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The sound of stress: Blunted cortisol reactivity to psychosocial stress in tinnitus sufferers

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Abstract

Clinical observations suggest that tinnitus is modulated by stress. However, there is little empirical data to support the link between stress and tinnitus. In this study, we measured the stress hormone cortisol to examine the reactivity of the hypothalamic-pituitary-adrenal (HPA) axis in tinnitus participants as well as in healthy controls without tinnitus. Eighteen participants with tinnitus and 18 controls without tinnitus were exposed to the Trier Social Stress Task and cortisol sampling and subjective ratings were obtained at regular intervals. Tinnitus participants displayed a blunted cortisol response to psychosocial stress, in comparison with healthy controls who had a typical cortisol release about 30 min after the beginning of the experiment. The blunted cortisol response displayed by the tinnitus participants suggests that they have an anomaly along the HPA axis. Their cortisol response is similar to that found in other bodily stress-related diseases and thus suggests that tinnitus is related to stress. However, tinnitus intensity might not be modulated by stress in a concurrent manner.

Keywords: Trier Social Stress Test; Tinnitus; Stress; Cortisol; HPA axis

Tinnitus is an illusory sound heard in the ears or head that is experienced by about 10.2% of the adult population, and the proportion of affected individual rises after 50 years of age [7]. A small proportion of these individuals experiences important psychological distress. There is now compelling evidence that tinnitus would be sustained by central structures. Recently, several mechanisms involving brain plasticity have been proposed [9], but, as of yet, there is no effective cure for this disorder.

Tinnitus has been compared to chronic pain because these two subjective sensations share many characteristics [10,31]. Both are permanent sensations that fluctuate over time. More specifically, the severity of tinnitus is reported by sufferers to be exacerbated by stress (e.g., [22,34,38]). In Ménière's disease and multiple sclerosis, for instance, there is support that exacerbation of symptoms is preceded by episodes of stress [1] or is linked with higher levels of stress hormones [26,39], although there are controversies regarding which symptoms are associated with stress [3] and the timeline between stress and exacerbation of symptoms [30].

Despite theoretical suggestions of a link between *tinnitus* and stress [2,25], this notion has received little empirical support. One study [37] reported that inpatients with sudden hearing loss and tinnitus had a higher number and greater stressfulness of events relative to a clinical Control group. Indirect support also indicates that subjective anxiety, perceived stress and tinnitus disturbance, as well as TNF-α, a stress-related immunological parameter, decreased in patients with tinnitus after a relaxation program [40]. These studies suggest, along with clinical observations, that stress levels may modulate tinnitus strength.

Recent psychoendocrine research has disclosed the important role of cortisol as a stress marker [5]. Cortisol secretion may be measured on a diurnal basis (e.g., basal) or in acute stressful situations (e.g., reactional). In a previous study [18], we measured basal cortisol in patients with tinnitus and in controls without tinnitus. Saliva samples were collected several times during a

Abbreviations: BDI-II, Beck depression Inventory; HPA, hypothalamic-pituitary-adrenal; PTA, Standard pure tone average for frequencies 500, 1000, 2000 Hz; S.D., standard deviation; TRQ, Tinnitus Reaction Questionnaire; TSST, Trier Social Stress Test; μg/dl, micrograms per decilitre

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given week. Circadian levels did *not* differ across groups when cortisol was averaged across days of the week, so all groups displayed "normal" levels. However, a greater number of patients with tinnitus had chronically elevated cortisol levels over a 1-week period relative to controls, that is, had a greater number of samples above the median, suggesting chronically elevated basal cortisol levels over a 1-week period. They also had greater intolerance to external sounds.

