

Three Years Later: Report on the State of Well-Being of Patients with Chronic Tinnitus Who Underwent Modified Tinnitus Retraining Therapy

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Key Words

Chronic tinnitus · Day ward therapy · Psychological intervention · Psychometric parameters · Sustained effect

Abstract

Successful management of patients with chronic tinnitus is an important health issue. One of the tinnitus management strategies used at our Tinnitus Center is a combination of tinnitus retraining therapy (TRT) with physiotherapy and psychological management [called modified TRT (MTRT)]. We have used this type of management for over a decade and have described the protocol in detail elsewhere. In the present study, we wanted to determine the effect of MTRT on the well-being of tinnitus patients 3 years after treatment onset. One hundred and thirty patients with chronic tinnitus were assessed using psychometric instruments immediately before 7-day MTRT, immediately after the therapy and 3 years later. Patients with very severe tinnitus-related distress associated with major depression and a risk of suicide were excluded from this study. MTRT resulted in a sustained reduction of tinnitus-related distress. Moreover, the quality of life of patients had increased, as assessed by a separate questionnaire. The effect of MTRT was influenced by the degree of tinnitus-related distress and by the patients' age, the latter being gender dependent. Hearing loss and tinnitus duration had only a minor influence on the therapeutic effect. Taken

together, we report a positive change in the state of well-being of patients with chronic tinnitus measurable with various psychometric instruments 3 years after the onset of MTRT.

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Introduction

Tinnitus is a phantom sound perceived only by the affected person. Tinnitus can be a symptom accompanying diverse health conditions, such as hearing loss, diabetes, cardiovascular or autoimmune diseases, some tumors and many other causes. The neurophysiological model of tinnitus proposed by Jastreboff and Hazell [1993] considers tinnitus to be a result of inappropriate networking between the auditory, limbic and sympathetic nervous systems. Tinnitus retraining therapy (TRT), which was developed based on a neurophysiological model, is often used for chronic, annoying tinnitus [Bauer and Brozski, 2011; Forti et al., 2009; Henry et al., 2006; Herraiz et al., 2005; Jastreboff and Jastreboff, 2000, 2003, 2004]. The aim of TRT is to habituate patients to the reactions induced by tinnitus and to habituate them to tinnitus perception. The efficacy of TRT was tested in several clinical studies; however, various modifications in the TRT clinical protocol applied by various tinnitus-treating centers

do not permit solid conclusions [Phillips and McFerran, 2010].

In our clinical experience, the addition of physiotherapy and psychological interventions to the core TRT protocol proved to be very helpful not only in the treatment of tinnitus but also of common comorbid conditions, such as mild-to-moderate depression, anxiety or insomnia. The physical therapy methods used in our center include manual therapy, aquatic bodywork and progressive muscle relaxation. Use of physical therapy for tinnitus treatment aims at physical/muscle relaxation, which in turn improves the quality of sleep, reduces emotional tension and improves cognition. Psychological treatment is often not only an option but a must, as every other tinnitus patient suffers from a comorbid mental condition [Zirke et al., 2010, 2013]. The clinical protocol used in our study was published in detail previously [Seydel et al., 2010]. Modified TRT (MTRT) was successfully used not only at our center but also by others [Hesse, 2008; Schaaf et al., 2010].

In our previous study, we determined the well-being of patients with chronic tinnitus following MTRT in an outpatient setting [Caffier et al., 2006; Mazurek et al., 2006]. We measured tinnitus-related distress with the German version of the Tinnitus Questionnaire (TQ) [Goebel and Hiller, 1998] and followed the patients for 1 or 2 years. Recently, we have demonstrated a positive effect of MTRT applied in the condensed form of a 7-day therapy in a day ward setting with follow-up counseling sessions up to 1 year after therapy onset [Seydel et al., 2010]. In that study, in addition to TQ, other psychometric instruments were used, namely the Perceived Stress Questionnaire (PSQ) and the General Depression Scale ['Allgemeine Depressionsskala' (ADS)]. Moreover, factors possibly influencing therapeutic efficiency such as gender, patients' age and duration of tinnitus were analyzed. We found that in the entire cohort of patients tested 1 year after the beginning of MTRT, the TQ score decreased significantly, whereas the scores indicating perceived stress or depression remained significantly unchanged. The efficacy of MTRT measured 1 year after its onset depended on the severity of disease, age and gender.

Here, we wanted to determine how long-lasting the efficacy of our treatment is. Therefore, in our present work, we focused on assessing the welfare of tinnitus patients 3 years after MTRT therapy onset. In addition to the psychometric tools used in our recent study [Seydel et al., 2010], we used the Anamnestic Comparative Self-Assessment (ACSA) to determine changes in quality of life.

Patients and Methods

This study was approved by the local ethics committee, and all participants gave their written consent. The entire study has been conducted according to the principles expressed in the Declaration of Helsinki.

One hundred and thirty patients (69 women and 61 men) with chronic tinnitus who were successively admitted to the day ward of our Tinnitus Center participated in the present study after signing the consent. The period of investigation was 4 years (July 2006 until May 2007, follow-up until April 2010). All patients had continuous tinnitus for at least 3 months. The patients were between 22 and 79 years old at the onset of the study, with an average age of 53.0 years [standard deviation (SD) 11.4]. The mean age of women was 51.4 years (SD 11.2) and of men 54.8 years (SD 11.5).

Patients with very severe tinnitus-related distress accompanied by major depression and a risk of suicide according to the ICD-10 (International Classification of Diseases) were excluded from this study and referred to another type of treatment (comprehensive inpatient treatment with psychological and psychotherapeutic approaches). The clinical protocol of MTRT and follow-up was not altered for the study and the only change was the addition of the ACSA questionnaire to monitor differences in the quality of life.

Patients' data were analyzed before the onset of therapy (T0), immediately after 7 days of therapy (T1) and 3 years later (T2).

The pretherapeutic mean hearing loss measured as an average of two contiguous test frequencies over the frequency range of 0.5–8 kHz was 25.3 dB (SD 15.9; range 2.5–108 dB) in the left ear and 23.4 dB (SD 16.1; range 2.5–100 dB) in the right ear without significant lateral differences (Mann-Whitney U test). Normal hearing (≤ 20 dB) was found in 38% of the left ears and 50% of the right ears. A low level of hearing loss (>20 –40 dB) was found in 46% of the left ears and 37% of the right ears. A higher level of hearing loss (>40 dB) was found in 16% of the left ears and 13% of the right ears.

