |
|--------------------|---------------------------|-----------------------------|--------------|
| Basic recording    | 228                       | 6                           | 0.9734       |
| Eyes open          | 228                       | 3                           | 0.9969       |
| Acoustic stimulation | 228                     | 10                          | 0.5910       |
| Photostimulation   | 228                       | 7                           | 0.8870       |
| Hyperventilation   | 228                       | 34                          | 0.0000       |
| Pathologic patterns | 152                      | 26                          | 0.0000       |

Number of tests performed: measurements of mean and maximal amplitudes of cortical activity gathered from each EEG electrode (together = 228 results to compare); number of significant tests: number of tests showing a significant difference ($p<0.05$) between the healthy and tinnitus groups based on Student’s t-test; significance: results of Student’s t-test for the whole analyzed condition. Significant differences between groups with regard to hyperventilation are explained in the Discussion (line 11).

In the present study, we compared spontaneous and sound-modulated electroencephalography (EEG) recordings between tinnitus patients and healthy controls.

## MATERIALS AND METHODS

The tinnitus patient group consisted of 50 individuals (24 women and 26 men) aged 20 to 63 (mean: 42.5) years with tinnitus who were not selected according to any tinnitus factors. The subjects’ tinnitus was subjective, located in the head. Acoustic stimulation (16 patients), atheromatosis (11 patients), hyperlipidemia (21 patients), arterial hypertension (5 patients), allergy (4 patients), depression (3 patients), occupational exposure to noise (2 patients), nicotinism and coronary disease (1 patient each). The features and outcomes of tinnitus were as follows:

- **a)** localization: right ear = 11 cases; left ear = 15 cases; bilateral = 24 cases;
- **b)** nuisance (minimal = 1, serious daily trouble = 10): 1-4 = 11 cases; 5-8 = 24 cases; 9-10 = 15 cases;
- **c)** effect of masking: present = 6 cases; lacking = 44 cases;
- **d)** time result: permanent tinnitus = 35 cases; interrupted tinnitus = 15 cases; and
- **e)** psychological effect: disturbed concentration = 32 cases; disturbed sleeping = 7 cases; nervousness = 11 cases.

The control group consisted of 25 healthy subjects (12 women, 13 men) aged 18-61 (mean: 40.4) years old with no otoneurologic symptoms. Hearing based on tonal audiometry was normal (not more than a 15-dB loss) in both ears. EEG recordings were obtained in the same manner as in the tinnitus group; acoustic stimulation was the same in every patient, presented through air conduction, with earphones applied to the ear that experienced the tinnitus or binaurally when the tinnitus was located in the head. Acoustic stimulation was performed in a silent room for 2 minutes. Hyperventilation was induced by taking 40 deep breaths per minute; at frequencies in the following sequence: 1, 3, 7, 10, 15, 20, 25, 30 and 50 Hz.

The control group consisted of 25 healthy subjects (12 women, 13 men) aged 18-61 (mean: 40.4) years old with no otoneurologic symptoms. Hearing based on tonal audiometry was normal (not more than a 15-dB loss) in both ears. EEG recordings were obtained in the same manner as in the tinnitus group; acoustic stimulation was the same in every case, and a 1000-Hz, 40-dB stimulus was presented.

### Ethics

The procedures were conducted in accordance with the ethical standards of the responsible committee on human...
RESULTS

Global differences were observed in the EEG recordings between the healthy subjects and tinnitus patients (Table 1). The responses to hyperventilation were significantly different. Therefore, we analyzed the type and localization of the significant changes. Spontaneous cortical activity with eyes closed revealed differences predominantly in the mean amplitude of the beta and delta waves between the groups. In the tinnitus patients, the power of the delta activity was decreased, whereas the power of the beta activity was increased (Table 2). Changes in the cortical activity under both the eyes-open and eyes-closed conditions were located strictly in the temporal regions. Tinnitus patients under acoustic stimulation showed amplitude changes in both the alpha and beta waves in the right temporal and frontal regions and the left occipital cortex (Table 3). Acoustic stimulation was followed by a decline in the beta power in the parietal region and an increase in the alpha power in the occipital and temporal regions. The mean and maximal amplitudes of the beta and alpha waves changed, and there were no regions in which the cortical activity remained the same (Table 4). Pathologic patterns were observed in the EEG recordings from tinnitus patients. Both the number and amplitude of the patterns described above were greater in the tinnitus patients than the healthy subjects (Tables 1 and 5).

When acoustic stimulation matched the pitch and intensity of the tinnitus in tinnitus patients, the total maximal power of the cortical activity increased in the frontal, central, parietal and temporal regions but only bilaterally in the central cortex (Table 6). Changes were detected in the mean amplitude of beta-1, beta-h, alpha-1 and delta waves and in the maximal amplitude of delta waves (Table 6).

DISCUSSION

EEG activity differed significantly between the healthy subjects and tinnitus patients. Changes in cortical activity were most frequently observed in the bilateral temporal lobes. Because these areas are involved in normal hearing, the pathology in tinnitus cases was suspected to be localized only in this region. This finding supports the hypothesis that tinnitus is not a “phantom” phenomenon but rather results from inappropriate cortical auditory perception, usually hyperactivity or activity, without any auditory input (8,9). The migration of tinnitus cortical generators over time is possibly represented by changes in activity in the auditory cortex, motor area, insula and prefrontal lobes (10).