These results suggest a dysregulated hypothalamo-pituitary-adrenal axis (or HPA axis, ultimately responsible for cortisol secretion) in tinnitus participants, plausibly related to a state of chronic stress. Although this finding does not tell if stress is a cause or a predisposing factor for tinnitus, it provides some support on the relationship between stress and tinnitus. However, a stronger test of the integrity of the HPA axis in tinnitus patients involves exposing them to an acute stressful situation where a punctual release of cortisol is required. Moreover, basal cortisol levels are not predictive of reactional levels. For instance, depressed patients with high basal levels have demonstrated abnormal activity of the HPA following pharmacological challenges [13,24,41] and patients with atopic dermatitis have normal basal cortisol levels and hyporesponse to acute stress [6]. Therefore, it is difficult to make specific predictions. Given our previous study, higher basal levels could reflect an anomaly in stress recovery, that is, there could be a normal response to stress followed by levels that do not return to normal levels. On the other hand, if tinnitus is like a chronic stressor, a possible outcome is a shutdown of the HPA axis when faced with an external, acute stress. If this is the case, then this shutdown should be evidenced by a hyporesponse to stress in tinnitus participants.

In this study, tinnitus participants and controls without tinnitus were exposed to a classic psychosocial laboratory stress task (the Trier Social Stress Test). We measured cortisol response as well as subjective feelings of stress and tinnitus strength (tinnitus participants) at several time intervals up to 1 h post-stress to measure both responsiveness to stress and recovery. TSST is one of the most robust tasks to elicit cortisol secretion in the laboratory [8]. We predict that if tinnitus is a stress-related pathology, aberrant cortisol patterns should be found in tinnitus participants as a group, irrespective of their tinnitus-related distress.

Eighteen adults with tinnitus (8 women, 10 men) and 18 adults without tinnitus (10 women, 8 men) participated in the study (see Table 1). They were recruited by posted ads in newspapers, via self-help groups, or had participated in our previous studies. All women were post-menopausal. The two groups were matched in age and education, and therefore groups did not differ on these factors ($p = .22$ for education and $p = .93$ for age). Wearing a hearing aid or a masker, or having been operated in the ears, were exclusion criteria.

Tinnitus was subjective and continuous in all cases, and had been present for at least six months (mean duration = 14.7 years ± 10.6). It was perceived bilaterally or mostly bilaterally (more intense in one ear than the other) in 14 cases, and was unilateral in 3 cases. One participant had unilateral tinnitus plus an intermittent tinnitus on the other side. Participants described their tinnitus percept as ringing (i.e., high-pitch, $n = 13$), buzzing (i.e., low-pitch, $n = 2$), or both ($n = 3$).

Inclusion criteria for all participants were stringent: All were in good health, and none had a medical condition or took medication that could interfere with the functioning of the HPA axis. None had neurological disease or a recent history of psychiatric disease, nor any dependence to alcohol or to any other drugs. All participants were non-smokers. Participants who took antidepressant drugs were not included. None of the women were taking hormone replacement therapy.

Hearing loss was assessed by an audiogram using insert phones (Interacoustics AC40, ANSI S3.6 norms, 1989). Pure tone averages (PTA) were calculated for standard frequencies 500–1000–2000 Hz and for high frequencies 4000 and 8000 Hz (HF). There were no overall differences between left and right ears or between men and women (all $ps < 1$), so data were collapsed across ears and gender. As expected, Tinnitus participants had higher thresholds than Controls (32.64 versus 18.61, $p < .05$ for PTAs, and 56.94 versus 40.83, $p < .05$ for HF).

Behavioral data were obtained with questionnaires that had good psychometric properties. Sensitivity to external sounds was assessed with the Hyperacusis questionnaire [27]. Depressive symptomatology (BDI-II, [4]) and alexithymia, i.e., inability to identify one's emotions [29] were also assessed (Table 2).

Salivary samples were taken with Salivettes (Starsteadt) and stored at −80 °C. All 216 salivary samples were recoded for blind cortisol analyzes before they were sent to the Douglas hospital center in Montreal. Cortisol levels were determined by specific radioimmunoassay using a commercial kit from DSL (DSL-2000; Sanofi Diagnostics, Montreal, Canada). The inter-assay coefficient of variation was 7.5% (on a range of 0.8–1.2 μg/dl dose).

