

PERSPECTIVES FOR TOTAL ELIMINATION OF TINNITUS PERCEPTION

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ABSTRACT

The goal of treatment based on the neurophysiological model of tinnitus is to induce and facilitate the habituation of tinnitus perception, thus resulting in a decrease of time that a patient is aware of tinnitus. Ultimately, the patient would perceive tinnitus only when focusing their attention on it. Gradual detuning of the neuronal networks involved in detecting the tinnitus signal may be the physiological mechanism responsible for this effect. If this detuning progresses further, it is possible to expect that the tinnitus-related neuronal activity will be filtered-out totally, resulting in the patient's inability to perceive tinnitus, even when attempting to do so. This effect can be expected to emerge in patients undergoing prolonged therapy. A survey revealed that, indeed, perception of tinnitus disappears totally for an average of 10.5 days in 19.6% of the patients who undergo habituation treatment. Furthermore, in cases where masking was implemented for several years, without inducing habituation, switching to the protocol with low level broad-band noise and directive counseling (retraining therapy) resulted in the rapid development of habituation.

In our clinic in London the treatment of tinnitus patients is based on a neurophysiological model of tinnitus¹⁻³, which is aimed at habituation of tinnitus-evoked aversive reactions and tinnitus perception^{4,5}. The first goal is to reach a point where the patient is aware of tinnitus but is no longer bothered or concerned by it, while the second, and primary aim is to reach the stage of habituation of the tinnitus perception, i.e., the patient is not aware of tinnitus presence except when focusing attention on tinnitus. The model predicts the possibility of some patients achieving habituation of tinnitus to such an extent that they will have periods of time when they are unable to evoke the perception of tinnitus, even when focusing attention upon it. We noticed that some patients do indeed report such a phenomenon. Accordingly, this study was aimed at investigating the prevalence and the extent of this phenomenon.

A total of 149 patients were included in this study. The longest time of observation was 15 years and 8 months, the shortest 7.5 months. Patients were asked to respond verbally to questions presented either face-to-face at clinical follow-up or over the telephone, following a specifically prepared questionnaire. For this paper only those variables will be presented which directly relate to the possibility and the extent of total blockage of the tinnitus signal, i.e., the patient is unable to evoke the perception of tinnitus, even when attempting to do so, and selected other variables which provide a base line for the extent of habituation:

- % of awareness of tinnitus at its start (AwS);
- % of awareness just before the beginning of treatment (AwB);
- % of awareness after one year of treatment (Aw1y);
- % of awareness now (AwN);

- presence/absence of periods when it was impossible to evoke tinnitus;
- duration of the absence of tinnitus, if it happened;
- time from the beginning of the treatment when annoyance decreased significantly;

Out of 149 patients, 143 (96.0%) reported improvement, with 28 (19.6% of improving) experiencing periods of time when tinnitus was totally absent and could not be evoked by focusing attention on it. The average duration of this period was 10.52 +/- 4.35 days (mean ± SEM). Table 1 presents the percentage of tinnitus awareness and its changes during the treatment. The means for changes were calculated as a mean of changes for individual patients.

Table 1: Awareness at the various stages of treatment

	AwB	Awly	AwN	(Awly-AwB)/AwB	(AwN-AwB)/AwB
better & disappearing	74.0±6.4 (28)	39.3±6.4 (26)	19.3±5.2 (26)	-34.3±5.6 (26)	-54.8±6.2 (26)
better & not disappearing	80.2±2.5 (115)	45.0±3.0 (98)	17.3±2.2 (98)	-34.7±3.2 (98)	-62.7±3.2 (98)
no better	80.8±9.9 (6)	73.3±11.4 (6)	82.5±10.7 (6)	-7.5±11.4 (6)	1.7±17.7 (6)

All data are in percentages ± SEM, with the number of cases in parentheses. AwB — awareness at the beginning of treatment; Awly — awareness after 1 year of treatment; AwN — awareness now; (Awly-AwB)/AwB — percentage change of awareness during first year of treatment; (AwN-AwB)/AwB — percentage change of awareness during entire treatment.

Due to very limited number of patients with no improvement, all the following analyses were performed only for patients reporting improvement. The population was divided into patients reporting total temporal disappearance of tinnitus and those who can always evoke tinnitus when focusing their attention on it.