Audiological, psychological and physical examinations were performed before the therapy onset. Every day, the patients practiced progressive muscle relaxation under supervision, which has been shown to be an effective technique for stress management [Storb and Strahl, 2006; Weber et al., 2002]. All patients took part in the following modules of MTRT: (1) counseling (comprising information about basic hearing physiology, the anatomy and function of the auditory system, the neurophysiological model of tinnitus generation, perception and factors possibly worsening the tinnitus perception and models of stress and stress management); (2) daily acoustic therapy (e.g. defocusing exercises to reduce the perception of tinnitus by intensifying external sounds); (3) physiotherapy and daily cognitive-behavioral group therapy dealing with dysfunctional cognition concerning tinnitus or anxiety, with sleep disturbance and stress management, and (4) 2 or 3 individual psychological consultations aimed at the identification and treatment of symptoms of stress, depression, anxiety and internal apprehension. These specific sessions were conducted by clinical psychologists and allowed individual treatment according to the degree of psychological comorbidities.

MTRT was conducted by an interdisciplinary team composed of otorhinolaryngology specialists, clinical psychologists, psychosomatic medicine specialists and physiotherapists. Psychosomatic medicine is a regular medical discipline studying the integration of

biological, psychological and social factors in medicine applied in the diagnosis and treatment of tinnitus [Hesse and Laubert, 2001]. The patients were not fitted with hearing aids at our center but were referred to a specialist. Following the 7-day therapy, patients were seen every 3 months for counseling and auditory check-up in the form of pure-tone audiometry, speech audiometry, auditory evoked potentials and tinnitus matching. The precise therapeutic and follow-up schedule has been described and published earlier [Seydel et al., 2010].

Psychometric Instruments Used in This Study

Tinnitus Questionnaire

The German version of the TQ is a psychometric instrument for the assessment of tinnitus-related annoyance [Goebel and Hiller, 1998]. The TQ has been evaluated in numerous studies and is often used in Germany to determine the tinnitus severity level [Adamchic et al., 2012]. The score of the TQ ranges from 0 to 84. The total score of the TQ can be split into 4 severity levels: low (1–30), moderate (31–46), severe (47–59) and very severe impairment (60–84). Tinnitus is regarded to be ‘compensated’ at a TQ level of ≤ 46 (no secondary symptoms) and ‘decompensated’ at a TQ level of ≥ 47 (permanent annoyance and psychological strain, accompanied by complaints such as depression, anxiety, impaired sleep and concentration) [Biesinger et al., 1998]. A total of 52 items are used to measure specific fields of tinnitus-related distress by means of subscales labeled ‘emotional distress’, ‘cognitive distress’, ‘intrusiveness’, ‘auditory perceptual difficulties’, ‘sleep disturbances’ and ‘somatic complaints’. Forty items are assigned to 6 subscales with 3 answers each. The sum of the subscales results in a global score of tinnitus distress. The remaining items allow additional reference to individual tinnitus annoyance. The TQ had high internal consistency, high convergence and discriminant validity and good change sensitivity in an unselected large multinational clinical sample and, thus, appears appropriate for evaluating the effects of tinnitus treatments in a cross-cultural context [Zeman et al., 2012]. It can be applied in comparative studies at different tinnitus-related institutions and for the evaluation of the relative effects of different treatment approaches. The split-half reliability is 0.94 and Cronbach’s α is 0.94 [Goebel and Hiller, 1998].

Perceived Stress Questionnaire

The PSQ measures subjective stress perception. It consists of 20 items (short version), allowing the subdivision into the 4 subscales ‘worries’ (anxiety concerning the future, general frustration), ‘tension’ (exhaustion, imbalance, lack of physical relaxation), ‘joy’ (satisfaction) and ‘demands’ (lack of time, deadline pressure, being stressed out by duties and responsibilities) indicating the global levels of perceived stress [Fliege et al., 2005; Levenstein et al., 1993]. The subscale ‘joy’ was recorded in the total score. Multiplication of the item scores of each subscale and of the total score by a factor of 100 results in a scale ranging from 0 to 100. According to Kocalevent et al. [2007], the cutoff score for a low level of perceived stress is 49 applying the PSQ-20. Split-half reliability is in the range of 0.80–0.88 and Cronbach’s α is 0.90.

General Depression Scale

Chronic tinnitus may be associated with depressive symptoms such as anxiety, low self-esteem or emotions such as hopelessness and helplessness. In our study, we used the full version of the General Depression Scale (ADS) introduced and validated by Hautz-

inger and Bailer [1993]. The ADS comprises 20 items; its total score ranges from 0 to 60 points. An ADS score >23 indicates depressive disorder.

Anamnestic Comparative Self-Assessment

The ACSA assesses the present subjective quality of life [Bernheim, 1986]. Patients are asked to rate their global well-being in comparison to their personal best (+5 on the rating scale) and worst (–5 on the rating scale) periods in life. ACSA is a one-dimensional rating scale with a total of 10 levels. The validation of the scale was based on a pilot study with cancer patients [Bernheim, 1986]. Split-half reliability is in the range of 0.78–0.98.

All outcome measures described in the present study have routinely been used in our clinical practice since the year 2003.

Statistics

Tinnitus parameters and hearing loss of the right and left side were compared using the Mann-Whitney U test. One-way ANOVA was used to analyze the changes in the psychometric scores following therapy. The scores of the subscales (TQ and PSQ) were analyzed by MANOVA followed by univariate tests. The influence of tinnitus severity level, gender, age or duration of tinnitus on the psychometric score was tested using three-way or two-way ANOVA. Bonferroni’s post hoc test was applied to compare individual scores. The correlation between the patients’ hearing ability and the therapy outcome after 3 years was analyzed using Spearman’s rank correlation. All statistical tests and graphics were made using Statistica 7.1 (StatSoft).

Results

Lasting Effect of MTRT on Tinnitus-Related Distress Evaluated by TQ, PSQ, ADS and ACSA

Three years after the onset of MTRT, patients reported a significant improvement in their state of well-being, as indicated by all psychometric instruments used (table 1). The post hoc test revealed a significant reduction of tinnitus distress (TQ) and depression (ADS) scores and an increase in the quality of life (ACSA scores) immediately after the 7-day therapy. Three years later, tinnitus distress and perceived stress had decreased even further, the ACSA scores indicating that the quality of life remained on a higher level, whereas the depression scores had increased.

For the TQ and PSQ subscales, a multivariate test (Wilk’s λ) revealed a significant score reduction with $F_{12, 764} = 4.90$ ($p < 0.0001$) for the TQ and $F_{8, 768} = 3.94$ ($p < 0.001$) for the PSQ. The univariate test results of the TQ and PSQ subscales following MANOVA are listed in table 2.