Participants were tested individually either at noon or at 3:30 p.m. in a counter-balanced order with the standard Trier Social Stress Test (or TSST, [28]). The protocol consists of a 10-min anticipation and preparation phase followed by a 10-min free

Table 1
Socio-demographic and tinnitus characteristics of the groups

	Tinnitus ($n = 18$)	Controls ($n = 18$)
Age in years (S.D.)	68.8 (5.7)	68.9 (5.5)
Education in years (S.D.)	13.49 (4.40)	14.9 (3.1)
Tinnitus duration in years		
Mean (S.D.)	14.67	–
Range	(1.5–35)	
Score on the Tinnitus Reaction Questionnaire (S.D.)	20.2 (17.7)	–

Table 2
Questionnaire data for the two groups

	Tinnitus ($n = 18$)	Controls ($n = 18$)
Hyperacusis Total score	19.89 (8.55)	11.56 (8.4)
Attentional subscale score	4.44 (3.0)	3.33 (2.79)
Social subscale score	8.83 (3.90)	3.78 (3.66)
Emotional subscale score	6.61 (2.83)	4.44 (2.90)
BDI-II score	9.17 (6.6)	4.9 (4.6)
Alexithymia score	66.2 (13.0)	62.89 (14.81)

speech and mental arithmetic task in front of a (sham) audience. The experimenter for this test, unknown to the participants, was blind to which group the participant belonged to. Six salivary cortisol samples were taken at regular intervals.

At each of the six intervals, participants rated their subjective stress levels on a Likert-type 10-point scale (0 = no stress, 10 = unbearable stress). In addition, tinnitus participants rated their tinnitus subjective strength on a similar scale (0 = no tinnitus, 10 = unbearable tinnitus). The entire procedure took about 1.5 h.

The study was approved by the Institutional ethics committee of the Institut universitaire de gériatrie de Montréal and was conducted with the consent of each participant.

Preliminary analyzes examined the influence of Time of testing (noon or 3:30 p.m.) on the data ($F < 1$). Mean raw cortisol levels (in μg/dl), subjective stress levels, and tinnitus intensity levels (Tinnitus group) were considered in independent ANOVAs with GROUP (Tinnitus versus Controls) as the between-subjects factor and Time (T0, $T+10$, $T+20$, $T+30$, $T+40$, $T+60$) as the within-subjects factor. ANOVAs and correlational analyses were also performed on questionnaire data. The SPSS package (version 11.0) was used.

There was a significant Group × Time interaction, F (5, 170) = 5.92, $p < .001$. In line with previous published reports on the TSST, the Control group displayed a significant increase in cortisol 20 min after exposure to the TSST ($T+30$) and cortisol levels rapidly declined to baseline values at +40 and +60 min. In contrast, the Tinnitus group did not display this increase of cortisol 20 min after exposure to TSST. This was supported by a significant group difference in cortisol levels at +30 min *only*, F (1, 34) = 11.2, $p < .003$, with the Control group showing increased cortisol levels when compared to the Tinnitus group. ANCOVAs were conducted with hearing loss (mean PTAs and High frequency hearing loss) as covariates on $T+30$. The difference between groups was still significant, F (1, 33) = 6.0, $p < .03$ (PTAs) and F (1, 33) = 8.33, $p < .01$ (HF). When BDI-II scores were put as a covariate on $T+30$, the difference between groups was also still significant, F (1, 33) = 9.43, $p < .001$ (Fig. 1).