Collected data allowed for basic characterization of the patient population and for assessing the effectiveness of the treatment over extensive periods of time. First, for evaluating the effectiveness of a treatment it is important to assess the homogeneity of our patients, as far as their awareness of tinnitus is concerned. Second, there is a possibility that patients recover spontaneously, with or without treatment. Third, while a neurophysiological model predicts lack of correlation of changes of awareness from the initial level of awareness at the beginning of the treatment, intuitive judgement, based on the cochlea-centric model predicts that patients with a higher severity of tinnitus should exhibit less improvement. Finally, it is interesting to find out if the level of awareness can be used as a predictor for cases when periods of total absence of tinnitus is experienced.

Figures 1-3 present level of awareness before, AwB (Fig 1), 1 year after the treatment, Awly, (Fig 2), and at the time of interview, AwN (Fig 3), relating these results to the AwB. Consistently, panel A shows raw data of awareness as a function of time, panel B shows change in awareness normalized as a percentage of AwB as a function of time, and panel C shows the change in awareness as a function of AwB. Furthermore, "all patients" are divided into patients who can always evoke perception of tinnitus when focusing their attention, labelled "tinnitus not disappearing" (open circles and dashed line), and those who experience periods when they are unable to evoke tinnitus perception, labeled "tinnitus disappearing" (full circles and solid line).

The level of AwB was stable over an analyzed period of 15 years and is close to 80% (Fig 1A). There was no significant correlation of AwB with time when treatment was initiated ($r=0.1583$, $n=114$, $t[112]=1.70$, N.S.; and $r=0.0142$, $n=28$, $t[26]=0.07$, N.S.; for groups with tinnitus disappearing and not-disappearing, respectively). These data indicate, that our population of patients was homogenous over an extensive period of time, and any time-dependent changes cannot be attributed to changes in the profile of patient's awareness. Notably, there was no difference between two subpopulations of patients. This

suggests that the initial level of awareness may not be a determinant for achieving the state of inability to recall tinnitus perception. The small number of patients and ceiling effect prevent us from making the final judgement, and more data are needed to clarify this issue.

For any type of study evaluating the effectiveness of the treatment it is imperative to establish the rate of spontaneous recovery. Thus, the difference between the level of AwB and AwS was normalized by dividing the difference (AwB-AwS) by AwB and plotted as the function of time (Fig 1B). There is a statistically significant tendency to increase the level of awareness during the pretreatment period by an average of 15.9% ($14.69 \pm 3.75\%$, mean \pm SEM, $n=110$, $t[109]=3.92$, $p<0.001$; and $21.11 \pm 6.24\%$, $n=25$, $t[24]=3.38$, $p<0.01$ for groups with tinnitus not-disappearing and disappearing, respectively), which is stable in the function of time. This contradicts the possibility that patients recover spontaneously; if anything, their awareness of tinnitus tends to increase, and further supports the homogeneity of our patient population.