We found a significant decrease of scores in the specific subscales representing tinnitus distress (TQ), namely in emotional and cognitive distress, in intrusiveness of tinnitus and in sleep disturbance. The post hoc test con-

Table 1. Changes in tinnitus-related distress evaluated using the TQ, PSQ, ADS and ACSA before (T0), immediately after (T1) and 3 years after MTRT (T2)

	Scores			F _(d.f.)	p
	T0	T1	T2		
TQ	35.6±15.0	28.0±14.9***	27.1±17.3****	11.4 _(2, 387)	<0.0001
PSQ	42.9±18.0	39.5±16.9	37.1±17.8*	3.5 _(2, 387)	<0.05
ADS	16.2±9.8	11.4±8.0***	14.9±10.2	9.0 _(2, 387)	<0.001
ACSA	4.33±2.26	5.50±2.06****	5.23±2.23**	10.2 _(2, 386)	<0.0001

Values are means ± SD. * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001 vs. T0 (Bonferroni's post hoc test).

Table 2. Changes in tinnitus-related distress evaluated using the subscales of the TQ and PSQ before (T0), immediately after (T1) and 3 years after MTRT (T2)

	Scores			F _{2, 387}	p
	T0	T1	T2		
TQ					
Em	9.9±5.1	7.1±5.0****	6.5±5.5****	15.8	<0.0001
Co	5.8±4.0	4.5±3.6*	4.2±4.0**	6.1	<0.01
Inti	9.9±3.2	7.6±3.4****	7.7±4.0****	17.1	<0.0001
Apd	4.9±3.5	4.0±3.0	4.4±3.5	2.2	n.s.
Sl	3.3±2.3	2.8±2.3	2.5±2.4*	3.5	<0.05
Som	1.9±1.6	2.0±1.8	1.7±1.7	0.6	n.s.
PSQ					
Worries	38.6±22.1	34.3±20.1	28.9±22.2***	6.6	<0.01
Tension	53.3±19.8	49.3±18.3	46.0±23.0*	4.1	<0.05
Joy	54.4±23.1	56.3±23.0	53.2±21.8	0.6	n.s.
Demands	47.2±23.9	43.1±23.4	40.5±23.5	2.7	n.s.

Values are means ± SD. Em = Emotional distress; Co = cognitive distress; Inti = intrusiveness of tinnitus; Apd = auditory perceptual difficulties; Sl = sleep disturbance; Som = somatic complaints; n.s. = not significant. * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001 vs. T0 (Bonferroni's post hoc test).

firmed the significance of this finding. The level of auditory perceptual difficulties and somatic complaints remained unaffected.

The perceived stress (PSQ) subscales 'worries' and 'tension' were also significantly reduced 3 years after the therapy onset, whereas the scores for 'joy' and 'demands' had not changed.

Clinical Significance of TQ, PSQ and ADS Scores

Seventy percent of patients (91 of 130) had lower tinnitus distress (TQ) scores by at least 5 points, indicating an effective clinical value of therapy 3 years after MTRT onset [Adamchic et al., 2012].

At the beginning of this study, 57 patients perceived stress above the normal range (score >49 points), whereas the rest (73 patients) scored within the normal limit [Kocalevent et al., 2007]. Three years later, 46% of patients (26 of 57) with initially higher scores of perceived stress had lower scores in the normal range. Except for 3 of 73 patients with initially normal stress levels, all remained in the low-score group.

One hundred and six patients initially presented with low depression scores (ADS), whereas the remaining 24 patients scored high according to Hautzinger and Bailer [1993]. Three years after therapy onset, 14 (58%) of 24 patients with an initially high ADS level scored low,

Table 3. Changes in tinnitus-related distress in patients with high and low level of tinnitus-related distress measured by the TQ, PSQ and ADS before (T0), immediately after (T1) and 3 years after MTRT (T2)

	Scores			F _(d.f.)	p
	T0	T1	T2		
TQ					
High level	56.9±7.9	46.7±12.2**	47.3±15.7*	6.2 _(2, 84)	<0.01
Low level	29.5±10.2	22.7±10.7****	21.3±12.8****	15.4 _(2, 300)	<0.0001
PSQ					
High level	59.7±11.7	53.5±13.0*	49.3±15.1***	8.7 _(2, 168)	<0.001
Low level	29.8±8.6	28.6±10.3	27.6±13.4	0.7 _(2, 216)	n.s.
ADS					
High level	32.3±6.2	19.1±10.9****	23.6±11.5**	11.1 _(2, 69)	<0.0001
Low level	12.6±6.1	9.7±6.0**	12.9±8.7	6.6 _(2, 315)	<0.01

Values are means ± SD. * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001 vs. T0 (Bonferroni's post hoc test).

while 10 patients (42%) remained in the group with a higher ADS level. Nine of 106 patients with an initially low ADS level had increased scores.

Therapy Outcomes in Patients with Different Degrees of Tinnitus Annoyance, Perceived Stress and Depression

In order to analyze the dependence of the therapy outcome on the degree of tinnitus-related distress, patients were split into two subgroups according to their TQ, PSQ and ADS score levels. There were 29 patients with a higher (TQ >46) and 101 patients with a lower level (TQ ≤46) of tinnitus annoyance; 57 patients with a higher (PSQ >49) and 73 patients with a lower level (PSQ ≤49) of perceived stress, and 24 patients with a higher (ADS >23) and 106 patients with a lower level (ADS <23) of depression.

The data were analyzed with a two-way ANOVA using time (T0, T1 and T2) and severity level of tinnitus as independent variables to analyze the interaction effect. The interaction effect was not significant for the TQ (F_{2, 384} = 0.48). However, the PSQ and ADS scores changed differently in the groups with a higher and a lower severity level over time (interaction effects F_{2, 384} = 3.82, p < 0.05, for the PSQ and F_{2, 387} = 10.5, p < 0.0001, for the ADS).

The groups with initially higher and lower severity level of tinnitus annoyance, perceived stress and depression were then analyzed separately using one-way ANOVA. Patients with higher or lower TQ had a long-lasting reduction of their tinnitus annoyance (table 3). Perceived stress was continuously reduced over the study period in the group with an initially higher PSQ level. Patients with

a higher depression level had a maximum reduction of their ADS scores immediately after the 7-day therapy and remained on a reduced level 3 years later. In contrast, patients with an initially lower depression level scored significantly lower only immediately after the end of therapy.