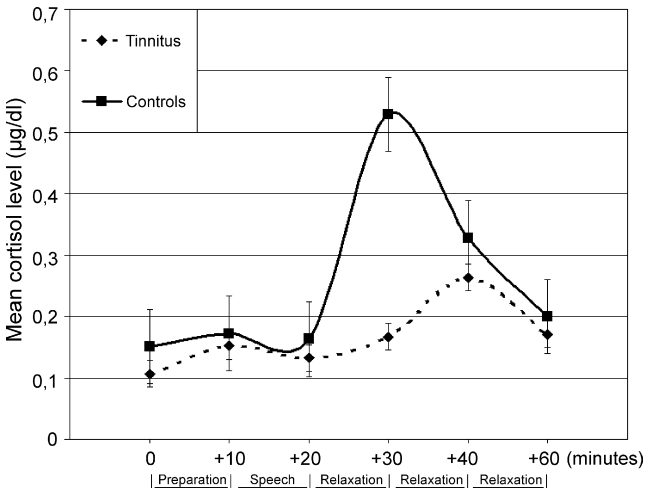

Fig. 1. Mean raw cortisol levels for the two groups in the TSST.

An additional ANOVA was performed on Tinnitus group data to verify whether the rise at Time +40 reflected a genuine (although delayed) increase in cortisol levels. The effect of Time was significant, F (5, 115) = 2.95, $p < .02$. Post hoc comparisons revealed that the difference between T0 and +40 was indeed significant at $p < .05$, but the other time points were not different from +40. Taken together, these results show that the Tinnitus group presented a delayed and blunted cortisol response to the psychosocial stressor.

On subjective Stress ratings, the Group and Time interaction was not significant ($F < 1$), nor was the main effect of group, F (1, 34) = 1.24, $p = .27$. There was, however, a significant main effect of Time, F (5, 170) = 22.47, $p < .001$. Post hoc comparisons revealed that ratings at +20 (mean rating = 4.56) were higher than at T0, +10, +30, +40, and +60 (means were 2.22, 3.12, 2.68, 2.11, and 1.83, respectively). Mean ratings at +10 were also significantly different from ratings at both T0 and +20 ($p < .05$). For the Tinnitus group, there was no effect of Time on tinnitus intensity ratings ($F < 1$).

On the Hyperacusis questionnaire, the Tinnitus group had scores close to the strong auditory sensitivity criterion of 28 established by Khalfa. The two groups differed on their total score, F (1, 36) = 8.69, $p < .007$, with means of 19.89 ± 8.54 and 11.6, ±8.4, respectively. The groups differed on the *Social* subscale, F (1, 36) = 16.11, $p < .001$ (means = 8.83 ± 3.90 and 3.78, ±3.66), but not on the *Emotional* subscale (with adjusted p), F (1, 36) = 5.15, $p < .04$ (means = 6.61 ± 2.83 and 4.44, ±2.90), or on the *Attentional* subscale, F (1, 36) = 1.33, $p = .26$ (means = 4.44 ± 3.0 and 3.33, ±2.79). When the covariate PTAs was added, the only significant difference remaining between groups was the Social subscale, F (1, 33) = 7.10, $p < .012$. Groups also differed on BDI-II scores, F (1, 36) = 5.16, $p < .03$ (means = 9.17 ± 6.56 and 4.89 ± 4.56), but not on alexithymia, $F < 1$.

Significant correlations were found between BDI-II and Hyperacusis Total scores, r (35) = .52, $p < .001$, Emotional subscale, r (35) = .49, $p < .002$ and Social subscale, r (35) = .52, $p < .001$. In the Tinnitus group, an additional significant correlation was found between TRQ and BDI-II scores, r (17) = .67, $p < .003$.

Our study provides the first direct physiological evidence that individuals with tinnitus present a blunted cortisol response to an acute stress. Despite subjective feelings of stress that were synchronized with, and were as important as those reported by controls, tinnitus participants showed a delayed and blunted responsiveness of their endocrine system to psychosocial stress.

