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Large–Scale Inverse and Forward Modeling of Adaptive Resonance in the Tinnitus Decompensation

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Abstract— **Neural correlates of psychophysiological tinnitus models in humans may be used for their neurophysiological validation as well as for their refinement and improvement to better understand the pathogenesis of the tinnitus decompensation and to develop new therapeutic approaches.**

In this paper we make use of neural correlates of top–down projections, particularly, a recently introduced synchronization stability measure, together with a multiscale evoked response potential (ERP) model in order to study and evaluate the tinnitus decompensation by using a hybrid inverse–forward mathematical methodology.

The neural synchronization stability, which according to the underlying model is linked to the focus of attention on the tinnitus signal, follows the experimental and inverse way and allows to discriminate between a group of compensated and decompensated tinnitus patients. The multiscale ERP model, which works in the forward direction, is used to consolidate hypotheses which are derived from the experiments for a known neural source dynamics related to attention.

It is concluded that both methodologies agree and support each other in the description of the discriminatory character of the neural correlate proposed, but also help to fill the gap between the top–down adaptive resonance theory and the Jastreboff model of tinnitus.

I. INTRODUCTION

Tinnitus is defined as "the perception of a sound that results exclusively from the activity within the nervous system without any corresponding mechanical, vibrating activity in the cochlear" [1]. Many of us have experienced a transient ringing, roaring or buzzing in the ears without any auditory stimulation, which often stems from a damage to the lower auditory system, e.g., after returning from a very loud environment where the outer hair cells of the cochlea are transiently damaged. While in the vast majority of the cases this sound disappears spontaneously in some cases it turns out to be a permanent sensation. For some people, the internal noise is not annoying and they get accustomed to it. They are referred as "compensated tinnitus patients". Minorities of other people, the decompensated tinnitus patients, are troubled by the noise and may develop psychiatric symptoms such as insomnia and depressions, which in some cases can even be a contributing factor to suicide [2]. However, it also seems likely that the presence of depression has major influence in the development of high psychological tinnitus impact. So far an objective diagnosis approach for tinnitus is not possible in a clinical setting [3]. Previous studies have shown that tinnitus is a body signal to which too much attention is paid and the degree of annoyance is determined exclusively or at least predominantly by non–auditory factors, see Section II-A. Also according to the neurophysiological tinnitus model of Jastreboff [1] and the model of Hallam [4], the development of high tinnitus related distress can be explained by the fixation of attention to the tinnitus. However the pathogenesis of the tinnitus is not completely understood up to now.

In this study, we analyze and quantify the tinnitus decompensation by focusing on two different methodologies, the inverse approach which is based on a phase stability measure of auditory late responses (ALRs) from tinnitus patients, and the forward approach provided by a mathematical multiscale ERP model [5].

II. METHODOLOGY

A. *Tinnitus Model of Adaptive Resonance*

According to the Jastreboff tinnitus model [1], the annoyance due to tinnitus is exclusively determined by non-auditory factors, especially the limbic and autonomic nervous system. In this model, there is an emotional weighting of the signal which either results in its habituation or amplification. While in compensated tinnitus patients a habituation is predominate, amplification and associated emotional negative reactions are the underlying mechanism in the tinnitus decompensation. The emotional weighting depends on several factors such as dysfunctional tinnitus related cognition or preexistent depression [2] but this is not completely understood. Neurobiological evidence of these psychologically driven top–down interaction may be provided by examinations in the bat [6]. These studies showed that the conditioning of an auditory with a pain stimulus results in a reorganization of the auditory cortex by top–down processes. Mapping these findings to the tinnitus model it can be assume that in the case of decompensated tinnitus patients there is also a signal, i.e., the tinnitus signal, which is related to negative association and may reorganize the auditory cortex in the sense above. A model which is in accordance to the findings of [7]. A mathematical framework of the cognitive tinnitus processing may be provided by adaptive resonance theory (ART) of Grossberg [8], in which top-down projections are the key mechanism for solving the