Influence of Hearing Ability on the Therapy Outcome

The correlation between the patients' hearing ability and the therapy outcome after 3 years was analyzed using Spearman's rank correlation. We found weak but statistically significant correlations between the hearing loss measured on the left side and the decrease of the TQ total score (r = -0.23, p < 0.01) and the following TQ subscales: emotional distress (r = -0.25, p < 0.01), cognitive distress (r = -0.21, p < 0.05) and intrusiveness (r = -0.24, p < 0.01). There was no correlation between hearing loss and score changes in PSQ, ADS and ACSA.

Influence of Gender, Age and Duration of Tinnitus on the Psychometric Parameters

Our recent studies have shown that factors like severity, hearing ability, gender, age and duration of tinnitus can influence outcome of MTRT [Mazurek et al., 2010a; Seydel et al., 2010]. In addition, preexisting tinnitus-related distress may depend on these factors [Seydel et al., 2013]. Therefore, we considered them in our analysis. As we knew that there is a lack of a linear relationship between tinnitus annoyance (perceived stress and depressive symptoms) and age or duration of tinnitus and that the greatest differences can be found between the gender-age groups (older men vs. women), we analyzed these particular factors using ANOVA rather than calculating

Fig. 1. Changes of the TQ scores assessed in three age groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.

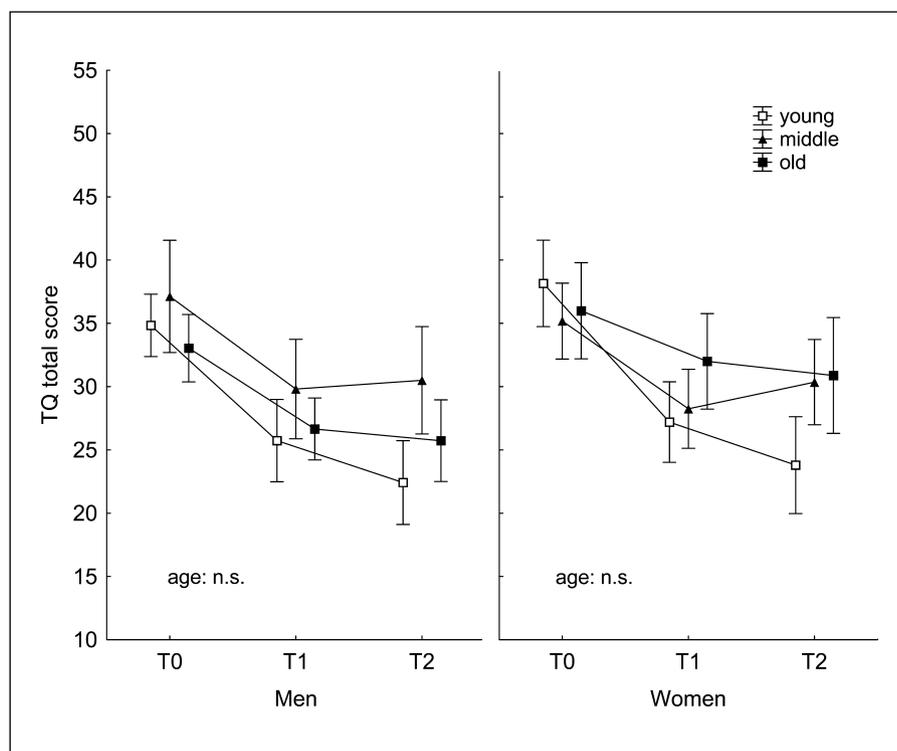


Table 4. Number of female and male patients in the groups divided by age and duration of tinnitus

Group	Years	Patients	
		female	male
Age			
Young	<50	25	19
Middle	50–60	28	16
Old	>60	16	26
Duration			
Short	<2	25	17
Middle	2–10	32	29
Long	>10	12	15

covariance analysis. The data of female and male patients were assigned to 3 age and 3 duration groups (table 4).

Age groups, gender and time after the onset of treatment (T0, T1 and T2) were analyzed using three-way ANOVA. In addition, two-way ANOVA was used to analyze gender groups separately. Because of the relatively small number of men and women in the groups ‘age’ or ‘duration’, the therapeutic effect was not analyzed there separately.

The total TQ score turned out to be reduced with time ($F_{2,372} = 10.4$, $p < 0.0001$). This was true for male ($F_{2,174} = 6.18$, $p < 0.01$) and female patients ($F_{2,198} = 4.54$, $p < 0.05$). The factor ‘age’ was not significant for either gender group (fig. 1).

Analysis of the total PSQ score demonstrated the influence of gender ($F_{1,372} = 5.12$, $p < 0.05$), age ($F_{2,372} = 40.0$, $p < 0.0001$) and time ($F_{2,372} = 4.22$, $p < 0.05$) on perceived stress. In addition, the interaction effect ‘gender \times age group’ was significant ($F_{2,372} = 12.0$, $p < 0.0001$). The effect of age was significant to a different degree in a gender-specific manner (men: $F_{2,174} = 65.9$, $p < 0.0001$; women: $F_{2,198} = 3.31$, $p < 0.05$) as analyzed by two-way ANOVA (fig. 2).

The ADS score was affected by time after treatment ($F_{2,372} = 9.01$, $p < 0.001$) and age ($F_{1,372} = 4.75$, $p < 0.01$). The factor ‘time’ was significant for men ($F_{2,174} = 3.78$, $p < 0.05$) and women ($F_{2,198} = 5.60$, $p < 0.01$); however, age had an influence on the ADS score only in male patients ($F_{2,174} = 5.86$, $p < 0.01$) with those patients who were >60 years old having the lowest scores (fig. 3).

The ACSA score was also affected by time after treatment ($F_{2,371} = 8.97$, $p < 0.001$) and by age ($F_{1,371} = 4.73$, $p < 0.01$). The factor ‘time’ was significant for men ($F_{2,173} = 4.86$, $p < 0.01$) and women ($F_{2,198} = 4.41$, $p <$

Fig. 2. Changes of the PSQ scores assessed in three age groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM.