This blunted response to stress was not related to depression, at least not to its major form, since tinnitus participants were within the "nondepressed" range, and that the group difference remained significant after factoring out BDI-II scores. Additionally, major depression is related to a *hyperactivity* of the HPA axis [35]. However, tinnitus is usually correlated with higher depression and anxiety scores (e.g., [16,23]) and subclinical depressive symptoms may also explain their sleep complaints [17]. Since TRQ scores were here correlated with BDI-II scores, the possibility that subclinical depression is a co-morbidity that

could be either a predisposing factor, a consequence of tinnitus, or share the same underlying cause, cannot be excluded. Nevertheless, the blunted response to stress found here characterizes a *diminished* glucocorticoid efficacy in tinnitus patients similar to the one that has been reported for a proportion of patients with stress-related disorders such as chronic fatigue syndrome, chronic pelvic pain, and fibromyalgia to name a few (see [12,14,15,19,20,36]). A triad of enhanced stress sensitivity, pain, and fatigue characterizes these disorders. Typically, one of these three symptoms is emphasized, and these disorders could share common mechanisms and development [11]. Given the findings of the present study, tinnitus appears to be a stress-related disorder. Also, tinnitus was previously found to be associated with greater sensitivity to sounds [18], a finding we replicated here with an independent group of participants. Hearing loss was responsible for this difference except for the Social subscale, which seems to be specifically attributable to tinnitus. Individuals with tinnitus tend to avoid noisy social situations, and this could contribute to their higher depression scores. Together, these symptoms can be related to increased stress sensitivity in individuals with tinnitus.

Our previous study on basal cortisol levels revealed an anomaly by showing chronically elevated basal cortisol levels. It is not uncommon to find that the basal and reactivity cortisol are seemingly conflicting, i.e., that basal levels seem to reflect an overactivity of the HPA axis and the reactional level seem to reflect an underactivity of the axis. The present findings, however, are much more robust than the subtle basal effects. Given the fact that tinnitus duration differed significantly between our two studies (5.5 versus 14.7 years), it is possible that the hyporeactive HPA axis might have developed after prolonged period of stress, together with a hyperactivity of the axis and excessive glucocorticoid release, as has been proposed by Hellhammer and Wade [21]. A combination of basal and reactional cortisol measurements within the same group of younger participants should be conducted to overcome the limitations of the present study and to shed light on this question.

Another important aspect is that our study did not provide support for the idea that tinnitus intensity was concurrent with subjective stress level. It is possible that a Likert-type scale was not sensitive enough a measure to capture subtle variations in tinnitus intensity, or that tinnitus intensity did not vary in the time window of the study. Another possibility is that psychosocial stress is not the appropriate condition to induce such intensity changes.

There are several mechanisms that might be responsible for this alteration in the stress response of the Tinnitus group. For example, it could be due to a reduced release of the appropriate hormone or releasing factor at any level of the HPA axis, a hypersecretion of one hormone/factor with subsequent down-regulation of the receptors, or inhibition of the HPA axis through enhanced negative feedback sensitivity. It is also possible that this is due to a more central mechanism involving the non-classical auditory pathways [32] or other brain structures such as the amygdala. A recent study [33], using voxel-based morphometry documented structural changes in the brains of tinnitus participants. Increases in the gray matter were found at the thalamic level, an important auditory relay. Additionally, gray matter decreases were found in the subcallosal region, including the nucleus accumbens. Interestingly, this region plays a central role in the reward circuit and in the stress response, and receives its input from the amygdala. The amygdala could therefore be a key structure in the perception or maintenance of tinnitus and of its bodily consequences such as the one shown here.

Future studies focusing on pharmacological challenge of the HPA axis in tinnitus participants and controls will be able to increase knowledge on the specific mechanisms involved in the case of tinnitus, and enable the development of new pharmacological treatments.