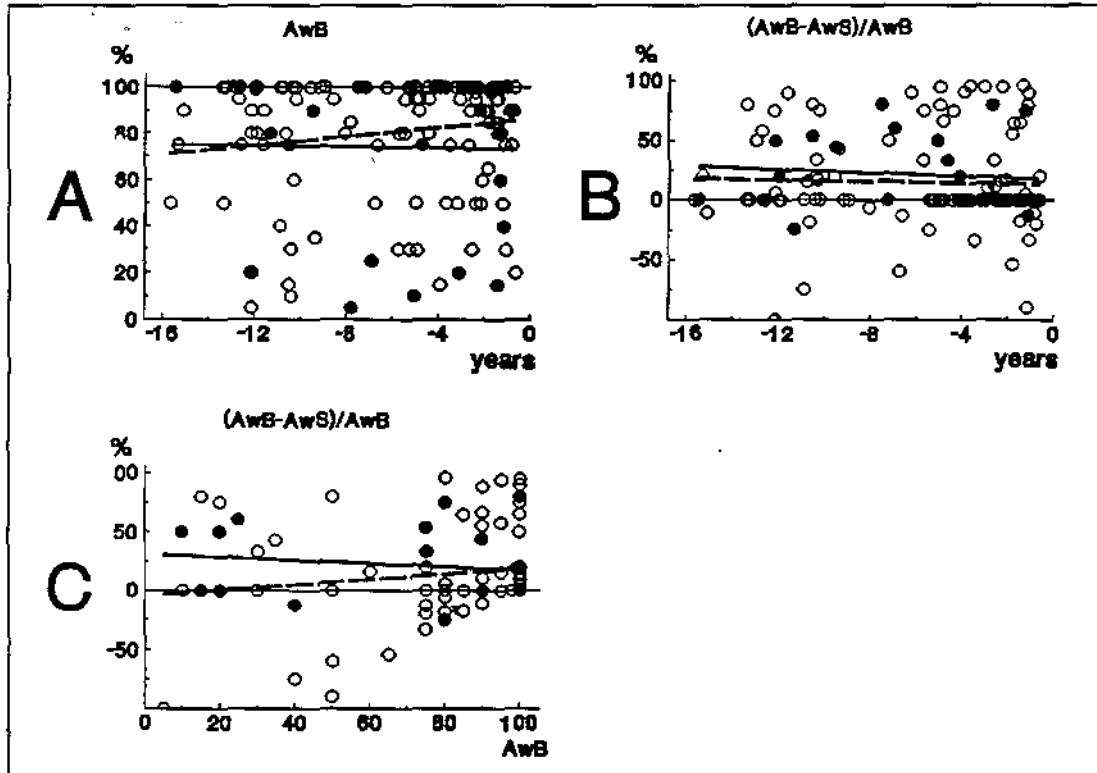


Figure 1: Characterization of the awareness at the beginning of the treatment (AwB). Panel A shows raw data for awareness at the beginning of the treatment (AwB) as a function of time when treatment was initiated. Panel B shows normalized change in awareness from the start of tinnitus to the beginning of treatment, i.e., $(AwB-AwS)/AwB*100$. Panel C shows the same normalized change but in function of AwB. In this and subsequent figures only patients reporting improvement are shown, and open circles and dashed line represent patients with not-disappearing tinnitus, while full circles and solid line represents patients with disappearing tinnitus.

A possibility that changes in the awareness are related to the level of awareness is explored using data presented in Fig 1C, which presents the same relative changes of awareness as shown in Fig 1B, but as a

function of AwB. There is no correlation between AwB-AwS and the level of AwB ($r=0.1595$, $n=110$, $t[108]=1.68$, N.S.; $r=0.1388$, $n=25$, $t[23]=0.21$, N.S.; for groups tinnitus not-disappearing and disappearing, respectively). There is no significant difference between the two subpopulations. Thus, while there is a significant tendency for increased awareness of tinnitus during the period of time from the start of tinnitus to the beginning of treatment, this increase does not depend on the AwB.

Next, we investigated Aw1y (Fig 2). The absolute level of Aw1y showed a significant tendency to decrease, suggesting that greater improvement occurred in recent years (Fig 2A). Linear regression analysis revealed borderline significance for dependence of the Aw1y on the time when the treatment was initiated ($r=0.1915$, $n=97$, $t[95]=1.90$, $p=0.06$; and $r=0.4191$, $n=26$, $t[24]=2.26$, $p<0.05$; for groups of tinnitus not-disappearing and disappearing, respectively).