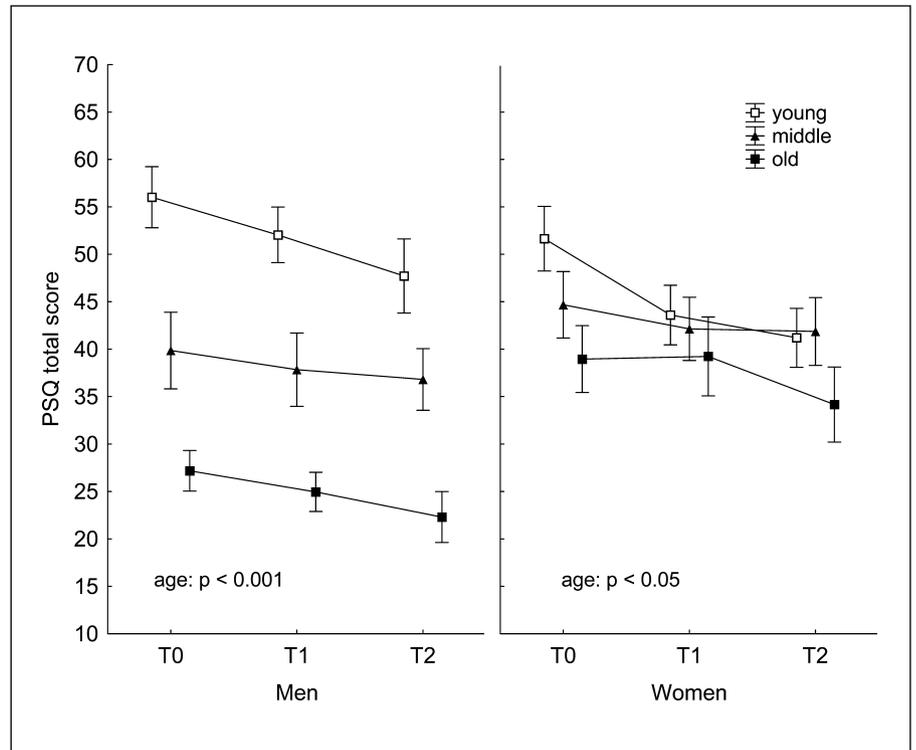


Fig. 3. Changes of the ADS scores assessed in three age groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.

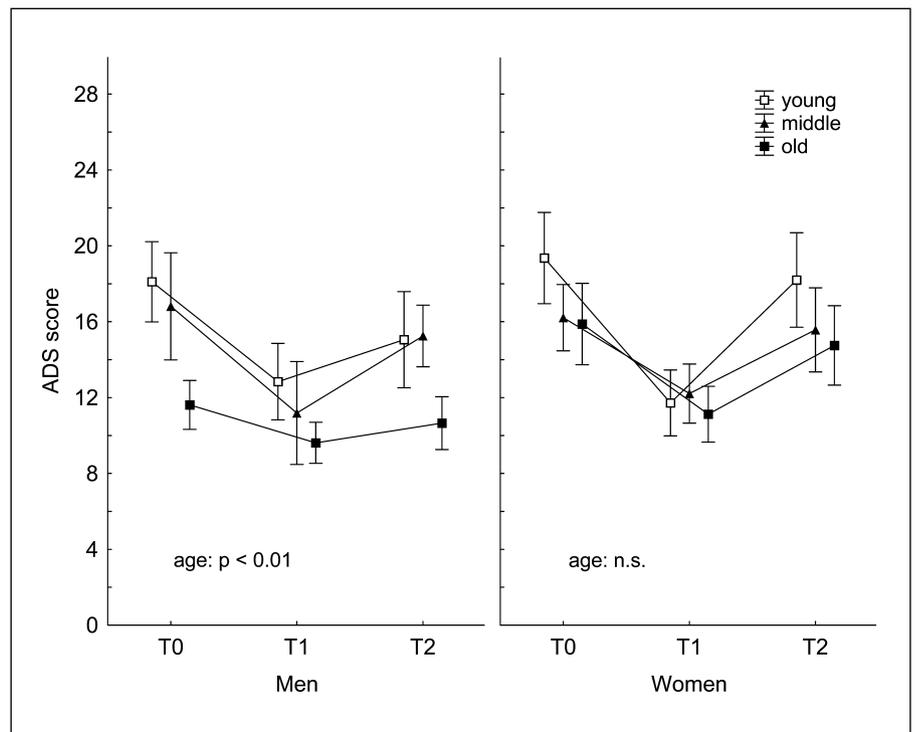
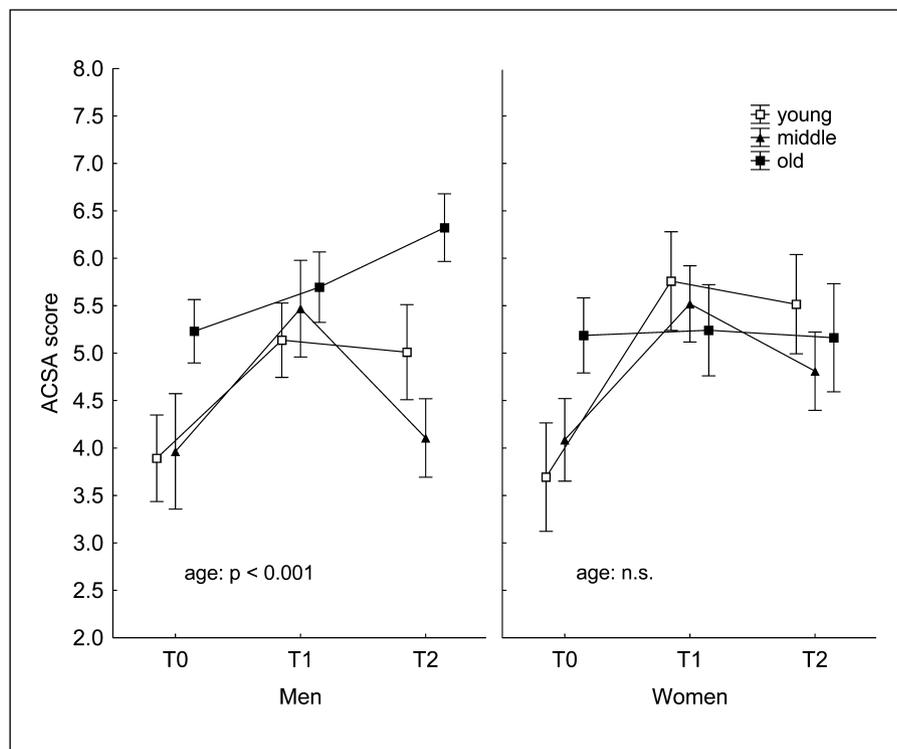


Fig. 4. Changes of the ACSA scores assessed in three age groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.



0.05), and the age also had an influence on the ACSA score in male patients ($F_{2, 173} = 7.98$, $p < 0.001$) with the patients who were >60 years old having the highest scores (fig. 4). The ACSA scores of female patients in the matching age group were not affected by time.

Tinnitus duration groups, gender and time after treatment (T0, T1 and T2) were analyzed using three-way ANOVA. In addition, two-way ANOVA was run for men and women separately.

