Proceedings of the 29th Annual International
Conference of the IEEE EMBS
Cité Internationale, Lyon, France
August 23-26, 2007.

The Role of Attention in the Tinnitus Decompensation: Reinforcement of a Large–Scale Neural Decompensation Measure

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Abstract— **Large–scale neural correlates of the tinnitus decompensation have been identified by using wavelet phase stability criteria of single sweep sequences of auditory late responses (ALRs). The suggested measure provided an objective quantification of the tinnitus decompensation and allowed for a reliable discrimination between a group of compensated and decompensated tinnitus patients. By interpreting our results with an oscillatory tinnitus model, our synchronization stability measure of ALRs can be linked to the focus of attention on the tinnitus signal. In the following study, we examined in detail the correlates of this attentional mechanism in healthy subjects. The results support our previous findings of the phase synchronization stability measure that reflected neural correlates of the fixation of attention to the tinnitus signal. In this case, enabling the differentiation between the attended and unattended conditions.**

It is concluded that the wavelet phase synchronization stability of ALRs single sweeps can be used as objective tinnitus decompensation measure and can be interpreted in the framework of the Jastreboff tinnitus model and adaptive resonance theory. Our studies confirm that the synchronization stability in ALR sequences is linked to attention. This measure is not only able to serve as objective quantification of the tinnitus decompensation, but also can be applied in all online and real time neurofeedback therapeutic approach where a direct stimulus locked attention monitoring is compulsory as if it based on a single sweeps processing.

I. INTRODUCTION

Tinnitus is defined as "the perception of a sound without the presence of an external sound source" [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. For compensated tinnitus patients, the internal noise is not annoying and a minority of the decompensated tinnitus patients, are troubled by the noise and may develop symptoms such as insomnia, concentration problems, and depressions which in some cases can even be a contributing factor to suicide [2]. It is commonly accepted 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. Conforming with the neurophysiological tinnitus model of Jastreboff [1] and the model of Hallam [3], the development of high tinnitus related distress can be explained by the fixation of attention to the tinnitus. The slope of the hearing loss in patients with high frequency hearing loss has been shown to be in some relation with tinnitus distress [4].

Most of the research in identifying the neural correlates of attentional effects at N1 and P2 reported the amplitude examination of large number of ALR sweeps due to poor signal-to-noise ratio. As a result, the evolution of sweep sequences, i.e., amplitude and phase fluctuations, are not locally reflected over the stimuli and sweep sequences, respectively, see [5], [6]. To solve these problems, we proposed a time-scale measure which is based on the phase information of single sweeps exclusively [7]. 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.

We have reported the implementation of wavelet phase synchronization stability of single sweeps of ALRs in objective quantification of the tinnitus decompensation [8]. Specifically, the synchronization stability which is according to the underlying model linked to the focus of attention on the tinnitus signal, discriminated between a group of compensated and decompensated tinnitus patients. Based on the tinnitus model, decompensated tinnitus patients pay too much attention to the tinnitus signal [9], [1], the signal tinnitus is expected by higher auditory areas in these patients, employing Adaptive Resonance Theory (ART) terms [10], and thus matches to 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 bursts applied in the study. Furthermore, the habituation effects over the ongoing experiment also have been examined using single sweeps approach. It has been shown that decompensated tinnitus patients cannot habituate to the stimuli and these findings are in accordance to [11] where decompensated tinnitus patients showed a less distinct habituation of the N1 minus P2 wave amplitude differences compared to compensated tinnitus patients using averaged ALR trials.