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stability–plasticity dilemma. ART is a representative theory of a fundamental paradigm shift in cognitive neuroscience [9]. ART claims that sensory processing is a highly active process with strong top–down interactions. The common mechanism of all these models is that sensory stimuli active top-down expectations whose signals are matched against the bottom-up data. Top–down expectations originating from learning processes focus the attention on information which matches to them (resonant state of ART). These expectations synchronize, amplify, and modify the activity of cells within the attentional focus and suppress the activity of others. Combining the Jastreboff tinnitus model with ART, similar mechanism of subcortical and cortico–cortical top-down interaction can be expected if attentional focus is on the signal tinnitus in decompensated tinnitus patients. Other signals such as stimuli used in the examinations are suppressed and lead to less synchronized responses in auditory cortex. As a result, neural correlates of these top–down projections might be reflected in the phase stability of single sweep sequences of ALRs. The combined model is illustrated in Fig. 1

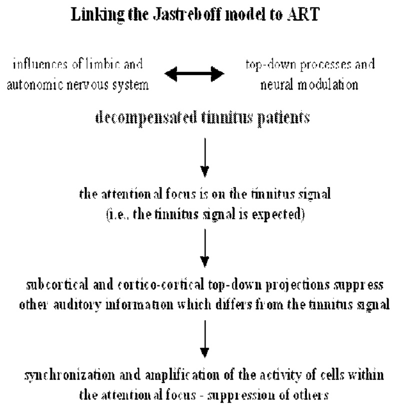

Fig. 1. Tinnitus model of adaptive resonance.

B. Multiscale ERP Model

The Multiscale ERP model employed in our study was suggested in [10]. It is based on a continuum model of corticothalamic dynamics that reproduces and unifies many features of ERPs by using averages over microstructures to produce mean–field equations that link the cellular level and neural network properties.

One of the main characteristics incorporated by the model is the neural response $S[V_a(r,t)]$ to the cell–body potential V_a as given by a sigmoidal type function

$$S[Va(r,t)] = \frac{Q_{max}}{1 + exp\{-[V_a(r,t) - \theta]/\sigma'\}},$$

where θ is the mean neural firing threshold relative to resting and $a = e, i$ is used to represent excitatory and inhibitory cortical population of neurons respectively. The potential V_a is a result of synaptic inputs from various types of afferent neurons that are summed after being filtered and smeared out in time as a result of receptor dynamics and passage trough the dendritic tree. It approximately obeys a differential equation

$$D_\alpha V_a(r,t) = \sum_b N_{ab} S_{ab} \phi_b(r, t - \tau_{ab}),$$

where

$$D_\alpha = \frac{1}{\alpha\beta}\frac{d^2}{dt^2} + (\frac{1}{\alpha} + \frac{1}{\beta})\frac{d}{dt} + 1,$$

$\frac{1}{\beta}$ and $\frac{1}{\alpha}$ represent the rise and decay times of the cell-body potential produced by an impulse at a dendritic synapse [10]. The crucial assumption in the model is that each part of the corticothalamic system produces a field ϕ_a of pulses, which travel at a velocity v_a through axons with a characteristic range r_a. Approximately, such pulses propagate according to the damped-wave equation

$$(\frac{1}{\gamma_a}^2\frac{\partial^2}{\partial t^2} + \frac{2}{\gamma_a}\frac{\partial}{\partial t} + 1 - r_a^2\nabla^2)\phi_a(r,t) = S[V_a(r,t)],$$

where $\gamma_a = v_a/r_a$ and r_a is the mean range of neural axons. The simulated ERPs can thus be generated by using a stimulus $\phi_n(k,w)$ of angular frequency w and wave vector k, which represents the thalamic stimulation, together with a function $\phi_l(k,w)$ relating cortical activity of a large neural population, to define a corticothalamic transfer function $\phi_l(k,w)/\phi_n(k,w)$, whose varying of parameters allows for the modulation of ERPs due to focal and non–focal attention.

Decompensated tinnitus patients pay too much attention to the tinnitus signal and cannot pay focal attention on a signal which differs from the tinnitus signal according to the model presented. The states of non–focal attention in decompensated and focal attention to an auditory stimulus which is different from the tinnitus signal in compensated tinnitus patients can be represented by this model.