Time ($F_{2, 372} = 10.0$, $p < 0.0001$) and gender ($F_{1, 372} = 4.41$, $p < 0.05$) significantly influenced the TQ scores, whereas tinnitus duration did not. In addition, the interaction effect 'gender \times tinnitus duration' was significant ($F_{2, 372} = 4.16$, $p < 0.05$). Unlike the factor 'duration', the factor 'time' was significant for men ($F_{2, 174} = 6.42$, $p < 0.01$) and women ($F_{2, 198} = 4.06$, $p < 0.05$) (fig. 5).

The PSQ score was influenced by tinnitus duration ($F_{2, 372} = 5.92$, $p < 0.05$), gender ($F_{1, 372} = 11.9$, $p < 0.01$) and time ($F_{2, 372} = 3.48$, $p < 0.05$). Separate gender-oriented analysis indicated that the factor 'tinnitus duration' was significant only for men ($F_{2, 174} = 8.33$, $p < 0.001$). Interestingly, male patients who had had tinnitus for more than 10 years perceived the lowest stress according to PSQ scores (fig. 6). An ANCOVA was used additionally with age as a covariate in order to rule out a possible

effect of tinnitus duration correlating with the men's age. The covariate 'age' was highly significant ($F_{1, 173} = 129.5$, $p < 0.0001$), but the factor 'tinnitus duration' remained significant ($F_{2, 173} = 6.32$, $p < 0.01$).

The ADS scores changed with time ($F_{2, 372} = 6.78$, $p < 0.01$) and were lower in men than in women ($F_{1, 37} = 6.55$, $p < 0.05$). Tinnitus duration did not affect the ADS scores. This was also true for men and women as analyzed separately by two-way ANOVA (fig. 7).

Analysis of the ACSA scores (three-way ANOVA) detected a significant effect of time after treatment ($F_{2, 371} = 9.34$, $p < 0.001$). The factors 'tinnitus duration' and 'gender' were not significant. Two-way ANOVA did not reveal a significant effect of tinnitus duration on the ACSA scores, neither for men nor for women (fig. 8).

Discussion

The goal of our present study was to assess the long-term effects (up to 3 years after therapy onset) of MTRT. Our results demonstrate significant improvement of patients' state of well-being reflected by reduced tinnitus annoyance (TQ), overall stress perception (PSQ) and depressive symptoms (ADS) and by improved quality of life

Fig. 5. Changes of the TQ scores assessed in three tinnitus duration groups of men and women before therapy (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.

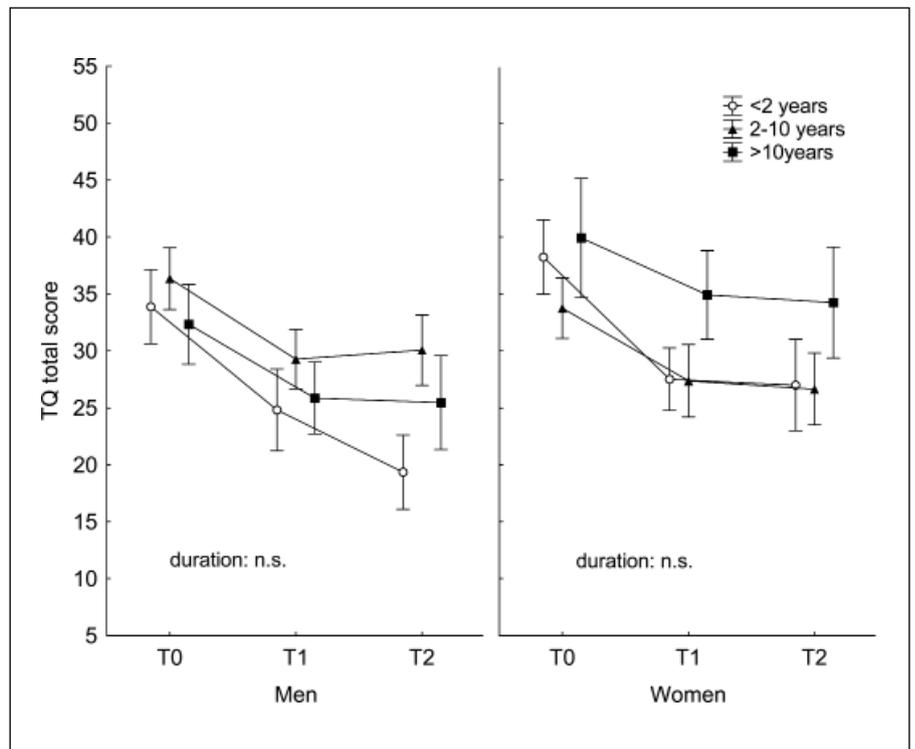


Fig. 6. Changes of the PSQ scores assessed in three tinnitus duration groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.

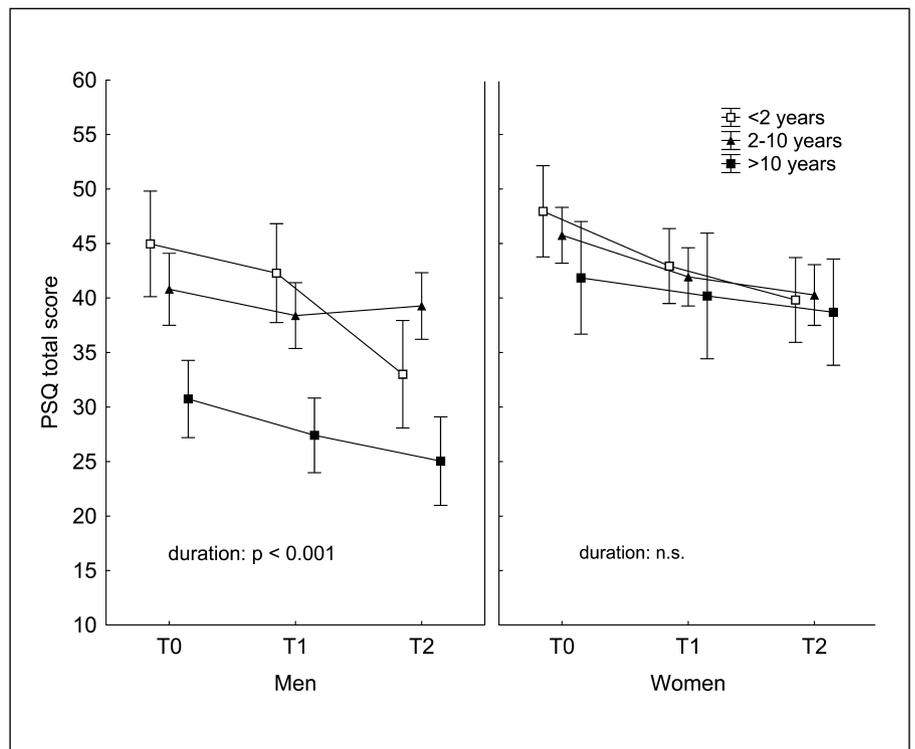


Fig. 7. Changes of the ADS scores assessed in three tinnitus duration groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.