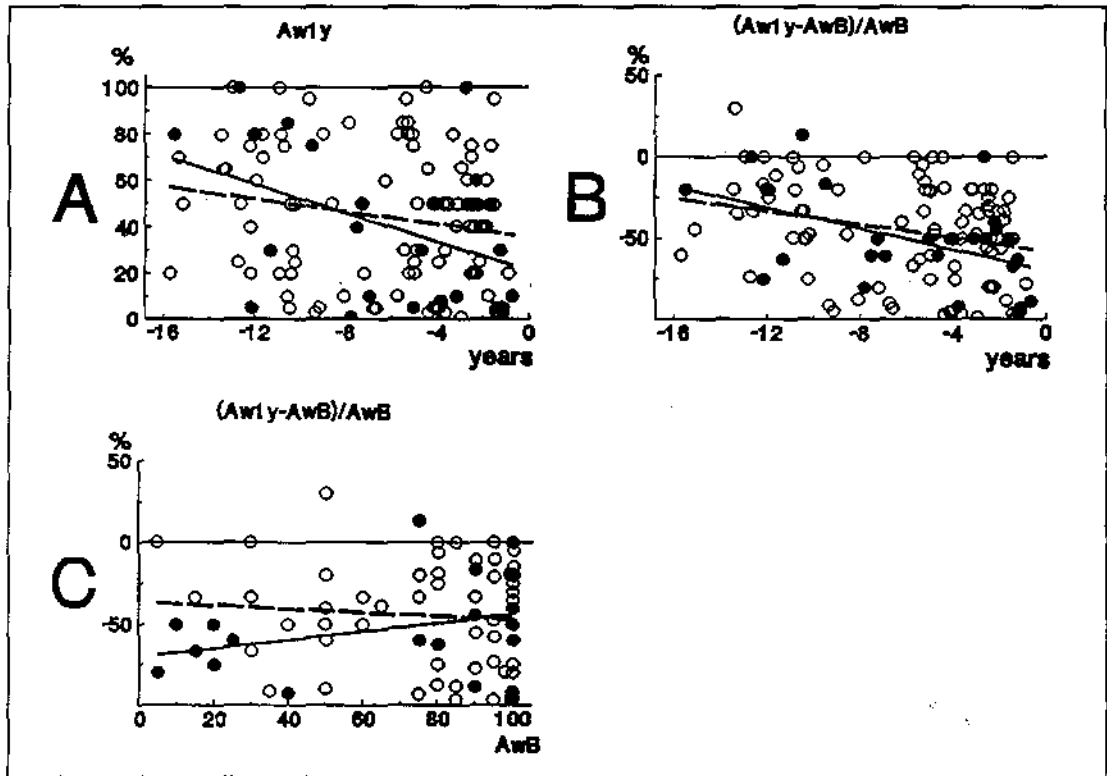


Figure 2: Characterization of the awareness after one year of treatment (Aw1y). Panel A shows raw data; panel B shows $(Aw1y-AwB)/AwB*100$ as a function of time; and panel C as a function of AwB.

Similar results were obtained after normalization of the Aw1y-AwB by dividing by AwB, showing significant dependence of the normalized change of awareness on time (Fig 1B; $r=0.2625$, $n=94$, $t[92]=2.61$, $p=0.01$; and $r=0.4783$, $n=26$, $t[24]=2.67$, $p<0.05$). Therefore, the results presented in Fig 2A and 2B suggest that our approach is presently more effective in inducing change of the awareness than it was in the past. While 15 years ago tinnitus awareness decreased on the average by only about 20% of the initial value, presently there is more than a 50% decrease.

Normalized changes of Aw1y do not show significant correlation from the level of AwB (Fig 1C; $r=0.089$, $n=94$, $t[92]=0.86$, N.S.; and $r=0.3157$, $n=26$, $t[24]=1.63$, N.S.). Thus, other factors are responsible for the observed increase of treatment effectiveness in decreasing of the level of tinnitus aware-

ness. One potential factor is a gradual shift from tinnitus masking, which would prevent habituation of tinnitus. However, a large proportion of patients were not masking their tinnitus in reality (but using "partial masking")⁶. Over the last 7 years there has been exclusive application of low level broad-band noise combined with directive counselling (retraining therapy) aimed at facilitating tinnitus habituation^{2,5}.

The dependence of the AwN on the time of treatment initialization is presented in Fig 3. The levels of AwN for both subpopulations of patients are close to 20%, and did not depend on the time of initialization of the treatment (Fig 3A; $r=0.0025$, $n=114$, $t[112]=0.27$, N.S.; and $r=0.0006$, $n=28$, $t=0.003$, N.S.). Furthermore, normalized AwN-AwB for both subpopulations did not depend on the time (Fig 3B; $r=0.045$, $n=114$, $t[112]=0.48$, N.S.; and $r=0.2157$, $n=26$, $t[24]=0.23$, N.S.) and decreased by about 76% in both groups. There is significant correlation between normalized change of awareness and the level of AwB for the not-disappearing group (Fig 3C, open symbols and dashed line; $r= -0.2557$, $n=114$, $t=2.80$, $p<0.01$), but not for the disappearing group ($r=0.2202$, $n=26$, $t=1.11$, N.S.). The negative correlation indicates that patients with larger AwB experience a larger relative improvement.