C. Auditory Late Response Phase Stability Measure

In our study, we employed the time-scale phase coherence measures based on the complex wavelet transform which take the non–stationary nature of evoked potentials into account in contrast to conventional coherence based on frequency information alone. Let $\psi_{a,b}(\cdot) = |a|^{-1/2}\psi((\cdot - b)/a)$ where $\psi \in L^2(\mathbb{R})$ is the wavelet with $0 < \int_{\mathbb{R}} |\Psi(\omega)|^2 |\Psi(\omega)|^{-1} d\omega < \infty$ ($\Psi(\omega)$ is the Fourier transform of the wavelet), and $a, b \in \mathbb{R}$, $a \neq 0$). The wavelet transform $\mathcal{W}_\psi : L^2(\mathbb{R}) \longrightarrow L^2(\mathbb{R}^2, \frac{dadb}{a^2})$ of a signal $x \in L^2(\mathbb{R})$ with respect to the wavelet ψ is given by the inner L^2–product $(\mathcal{W}_\psi x)(a,b) = \langle x, \psi_{a,b}\rangle_{L^2}$. The wavelet phase coherence defined in [14] is mainly applied to measure the degree of phase locking of two signals in time, e.g., obtained from two different sites. For the determination of the phase stability, we need an adaptation of the derived phase locking measure between two signals to our problem, see [11] for more details. In this study, we used the 6th-derivative of the complex Gaussian function as wavelet. The phase stability $\Gamma_{a,b}$ of a sequence $\mathcal{X} = \{x_m \in L^2(\mathbb{R}) : m = 1, \ldots, M\}$ of M sweep is defined by

$$\Gamma_{a,b}(\mathcal{X}) := \frac{1}{M}\left|\sum_{m=1}^{M} e^{\imath \arg((\mathcal{W}_\psi x_m)(a,b))}\right|. \qquad (1)$$

It is obvious to see that the phase stability in (1) is a value in $(0, 1)$. We have a perfect neural synchronization stability for a particular a' and b' for $\Gamma_{a',b'} = 1$ (perfectly coherent phases) and a decreasing stability for smaller values due to phase jittering.

D. Patients and Data

500 ERPs and sweeps, respectively, that represent focal and non–focal attentive processes were simulated by the multiscale ERP model so as to generate the forward data to be analyzed by the phase stability measure in (1).

Experimental data was obtained from a total of 29 tinnitus patients, who were divided in two groups: compensated patients (tinnitus of degree 1 and 2, 18 patients) and decompensated patients (tinnitus of degree 3 and 4, 11 patients) by the 4 degree tinnitus differentiation scheme in [12] which is a German version of the questionnaire by Hallam. There is no significant difference of the age and gender distribution among the group of compensated and decompensated patients. Also there was no significant difference between the groups regarding tinnitus pitch which ranged between 125 and 10000 Hz there was no significant difference between the groups at any measured frequency. However there was significant difference between the groups regarding the time since the appearance of the tinnitus (mean of 40,93 months in the compensated group and 92,71 months in the decompensated group). ALRs were obtained using a commercially available device in a sound-proof chamber. In each measurement, tone bursts were presented with a stimulation rate of 1 burst per 2.5s at 80dB. Artifacts were excluded from the analysis by the internal artifact filter of the system. Single sweeps were recorded using electrodes placed at the left and right mastoid, the vertex, and the upper forehead. Electrode impedances were below 5k in all measurements (filter: 5Hz-200Hz, sampling frequency: 500Hz). The distance of the auditory stimulus from the tinnitus signal was at least 1kHz for all patients so that they do not coincide in frequency. In patients with a one-sided tinnitus, the contralateral ear to the tinnitus was stimulated according to [13].

III. RESULTS

In Fig. 2 the averaged neural synchronization stability is shown for the group of compensated and decompensated tinnitus patients for $a = 40$. It is noticeable that the major differences of the phase stability are associated with the time interval between 100ms and 200ms where the N1 (approx. 100–150ms) and the P2 (approx. 150–200ms) waves are located. In this interval, the difference between the two groups is significant (Wilcoxon test, significance level $p<0.05$). The neural activity reflected in these waves is presumably associated with the auditory cortex [14].

Due to the subjective evaluation, we expect a rather strong overlaps between groups of patients, especially between the tinnitus of degree 2 and 3. Therefore, we focus our interest in patients with tinnitus of degree 1 (T1 group) and 4 (T4 group), i.e., the most compensated and decompensated ones, for the experiments in which we analyze the evolution of the phase stability over the sweep sequence. In figure 4, we show an example of the evolution of phase for T1 and T4 patients, specifically the quantity $\left|e^{\imath \arg(\mathcal{W}_\psi x_m)(a,b)}\right|$ $m = 1, \ldots, M$ (each circle represents one sweep). It is clear that the summation of the individual sweeps for the T1 patient result in a much larger values than the decompensated T4 patient which is expected in our approach.