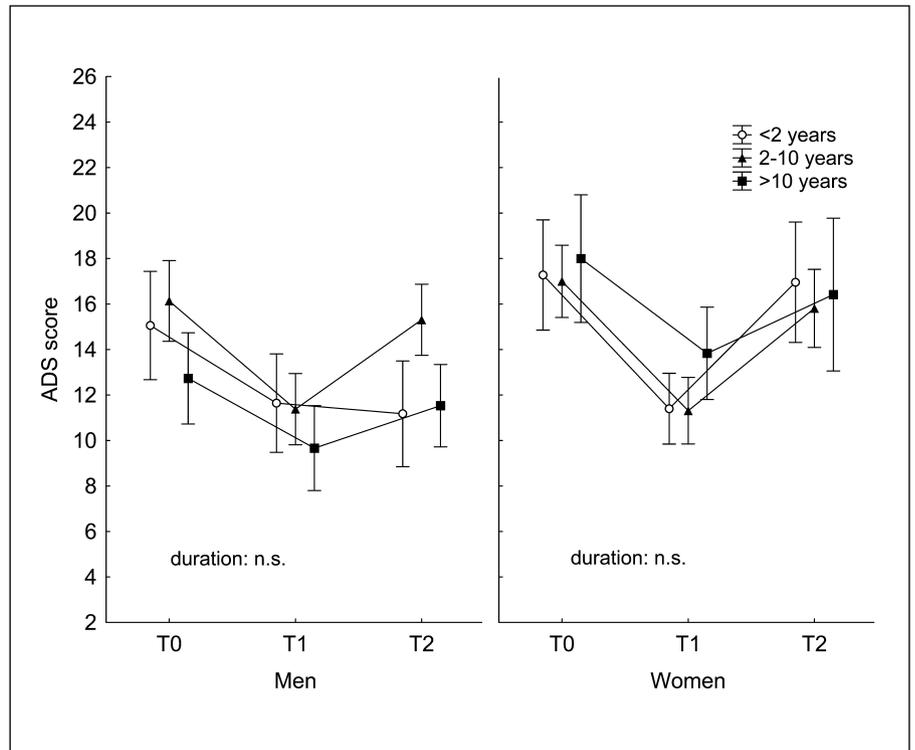
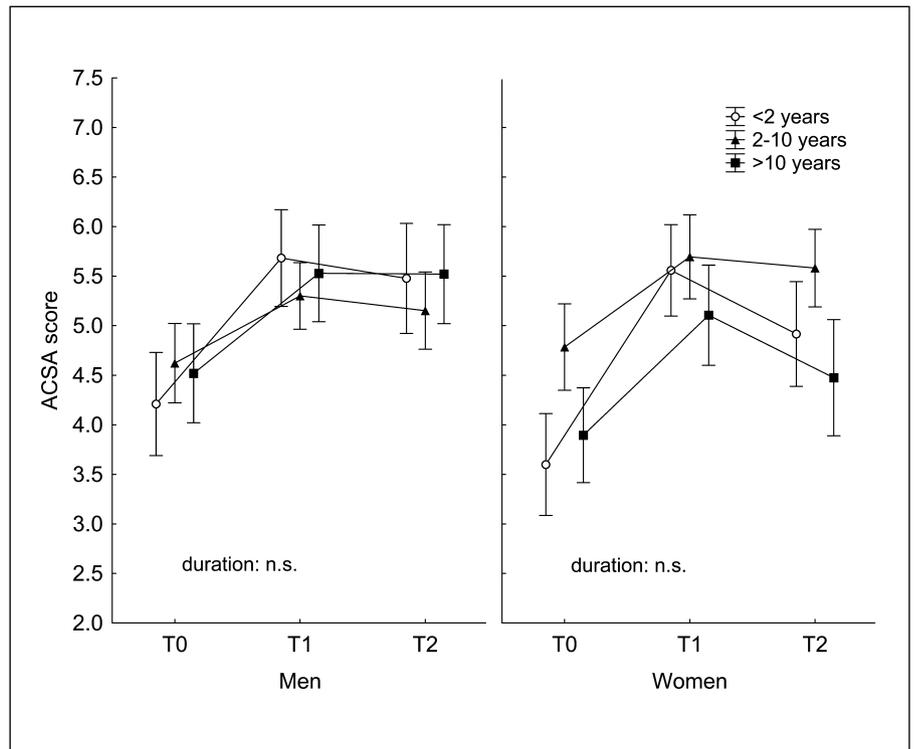


Fig. 8. Changes of the ACSA scores assessed in three tinnitus duration groups of men and women before MTRT (T0), immediately after therapy (T1) and 3 years later (T2). Values are means \pm SEM. n.s. = Not significant.



(ACSA). The therapeutic effect depended partly on the initial tinnitus severity level. The scores obtained by patients with initially normal levels of perceived stress (PSQ) and depression (ADS) are not expected to be modulated by therapeutic interventions [Hautzinger and Bailer, 1993; Kocalevent et al., 2007]. Therefore, it is essential to divide patients into groups according to different tinnitus severity levels and to separately analyze patients with an initially high tinnitus distress score. Moreover, our results imply that patients' age and gender may be possible predictors of therapeutic success. The degree of hearing loss and duration of tinnitus could also play a role in therapy outcome [Mazurek et al., 2010a]. Our previous study demonstrated a decrease of TQ and ADS scores in the therapy group, whereas the scores of the control group did not change significantly [Seydel et al., 2010].

Reduction of tinnitus annoyance measured in our present work with the TQ is comparable to the findings of other studies. However, evaluation time in these studies was limited to 1 year [Biesinger et al., 1998; Delb et al., 2002; Eysel-Gosepath et al., 2004; Hesse and Laubert, 2001; Mazurek et al., 2006, 2009; Seydel et al., 2010]. A novel finding here is a significantly sustained reduction in tinnitus-related distress lasting up to 3 years after therapy onset. Of all TQ subscales, emotional distress, cognitive distress and intrusiveness were the most reduced by MTRT. In addition, sleep disturbance was reduced. Sleep complaints of tinnitus patients may be explained by hyperacusis and a stronger focus on tinnitus due to a missing background noise at night [Hebert and Carrier, 2007]. The focus on tinnitus may be distracted by using relaxation techniques [Biesinger et al., 1998]. Internalizing these techniques and application of coping strategies usually takes some time [Ohm, 2003].