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References

[1] K.D. Ackerman, R. Heyman, B.S. Rabin, B.P. Anderson, P.R. Houck, E. Frank, A. Baum, Stressful life events precede exacerbations of multiple sclerosis, Psychosom. Med. 64 (2002) 916–920.
[2] D. Alpini, A. Cesarani, Tinnitus as an alarm bell: stress reaction Tinnitus model, ORL J. Otorhinolaryngol. Relat. Spec. 68 (2006) 31–36.
[3] G. Andersson, C. Hägnebo, L. Yardley, Stress and symptoms of Meniere's disease: a time-series analysis, J. Psychosom. Res. 43 (1997) 595–603.
[4] A.T. Beck, Beck Depression Inventory II, The Psychological Corporation, Harcourt Canada Assessment Company, Toronto, 1997.
[5] M. Biondi, A. Picardi, Psychological stress and neuroendocrine function in humans: the last two decades of research, Psychother. Psychosom. 68 (1999) 114–150.
[6] A. Buske-Kirschbaum, A. Geiben, H. Hollig, E. Morschhauser, D. Hellhammer, Altered responsiveness of the hypothalamus-pituitary-adrenal axis and the sympathetic adrenomedullary system to stress in patients with atopic dermatitis, J. Clin. Endocrinol. Metab. 87 (2002) 4245–4251.
[7] A.C. Davis, Hearing in Adults, Whurr, London, UK, 1995.
[8] S.S. Dickerson, M.E. Kemeny, Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research, Psychol. Bull. 130 (2004) 355–391.
[9] J. Eggermont, L. Roberts, The neuroscience of tinnitus, Trends Neurosci. 27 (2004) 876–882.
[10] R.L. Folmer, S.E. Griest, W.H. Martin, Chronic tinnitus as phantom auditory pain, Otolaryngol. Head Neck Surg. 124 (2001) 124.
[11] E. Fries, J. Hesse, J. Hellhammer, D.H. Hellhammer, A new view on hypocortisolism, Psychoneuroendocrinology 30 (2005) 1010–1016.
[12] P.W. Gold, G.P. Chrousos, Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs low CRH/NE states, Mol. Psychiatry 7 (2002) 254–275.
[13] P.W. Gold, D.L. Loriaux, A. Roy, M.A. Kling, J.R. Calabrese, C.H. Kellner, L.K. Nieman, R.M. Post, D. Pickar, W. Gallucci, P. Avgerinos, S. Paul, E.H. Oldfield, G.B. Cutler, G.P. Chrousos, Responses to corticotropin-releasing hormone in the hypercortisolism of depression and Cushing's disease. Pathophysiologic and diagnostic implications, N. Engl. J. Med. 314 (1986) 1329–1335.
[14] E.N. Griep, J.W. Boersma, E.G. Lentjes, A.P. Prins, J.K. van der Korst, E.R. de Kloet, Function of the hypothalamic-pituitary-adrenal axis in patients with fibromyalgia and low back pain, J. Rheumatol. 25 (1998) 1374–1381.