In the following study, we examined in detail the correlates of the attentional mechanism that demonstrated in the previous study by using a maximum entropy auditory paradigm principle in healthy subjects [12]. Attention was manipulated by requiring the subjects to attend to the auditory stimuli in a specified ear while ignoring signal presented concurrently in the other ear. The results support our previous findings

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of the phase synchronization stability measure that reflected neural correlates of the fixation of attention to the tinnitus signal. In this case, enabling the differentiation between the attended and unattended conditions. More importantly, we show that the wavelet phase synchronization of ALR single sweeps allows for a direct online monitoring of phase locked auditory attention as a single sweep processing is employed. Such an online monitoring cannot be implemented by known procedures as they are based on large–scale averages of ALRs. This measure is not only able to serve as objective quantification of the tinnitus decompensation, but also can be applied in all online and real time neurofeedback therapeutic approach where a direct stimulus locked attention monitoring is mandatory.

II. METHODS

A. Oscillatory Tinnitus Model

Based on 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 [13]. 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 the tinnitus signal, which is related to negative association and may reorganize the auditory cortex in the sense above. A mathematical framework of the cognitive tinnitus processing may be provided by Adaptive Resonance Theory (ART) of Grossberg [10], in which top-down projections are the key mechanism for solving the stability–plasticity dilemma. ART is a representative theory of a fundamental paradigm shift in cognitive neuroscience [14]. ART claims that sensory processing is a highly active process with strong top–down interactions. Many cognitive models based on ART have been suggest so far [10] and recently ART has also been adapted to the auditory system for auditory scene analysis and source segregation [15]. 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.

B. ALR Phase Stability

In our studies, we employed the time–scale 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 the frequency information alone. This wavelet coherence increases with the correlation of the envelopes between two signals as well as if their phase shows smaller variations in time [7].

In contrast to the analysis of averaged potentials, the amplitude information of single sweep event–related potentials, i.e., the response to individual events, turned out to be fragile in some cases [5]. Large amplitude fluctuations can easily be introduced by slight accidental changes in measurement setup over time. Since the signals exhibit a high degree of variance from one sweep to another, even robust amplitude independent synchronization measures such as the time–scale entropy [16] can hardly be applied to assess their synchronization stability.

To be independent from amplitude fluctuations one can focus on the wavelet phase coherence exclusively [7]. The wavelet phase coherence defined in [7] is mainly applied to measure the degree of phase locking of two signals in time, e.g., obtained from two different sites. Although such large–scale measures of cortical potentials based on synchronization provided no direct link between effects at the scale of neurons, recent multiscale models of event related potentials [17] representing corticothalamic loops may also justify their use, see [18].

Note that the estimation of the phase relation from experimental data represents an inverse problem in a mathematical sense. It has thoroughly been investigated in nonlinear dynamics, in particular for weakly coupled self–sustained chaotic oscillators, see [19] for a review. The role of phase locking in modern biosignal processing in a more general sense as presented here can be found in [20].

For the determination of the synchronization stability, we need an adaptation of the derived phase locking measure between two signals to our problem, see [8] for more details. Let

$$\psi_{s,\tau}(\cdot) = |s|^{-1/2}\psi((\cdot - \tau)/s) \tag{1}$$

where $\psi \in L^2(\mathbb{R})$ is the wavelet with $0 < \int_{\mathbb{R}} |\Psi(\Omega)|^2 |\Psi(\Omega)|^{-1} \mathrm{d}\Omega < \infty$ ($\Psi(\Omega)$ is the Fourier transform of the wavelet ψ), and $s, \tau \in \mathbb{R}$, $s \neq 0$). The wavelet transform

$$\mathcal{W}_\psi : L^2(\mathbb{R}) \longrightarrow L^2(\mathbb{R}^2, \frac{\mathrm{d}s\mathrm{d}\tau}{s^2}) \tag{2}$$

of a signal $f \in L^2(\mathbb{R})$ with respect to the wavelet ψ is given by the inner L^2–product

$$\begin{aligned}(\mathcal{W}_\psi f)(s,\tau) &= \langle f, \psi_{s,\tau}\rangle_{L^2} \\ &= \int_{\mathbb{R}} f(t)\psi_{s,\tau}(t)dt. \end{aligned} \quad (3)$$

In this study, we used the 4th–derivative of the complex Gaussian function as wavelet.