Tinnitus may be a symptom of a preexisting distress. However, tinnitus may also act as a stressor itself and have a negative effect on the process of habituation [Biesinger et al., 1998; Mazurek et al., 2010b]. This demonstrates the importance of including stress management in tinnitus therapy. The mean total PSQ score in our sample before therapy onset was 42.9 points, which is below the cutoff score of 45 indicating a pathological stress level. During the course of this study, we found progressive reduction of the PSQ score, which was significant 3 years after therapy onset. Particular improvement was seen in the subscales 'worries' and 'tension'. In the group with a high stress level, a score reduction from 59.7 to 49.3 points was found. An initially low level of perceived stress is unlikely to be changed into an even lower one. In a previous study, we investigated the PSQ scores 6 months and 1 year after

the onset of MTRT and did not find a significant decrease [Seydel et al., 2010]. Even though the total PSQ score did not change over time, the scores of the subscales 'worries' and 'tension' decreased significantly 6 months and 1 year after therapy onset [Seydel et al., 2010]. Identification and modulation of dysfunctional cognition requires a longer period of time, as it does for new coping strategies. Consequently, the results of our study indicate a successful and lasting implementation of strategies learned during the 7-day MTRT. The decline of the perceived stress score indicates effective coping with the stressor 'tinnitus' and different individual stress factors. The score decrease of the PSQ subscales 'worries' and 'tension' is likely to represent functional coping and efficient relaxation techniques. On the other hand, PSQ scores of patients with an initially higher level of perceived stress were reduced by 6 points already 7 days after therapy onset and by 10 points 3 years later. In contrast to our present findings, Weber et al. [2002] found a significant decrease of the PSQ score in the subscale 'tension' at the end of a 10-week relaxation training for tinnitus patients. Additionally, the subscale score 'joy' increased. However, in that study, the therapeutic protocol differed from that used in the present study, long-term effects were not assessed and information about duration of tinnitus and gender was missing. In addition, the average age of participants in that study was 43.2 years (SD 9.7), which was significantly lower than in our present study. Also, Londero et al. [2006] achieved significant reduction in 'general distress' and 'severe distress' 1 year after therapy onset. Interestingly, patients in that study were also younger than in our study.

Tinnitus patients are frequently diagnosed with mood affective disorders [Zirke et al., 2010, 2013]. It is still unclear whether a depressive disorder is a predisposing factor or a result of tinnitus [Gerhards and Brehmer, 2010; Olderog et al., 2004]. Nevertheless, depression can induce inadequate strategies of coping with tinnitus [Herraiz et al., 2005; Konzag et al., 2005]. Because of a high comorbidity and resulting requirement for psychotherapeutic intervention, the assessment of depressive symptoms at our center has permanently been incorporated into tinnitus diagnostic procedures. The initial mean ADS score of 16.2 points determined in our study indicates mild depression. Low starting scores may explain the rather minor reduction of the depression score by 8.0% following the 3-year period after therapy onset. In agreement with this, patients with initially more pronounced depressive symptoms (mean ADS level of 32.3 points) benefited from MTRT to a higher and long-lasting degree (27%). Our previous study demonstrated a similar effect in pa-

tients with an initially high ADS score 1 year after the end of therapy [Seydel et al., 2010].

Tinnitus patients frequently report compromised quality of life. MTRT positively influenced quality of life as measured by the ACSA. Increased ACSA scores were found already 7 days after therapy onset and 3 years after therapy. ACSA scores were associated with the statement 'personal best period in life'. Weber et al. [2002] observed a similar trend after a 10-week relaxation training. The improvement in quality of life could be a result of reduced tinnitus distress or of improved coping strategies. Furthermore, the decline of stress (PSQ) and depression levels (ADS) could be attributed to a better quality of life.

In order to identify possible predictors of successful therapy, we analyzed the influence of gender, age, duration of tinnitus and hearing loss on therapy outcome. The long-term outcome of MTRT measured by tinnitus annoyance (TQ) was neither influenced by age nor by duration of tinnitus. However, there were gender differences indicating that to some extent women benefit more than men from the therapy. The important role that gender and age play in MTRT outcome was already demonstrated in our previous studies with a larger number of tinnitus patients [Seydel et al., 2006, 2013]. Here, due to a rather small number of patients per age and tinnitus duration groups, the therapeutic effect could not be compared between the groups.

The perceived stress (PSQ) was influenced by age in both gender groups, but to a higher degree in men than in women. Duration of tinnitus influenced the PSQ scores only in men. Our recent study demonstrated that older male tinnitus patients have reduced perceived stress scores [Seydel et al., 2013]. In a population-based survey, Kocalevent et al. [2007] found that the stress score decreases with age starting from 55 years. The total PSQ score of the general population was shown to be slightly higher in women than in men.

The age of patients influenced depression and quality of life scores, but only in men, which was possibly caused by a larger old-age group, in which the lowest ADS scores and the highest ACSA scores were observed.

The degree of hearing loss influenced the reduction of tinnitus annoyance (TQ) after 3 years. This finding confirms our previously described negative correlation between TQ scores and hearing ability [Mazurek et al., 2010a]. In our present study, patients with better hearing responded better to MTRT than patients with a higher degree of hearing loss. This was true for patients with more pronounced hearing impairment on the left side and was possibly due to a generally higher degree of hearing loss on that side or to higher tinnitus annoyance found in pa-

tients with left-sided tinnitus in our previous study [Mazurek et al., 2010a]. Although reduction of stress and depressive symptoms and improved quality of life were not influenced by hearing loss, our results suggest that fitting the hearing-impaired patients with a hearing aid may be an essential element of tinnitus treatment.

Conclusions

MTRT conducted at our outpatient department was demonstrated to be an effective intervention in patients with chronic tinnitus. The aim of therapy was to promote a long-term tinnitus habituation and long-term reduction of tinnitus-related distress and comorbid psychological and somatic symptoms. MTRT appears to be an effective way of tinnitus treatment and is associated with a short- and long-term reduction of tinnitus annoyance (TQ), perceived stress (PSQ) and depressiveness (ADS), partly dependent on the initial severity level. In addition, an increase of global quality of life (ACSA) was achieved.

Taken together, we observed an improved state of well-being in a cohort of tinnitus patients who had been treated with MTRT 3 years earlier. Interestingly, the psychometric instrument ACSA indicated an improvement in the quality of life of treated tinnitus patients over the 3-year study period. A direct causative link between the MTRT and the patients' state of well-being 3 years after therapy onset remains to be determined.

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Disclosure Statement

None of the authors reports potential conflicts of interest.

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