The changes in cortical activity in the tinnitus patients included decreased delta wave amplitudes and increased beta-1, beta-h, and alpha-1 wave amplitudes. According to Vanneste (10), high-frequency waves are associated with...
Table 6 - Significant differences between EEG recordings with eyes closed and EEG recordings during phonostimulation in the tinnitus patients.

| Group         | Variable         | Eyes closed | Phonostimul. | Significance of Levene’s test | Variance in 2 groups | Statistics t | Df | Significance of t test (2 tail) 95% CI |
|---------------|------------------|-------------|--------------|------------------------------|----------------------|--------------|----|-----------------------------------|
| Tinnitus group | Amax for Fp1Fpz  | 47.6        | 20.7         | 68.0                         | 57.5                 | 0.002        | Different | 2.37 | 61.51 | 0.021 | -37.7 | -3.2 |
|               | Amax for FzFpz   | 5.1         | 12.3         | 17.3                         | 27.2                 | 0.000        | Different | -2.89 | 68.33 | 0.005 | -20.6 | -3.8 |
|               | Amax for C3Fpz   | 1.54        | 3.74         | 4.23                         | 4.36                 | 0.001        | Different | -2.31 | 95.82 | 0.023 | -3.49 | -0.27 |
|               | Amax for C4Fpz   | 6.0         | 9.6          | 15.1                         | 19.8                 | 0.026        | Different | -2.92 | 70.93 | 0.005 | -15.3 | -2.9 |
|               | Amax for CzFpz   | 2.24        | 3.48         | 4.16                         | 3.87                 | 0.047        | Different | -2.61 | 96.90 | 0.011 | -3.38 | -0.46 |
|               | Amax for PzFpz   | 15.1        | 7.4          | 21.5                         | 15.6                 | 0.004        | Different | -2.63 | 69.98 | 0.010 | -11.3 | -1.6  |
|               | Amax for T6Fpz   | 7.5         | 10.1         | 13.3                         | 14.2                 | 0.053        | Equal      | -2.36 | 98   | 0.020 | -10.7 | -0.9 |
|               | Average for Fp2Fpz | 11.26      | 4.12         | 13.86                        | 6.99                 | 0.063        | Equal      | -2.27 | 98   | 0.026 | -4.88 | -0.32 |
|               | Amax (D) for F3Fpz | 16.9       | 7.5          | 21.0                         | 11.8                 | 0.156        | Equal      | -2.08 | 98   | 0.040 | -8.0  | -0.2  |
|               | Amax (D) for T6Fpz | 11.38      | 4.25         | 13.52                        | 6.26                 | 0.024        | Different | -2.00 | 86.22 | 0.049 | -4.27 | -0.01 |
|               | Aav (D) for Fp2Fpz | 12.94      | 5.31         | 15.84                        | 8.19                 | 0.039        | Different | -2.10 | 84.02 | 0.039 | -5.64 | -0.16 |
|               | Aav (Al) for F3Fpz | 18.12      | 6.22         | 15.96                        | 3.65                 | 0.009        | Different | -2.12 | 79.17 | 0.037 | -0.13 | 4.19 |
|               | Aav (Bl) for F4Fpz | 21.9       | 10.4         | 26.7                         | 12.2                 | 0.648        | Equal      | -2.12 | 98   | 0.036 | -9.3  | -0.3  |
|               | Aav (Blh) for C3Fpz | 21.7       | 6.4          | 25.3                         | 9.2                  | 0.245        | Equal      | -2.24 | 98   | 0.027 | -6.7  | -0.4  |
|               | Aav (Blh) for O1Fpz | 30.6       | 18.8         | 39.7                         | 19.2                 | 0.737        | Equal      | -2.38 | 98   | 0.019 | -16.6 | -1.5  |

Abbreviations: Aav: average amplitude; Amax: maximal amplitude; 95% CI: 95% confidence interval; SD: standard deviation. Rhythms: A = alpha, B = beta, D = delta. Cortical regions: T = temporal, P = parietal, F = frontal, O = occipital, C = central.
and increased alpha-1, beta-1 and beta-h wave amplitudes demonstrate a pathologic pattern;
3. Significant alterations in spontaneous cortical activity induced by acoustic stimulation were only observed in the tinnitus patients, and despite individual matching of the applied sound, the pathologic changes only slightly improved;
4. The usefulness of sound therapy for tinnitus should be considered together with the results of other objective studies, e.g., positron emission tomography; and
5. EEG is an effective method for evaluating cortical modification after sound stimulation, but some psychological limitations to this method should be taken into consideration.

AUTHOR CONTRIBUTIONS
Pawlak-Osińska K conceived the idea and wrote the manuscript. Kazmierczak W prepared the manuscript for publication. Kazmierczak H conducted the literature review. Wierzchowska M collected and prepared the data. Matuszewska I obtained the EEG recordings.

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