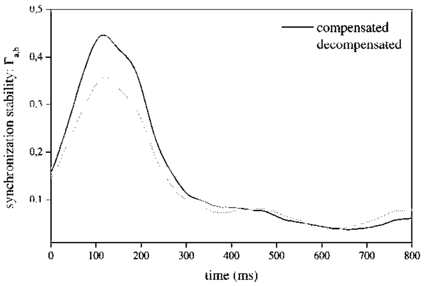

Fig. 2. The averaged difference of the phase stability for $a = 40$ as example.

In Fig. 3, it is shown the phase difference between consecutive pairs of sweeps, i.e.,

$$\frac{1}{2}\left|e^{\imath \arg(\mathcal{W}_\psi x_m)(a,b)} + e^{\imath \arg(\mathcal{W}_\psi x_{m+1})(a,b)}\right|,$$

$m = 1, \ldots, M-1$ of a total of 1000 sweeps, averaged for the T1 and T4 group, respectively. A rather slight habituation in the compensated patients (T1) as reflected in the decreasing of the phase stability between consecutive pairs of sweeps is noticeable.

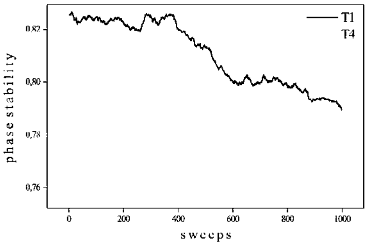

Fig. 3. The mean phase stability of consecutive sweeps for tinnitus patients of degree 1 (T1) and degree (T4) (smoothed).

Fig. 5 depicts our findings by using the simulated focal and non–focal ERPs together with the phase stability measure. It is clearly noticeable that in the case of non–focal attention, the ERP and sweep sequence, respectively, is unstable as in the case of decompensated tinnitus patients in Fig. 4. For focal attention, we have a rather stable synchronization as for the compensated patient.

IV. DISCUSSION

The neural synchronization stability measure in this study is evaluated by using a time–scale measure that is based on the phase information exclusively. It is important to note that this measure is not applied as direct time locking measure

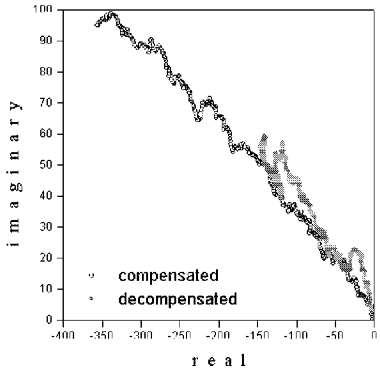

Fig. 4. The evolution of ALR sweeps in the complex plane for a T1 and T4 patient.

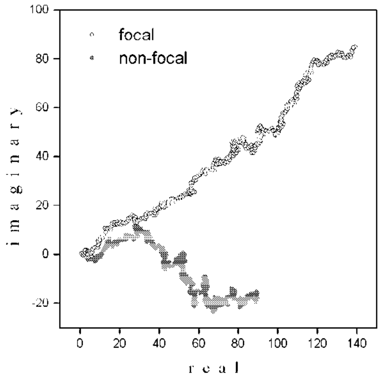

Fig. 5. The evolution of simulated ALR sweeps in the complex plane for focal and non-focal attention.

since the responses in both groups are stimulus locked. We evaluated the quality and stability of the response over the stimulus sequences in terms of the time-resolved phase information. This measure is independent from the fragile amplitude information and its use is fully supported and justified by the multiscale event related model that we used to simulate sweeps that reflect focal and non focal attention. Such ERP model is based on feedback top–down projections between the cortex and thalamus [10], and so it clearly establishes and connection between the Jastreboff tinnitus model and the ART Grossberg Theory. Since decompensated tinnitus patients pay too much attention to the tinnitus signal [15], [1], the signal tinnitus is expected by higher auditory areas in these patients, employing ART terms, it matches the top–down projections which synchronize the cells within the focus of attention to this particular signal. The activity of other cells is suppressed such that these patients can hardly synchronize to other signals like the tone burst applied in this study. In other words, they cannot habituate to the stimuli. The numerical results of both inverse and forward approaches immediately establish a conceptual mapping between focal and non–focal attention and compensated–decompensated tinnitus, but yet such mapping that arose from considering inverse–forward methodologies remains to be improved by numerous physiological experiments and a careful tuning of model parameters.