[15] A. Gur, R. Cevik, K. Nas, L. Colpan, S. Sarac, Cortisol and hypothalamic-pituitary-gonadal axis hormones in follicular-phase women with fibromyalgia and chronic fatigue syndrome and effect of depressive symptoms on these hormones, Arthritis Res. Ther. 6 (2004) R232–R238.
[16] J. Harrop-Griffiths, W. Katon, R. Dobie, C. Sakai, J. Russo, Chronic tinnitus: association with psychiatric diagnosis, J. Psychosom. Res. 31 (1987) 613–621.
[17] S. Hébert, J. Carrier, Sleep complaints in elderly tinnitus patients: a controlled study, paper submitted for publication.
[18] S. Hébert, P. Paiement, S.J. Lupien, A physiological correlate for the intolerance to both internal and external sounds, Hear. Res. 190 (2004) 1–9.
[19] C. Heim, U. Ehlert, J.P. Hanker, D.H. Hellhammer, Abuse-related posttraumatic stress disorder and alterations of the hypothalamic-pituitary-adrenal axis in women with chronic pelvic pain, Psychosom. Med. 60 (1998) 309–318.
[20] C. Heim, U. Ehlert, D.H. Hellhammer, The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders, Psychoneuroendocrinology 25 (2000) 1–35.
[21] D.H. Hellhammer, S. Wade, Endocrine correlates of stress vulnerability, Psychother. Psychosom. 60 (1993) 8–17.
[22] J.L. Henry, P.H. Wilson, The Psychological Management of Chronic Tinnitus, Allyn Bacon, Boston, 2001.
[23] K.M. Holgers, S. Erlandsson, M.L. Barrenäs, Predictive factors for the severity of tinnitus, Audiology 39 (2000) 284–291.
[24] F. Holsboer, U. Von Bardeleben, A. Gerken, G.K. Stalla, O.A. Muller, Blunted corticotropin and normal cortisol response to human corticotropin-releasing factor in depression, N. Engl. J. Med. 311 (1984) 1127.
[25] K.C. Horner, The emotional ear in stress, Neurosci. Biobehav. Rev. 27 (2003) 437–446.
[26] K.C. Horner, R. Guieu, J. Magnan, A. Chays, Y. Cazals, Prolactinoma in some Ménière's Patients—is stress involved? Neuropsychopharmacology 26 (2001) 135–138.
[27] S. Khalfa, S. Dubal, E. Veuillet, F. Peretz-Dias, R. Jouvent, L. Collet, Psychometric normalization of a hyperacusis questionnaire, ORL J. Otorhinolaryngol. Relat. Spec. 64 (2002) 436–442.
[28] C. Kirschbaum, K.M. Pirke, D.H. Hellhammer, The "Trier Social Stress Test"—a tool for investigating psychobiological stress responses in a laboratory setting, Neuropsychobiology 28 (1993) 76–81.
[29] G. Loas, D. Fremaux, M.P. Marchand, C. Chaperot, R. Dardennes, L'alexithymie chez le sujet sain: validation de l'échelle d'alexithymie de Toronto (TAS) dans une population "tout venant" de 144 sujets, application au calcul de la prévalence, Ann. Med. Psychol. 151 (1993) 660–663.
[30] D. Mohr, D. Pelletier, A temporal framework for understanding the effects of stressful life events on inflammation in patients with multiple sclerosis, Brain Behav. Immun. 20 (2006) 27–36.
[31] A.R. Møller, Similarities between chronic pain and tinnitus, Am. J. Otol. 18 (1997) 577–585.
[32] A.R. Møller, M.B. Møller, M. Yokota, Some forms of tinnitus may involve the extralemniscal auditory pathway, Laryngoscope 102 (1992) 1165–1171.
[33] M. Muhlau, J.P. Rauschecker, E. Oestreicher, C. Gaser, M. Rottinger, A.M. Wohlschlager, F. Simon, T. Etgen, B. Conrad, D. Sander, Structural brain changes in tinnitus, Cereb. Cortex 16 (2006) 1283–1288.
[34] R.H. Nodar, "C.A.P.P.E."—a strategy for counseling tinnitus patients, Int. Tinnitus J. 2 (1996) 111–113.
[35] C. Pariante, A.H. Miller, Glucocorticoid receptors in major depression: relevance to pathophysiology and Treatment, Biol. Psychiatry 49 (2001) 291–404 (review).
[36] A.D. Roberts, S. Wessely, T. Chalder, A. Papadopoulos, A.J. Cleare, Salivary cortisol response to awakening in chronic fatigue syndrome, Br. J. Psychiatry 184 (2004) 136–141.
[37] C. Schmitt, M. Patak, B. Kröner-Herwig, Stress and the onset of sudden hearing loss, Int. Tinnitus J. 6 (2000) 41–49.
[38] R.S. Tyler, Tinnitus Handbook, Singular, San Diego, 2000.
[39] N. van Cruijsen, R.P. Dullaart, H.P. Wit, F.W.J. Albert, Analysis of cortisol and other stress-related hormones in patients with Ménière's disease, Otol. Neurotol. 26 (2005) 1214–1219.
[40] C. Weber, P. Arck, B. Mazureck, B.F. Klapp, Impact of a relaxation training on psychometric and immunologic parameters in tinnitus sufferers, J. Psychosom. Res. 52 (2002) 29–33.
[41] E.A. Young, J. Kotun, R.F. Haskett, L. Grunhaus, J.F. Greden, S.J. Watson, H. Akil, Dissociation between pituitary and adrenal suppression to dexamethasone in depression, Arch. Gen. Psychiatry 50 (1993) 395–403.