Note that the scale s can always be associated with a pseudo-frequency F_a in Hz by

$$F_a = F_\psi / s.\Delta$$

where Δ is the sampling period and F_ψ is the center frequency of the wavelet ψ [21].

The synchronization stability $\Gamma_{s,\tau}$ of a sequence $\mathcal{F} = \{f_m \in L^2(\mathbb{R}) : m = 1, \ldots, M\}$ of M sweeps is defined as

$$\Gamma_{s,\tau}(\mathcal{F}) := \frac{1}{M}\left|\sum_{m=1}^{M} e^{\imath \arg((\mathcal{W}_\psi f_m)(s,\tau))}\right|. \quad (4)$$

Apparently, the value for synchronization stability in (4) is in the range of $(0, 1)$. We have a perfect neural synchronization stability for a particular s' and τ' for $\Gamma_{s',\tau'} = 1$ (perfectly coherent phases) and a decreasing stability for smaller values due to phase jittering.

C. Subjects and Materials

A total of 10 student volunteers from Saarland University with normal hearing participated in the study. ALRs were acquired through commercially available amplifier (g.tec USBamp, Guger Technologies Austria). We delivered 3 pure tones in random order to the right ear at randomized inter-stimulus interval (ISIs). Meanwhile, the left ear was presented with music. Subjects were required to detect the target tones in the first part of the experiment and then ignore the stimuli in the second part of the experiment. Single sweeps, i.e., the responses to the individual stimulus were recorded using electrodes placed at the left and right mastoid, the vertex, and the upper forehead. Electrodes impedances were below 5kΩ in all measurements (filter: 1Hz–30Hz, sampling frequency: 512Hz). Reader may refer to [12] for details on the experiment setup.

III. RESULTS AND DISCUSSIONS

A total of 29 tinnitus patients entered the first study. They were separated into a group of 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 [22] which is a German version of the questionnaire by Hallam. See [8] for more information on the study.

Fig. 1 shows the averaged synchronization stability for the group of compensated and decompensated tinnitus patients for $s = 40$ as example. Note that the scale can always be associated with a pseudo frequency as described in the II-B. For this scale, the temporal resolution is rather satisfactory and the differences in this frequency band are also clearly noticeable [8].

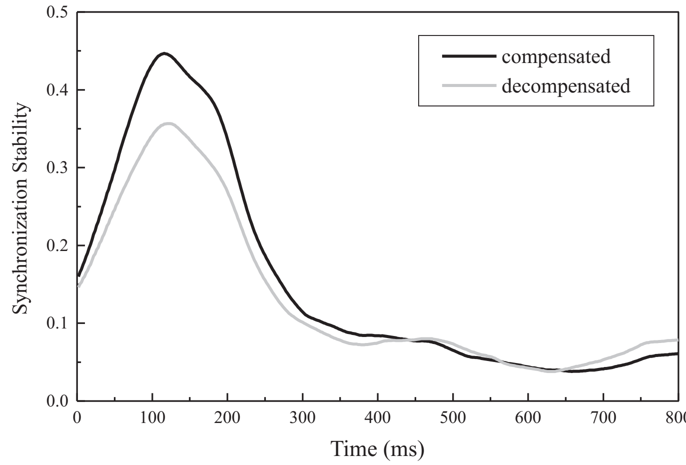

Fig. 1. The averaged difference of the synchronization stability for $s = 40$ as example.

The most significant differences (Wilcoxon test, significance level $p<0.05$) of the synchronization stability are found within the time interval between 100ms and 200ms where the N1 (approx. 100–150ms) and the P2 (approx. 150–200ms) waves are located. The neural activity reflected in these waves is presumably associated with the auditory cortex [23], [24].

Fig. 2 showed the phase stability of a subject for both conditions (attended and unattended) for 3 different types of stimuli tones for $a = 40$ as example. Note that difference in the stimulus pitch (different tones) results in different phase stability.