V. CONCLUSION

Based on a model of adaptive resonance for the tinnitus neurophysiology, we derived an objective measure of the degree of tinnitus decompensation in large-scale brain data. The synchronization stability of ALR sequences is obtained by employing the wavelet phase coherence and this measure significantly discriminates the compensated and decompensated tinnitus patients. ART provides a mathematically well founded framework for Jastreboff tinnitus model to derive a tinnitus model of adaptive resonance. By means of applying the ERP model we were able to support the link between ART and Jastreboff model. It is concluded that neural correlates of the involved processes are globally reflected in the synchronization stability of ALR sequences which might be useful as objective tinnitus decompensation measure.

REFERENCES

[1] P. J. Jastreboff, "Phantom auditory perception (tinnitus): mechanism of generation and perception," *Neuroscience Research*, vol. 8, pp. 221–254, 1990.

[2] W. Delb, R. D'Amelio, O. Schonecke, and H. Iro, "Are there psychological or audiological parameters determining the tinnitus impact," in *Proceedings of the 6th tinnitus seminar*, J. W. P. Hazell, Ed., Cambridge, UK, 1999, pp. 446–451, Oxford University Press.

[3] V. Walpurger, G. Herbing-Lennartz, H. Denecke, and R. Pietrowsky, "Habituation deficits in auditory event related–potentials in tinnitus complainers," *Hearing Research*, vol. 181, pp. 57–64, 2003.

[4] S. D. Stephens, R. S. Hallam, and S.C. Jakes, "Tinnitus–a management model," *Clin. Otolaryngol. Allied Sci.*, vol. 11, pp. 227–238, 1986.

[5] C. J. Rennie, P. A. Robinson, and J.J. Wright, "Unified neurophysical model of EEG spectra and evoked potentials," *Biol. Cybernetics*, vol. 86, pp. 457–471, 2002.

[6] W. Ji and N. Suga, "Development of the reorganization of the auditory cortex caused by fear conditioning: "effect of entropine"," *J. of Neuroscience*, vol. 90, pp. 1904–1909, 2003.

[7] W. Mühlnickel, T. Elbert, E. Taub, and H. Flor, "Reorganization of the auditory cortex in tinnitus," in *Proc. of the National Academy of Sciences*, 1998, vol. 95, pp. 10340–10343.

[8] S. Grossberg, "Linking attention to learning, expectation, competition, and consciousness," in *Neurobiology of Attention*, L. Itti and J. Tsotsos, Eds., 2005, pp. 652–662.

[9] A. K. Engel, P. Fries, and W. Singer, "Dynamic predictions: Oscillations and synchrony in top–down processing," *Nature Review Neuroscience*, vol. 2, pp. 704–718, 2001.

[10] J. J. Robinson, C. J. Rennie, D.L. Rowe, S.C. O'Connor, and E. Gordon, "Multiscale brain modeling," *Philo. Transactions*, vol. 360, pp. 1043–1050, 2005.

[11] D. J. Strauss, W. Delb, R. D'Amelio, and P. Falkai, "Neural synchronization stability in the tinnitus decompensation," in *Proceedings of the 2st Int. IEEE EMBS Conference on Neural Engineering*, Arlington, VA, USA, 2005, pp. 186–189.

[12] W. Goebel and W. Hiller, *Tinnitus–Fragebogen (TF). Ein Instrument zur Erfassung von Belastung und Schweregrad bei Tinnitus*, Hofgrefe, Göttingen, Germany, 1998.

[13] A. H. Lockwood, R. J. Salvi, M. L. Coad, M. L. Towsley, D. S. Wack, and B. W. Murphy, "The functional neuroanatomy of tinnitus: evidence for limbic system links and neural plasticity," *Neurology*, vol. 50, pp. 114–120, 1998.

[14] J. W. Hall, *Handbook of Auditory Evoked Responses*, Allyn and Bacon, Needham Heights, MA, 1992.

[15] R. S. Hallam, S. C. Jakes, and R. Hinchcliffe, "Cognitive variables in tinnitus annoyance," *British Journal of Clinical Psychology*, vol. 31, pp. 613–621, 1988.