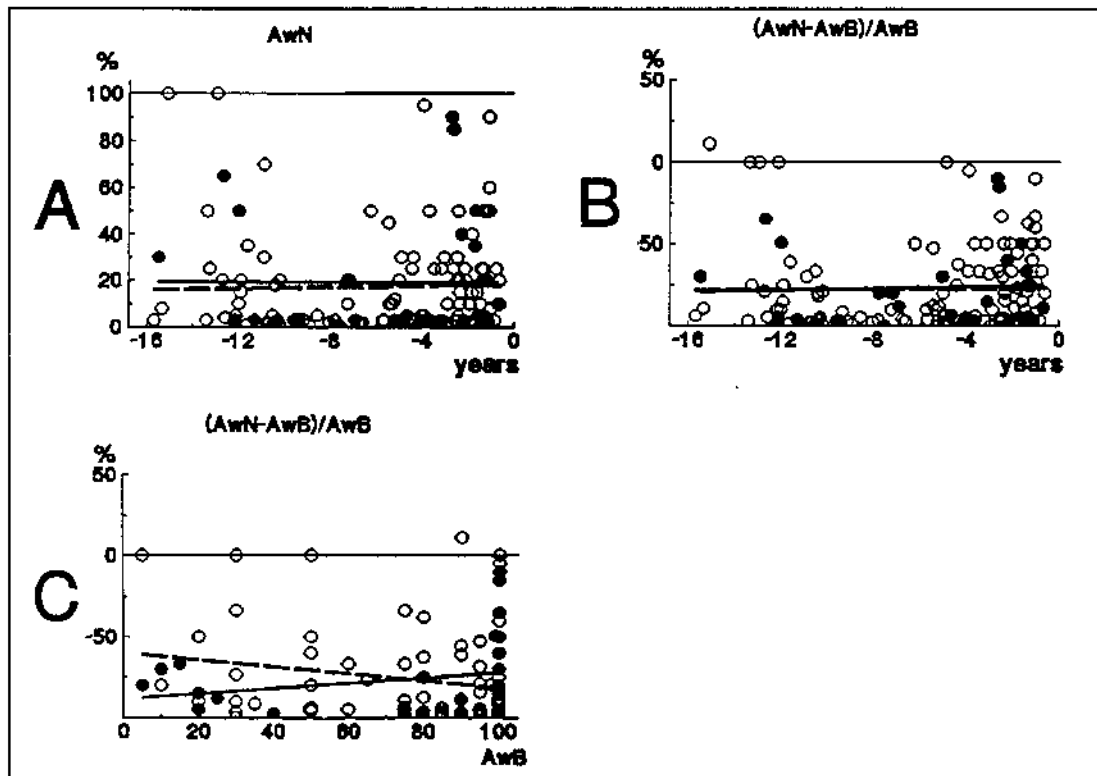


Figure 3: Characterization of the present level of awareness (AwN). All panels are analogical to previous figures.

An expectation could be that the time of significant improvement reported by patients should depend on the level of AwB, due to the expectation that more severe tinnitus should take more time for improvement. Furthermore, a difference could be expected between the patients who are able and the patients who are not able to evoke tinnitus. Results presented in Fig 4 contradict this expectation ($r=0.020$, $n=101$, $t[99]=0.20$, N.S., and $r=0.223$, $t[25]=1.14$, N.S.).

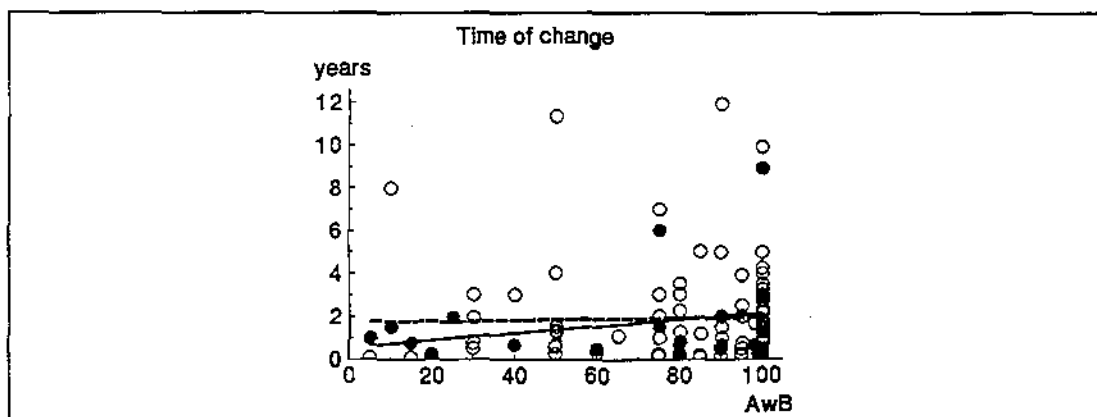


Figure 4: Dependence of the time, when patients reported significant improvement as a function of the AwB.

In conclusion, our results show that about 20% of patients experience periods of time when the tinnitus signal is blocked to the extent that the patient is unable to recall it. The average period of time was about 10 days. This does not depend on the pre-treatment level of awareness. Furthermore, all studied relationships between the time of starting treatment and the awareness of tinnitus and its changes were practically identical for patients experiencing or not experiencing the periods of tinnitus block. The data also show the increased effectiveness of treatment during the first year for patients treated more recently. Notably, there is a significant increase of the level of awareness between the start of tinnitus and the beginning of the treatment, which argues against the possibility of attributing the decrease of tinnitus awareness to spontaneous recovery. The combined results of this study support a neurophysiological model of tinnitus and indicate the possibility of achieving a state where the tinnitus signal is filtered so efficiently that the patient is unable to evoke tinnitus by focusing their attention on it. Further studies are needed to establish whether it is possible to facilitate the occurrence of this stage and induce it in a larger proportion of patients.

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