Due to the factors of measurement instabilities in data acquisition, we normalized the data that we gathered. The normalized averaged difference of the synchronization stability for all subjects in attended and unattended conditions (for the target tones) is depicted in Fig. 3. Again, the major and significant differences was expected at the time interval where the N1 and the P2 waves are located. Herein, the measure enable the differentiation between the attended and unattended conditions. The results obtained support our findings in previous study on the discrimination of decompensated and compensated tinnitus patients based on phase synchronization stability of a single sweep analysis which is linked to attention.

An experiment of multi–channel EEG recording has been conducted as well and the results can be found in [12].

IV. CONCLUSIONS

We have presented a new scheme for the objective quantification of the tinnitus decompensation using the synchronization stability of ALR sequences. This synchronization stability is significantly different in a group of compensated and decompensated tinnitus patients. The presented model linking ART to the Jastreboff tinnitus allowed an ART based

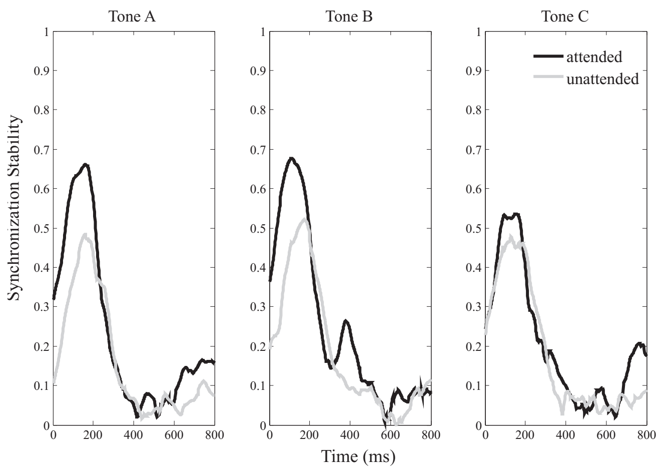

Fig. 2. The difference of the synchronization stability for a subject ($a = 40$ as example) for 3 different tones.

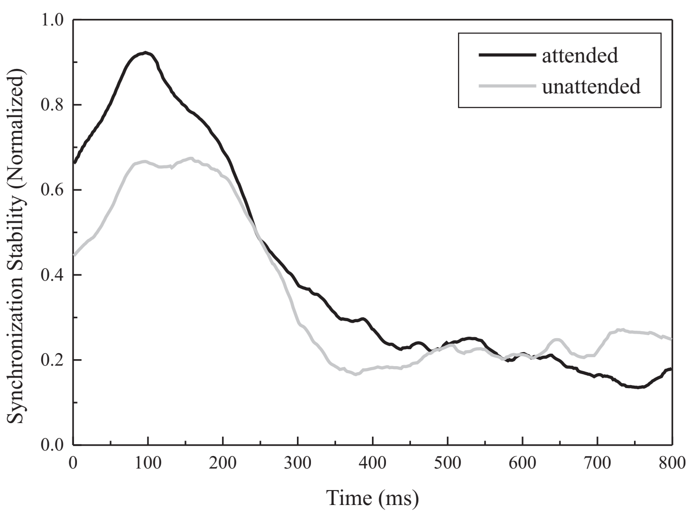

Fig. 3. The normalized averaged difference of the synchronization stability (for the target tones) $s = 40$ as example.

interpretation of the obtained results. In our subsequent study, the synchronization stability again able to differentiate between the attended and unattended conditions. This finding confirm that the synchronization stability in ALR sequences is linked to attention.

It is concluded that the synchronization stability of ALR sequences can be used in the objective quantification of the tinnitus decompensation. Due to the analysis of single sweeps, the presented approach provides a direct or real time monitoring and might thus be used in therapeutic neurofeedback based control system, which has potential application in a clinical treatment for tinnitus patients.

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