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Stochastic Resonance in Brain Activity Elicited by Auditory Stimuli

K. Tanaka, I. Nemoto, M. Kawakatsu and Y. Uchikawa, *Member, IEEE*

Abstract—**We measured auditory steady state responses (ASSRs) in magnetoencephalogram to an ongoing sinusoidal amplitude modulated tone presented to the subject's left ear while bursts of white noise of various intensities were presented to the right ear. Because the power and coherence as functions of the noise to signal ratio differed considerably among subjects, we used their maximum values as test statistics for testing the group data. The results showed a significant enhancement in the phase coherence of ASSRs obtained over the right temporal regions by the presence of white noise of appropriate intensity. The observed stochastic resonance (SR) most likely occurred within the central nervous system. Our finding may be quite important as mechanisms of SR in biological systems are mostly unknown.**

I. Introduction

Stochastic resonance (SR) in neuronal system has been well established experimentally through controlled addition of external noise [1]. A certain amount of noise has been shown to improve [2]. We showed also the presence of SR in auditory steady state responses (ASSRs) in magneto- encephalogram (MEG) [3, 4]; we presented an amplitude- modulated tone superimposed with white noise and found that the phase coherence of the evoked responses increased when there was a small amount of noise.

The ASSRs to sinusoidal amplitude-modulated (SAM) tones have been studied extensively. The ASSR oscillates at the frequency of acoustic amplitude modulation, and its power is greatest when the modulation frequency is in the 40-Hz range [5]. The mechanisms of the generation of ASSRs and its phase synchronization are not known. Ross et al. showed that ASSR was explained equally well by the hypothesis of linear overlapping of successive middle latency responses and by that of synchronization of gamma-band responses [5]. We have studied the phase synchronization behavior in ASSRs to optimal chirp tones [6]. We also speculated from the result that synchronization of an ongoing 40 Hz component (gamma component) in MEG was at least partly responsible for the ASSR although superposition of middle latency evoked response to each cycle of the stimulus was also a candidate [6]. Our finding that ASSRs demonstrated SR behavior indicated the presence of some nonlinear mechanism in the generation of ASSRs.

In the present study, we presented an ongoing SAM tones to the left ear and the white noise of various intensities to the right ear separately. If this procedure also produced any SR effect, one could conclude that this SR occurred after the right and left auditory signals interacted with each other and not in the periphery.

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K. Tanaka is with Division of Science and Engineering, Tokyo Denki University, Saitama, JAPAN. (e-mail: ktanaka@mail.dendai. ac.jp).

I. Nemoto. is with the School of Information Environment, Tokyo Denki University, Chiba, JAPAN. (e-mail: nemoto@sie.dendai.ac.jp).

M. Kawakatsu, is with the School of Information Environment, Tokyo Denki University, Chiba, JAPAN. (e-mail: kawakatu@sie.dendai.ac.jp).

Y. Uchikawa is with Division of Science and Engineering, Tokyo Denki University, Saitama, JAPAN. (e-mail: uchikawa@f.dendai. ac.jp).

II. Methods

A. Subjects

Six male subjects (21-34 years), four of them right-handed (two left-handed), without histories of hearing loss or neurological disorder participated in the study. Written forms of informed consent was obtained from all of them and the experiments were conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Tokyo Denki University. The subjects were instructed to watch a self-selected silent movie and ignore the auditory stimuli.

B. Auditory stimuli

A 1 kHz sinusoidal wave was amplitude modulated with modulation frequency 40-Hz and depth 1.0 to obtain the SAM tone. The SAM tone was presented continuously to the subject's left ear during an experimental run. The designed frequency band of the white noise ranged from 50 to 10,000 Hz. The intensity of the SAM tone was set at 40 dB (SL: sensation level) above its threshold measured without noise for each subject. We also measured the threshold of hearing for the white noise for each subject using only the noise. About 100 bursts of white noise, each lasting for 1.0 s, were presented to the right ear in one experiment run to obtain the average ASSR over the 100 epochs. The ASSRs were measured for six noise levels, noise-free ($-\infty$ dBSL), and the five levels from -6 to 6 dBSL separated by 3 dBSL increments. Stimuli were generated with an Apple Macintosh computer driving Sound Generator and delivered via Eartone ER2 transducer to the subject's ear through a plastic tube of length 1.7 m. The inter-stimulus intervals of white noise were randomized between 0.75 s and 1.25 s. Six runs for the 6 noise intensities were done in random order, each being separated from another by a ~2 min resting period.

C. MEG data acquisition and processing

MEG recordings were made with a 122-channel whole head planar gradient MEG system (Neuromag-122™) in a magnetically shielded room of Tokyo Denki University. The signals were band-pass filtered from 0.03 to 100 Hz and digitized at 1 kHz. At least 100 epochs were recorded for averaging.

Since the planer-gradiometer type MEG equipment consisted of two orthogonal channels at each sensor location, we used the signal vector $\mathbf{x}(t_i)=(x_1(t_i), x_2(t_i))^T$ measured at the maximally responding sensor site over the right and left temporal regions in each subject. The principal component analysis was applied to this vector process to obtain a scalar process $\xi(t)$ associated with the largest of the two eigenvalues of the covariance matrix $\mathbf{C}$ of the averaged response $\bar{\mathbf{x}}(t_i)$:

$$\mathbf{C}=\frac{1}{I-1}\sum_{i=1}^{I}(\mathbf{x}(t_i)-\bar{\mathbf{x}})(\mathbf{x}(t_i)-\bar{\mathbf{x}})^T,\ \bar{\mathbf{x}}=\frac{1}{I}\sum_{i=1}^{I}\mathbf{x}(t_i)\ .\cdots\cdots(1)$$

The time t_i, i= 1,…,I runs through the 1 s epoch corresponding to a noise burst. For quantifying the degree of synchronization, we used the phase coherence estimated for the latter 500 ms period (during steady state) of the 1 s epoch by

$$\left|\hat{C}_\varphi\right|^2=\left(\frac{1}{N}\sum_{k=1}^{N}\frac{X_k(\omega)}{A_k(\omega)}\right)^2+\left(\frac{1}{N}\sum_{k=1}^{N}\frac{Y_k(\omega)}{A_k(\omega)}\right)^2\cdots\cdots\cdots(2)$$

$$A_k(\omega)=\sqrt{(X_k(\omega))^2+(Y_k(\omega))^2}$$

where $X_k(\omega)$ and $Y_k(\omega)$ are respectively, the real and imaginary parts of the discrete Fourier transform of $\xi(t)$ for $0.5 < t < 1$ with the angular frequency $\omega = 80\pi$ and N is the number of epochs to be analyzed (usually 100). The power of the 40 Hz component was obtained by

$$P(\omega)=\sum_{k=1}^{N}(A_k(\omega))^2/N\ .\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(3)$$

D. Statistics used for statistical analysis

We applied statistical analysis both to individual subject's data and to the group data. The power defined by (3) and the phase coherence by (2) may be directly used for the usual repeated measures Dunnett's multiple comparison on the group data. However, this test may not be powerful enough to detect significant effect of the noise because of large variations among subjects. Considering that only significant increase in power or coherence relative to their values at noise-free condition (-∞ dBSL) is necessary to be shown for indicating the presence of SR (regardless of the value of stimulus intensity of noise at which the increase happens), their maximum values may be used as the statistics for the purpose as shown in the next section.

For the tests of individual data and group data, we need statistics of which the distributions can be reasonably assumed. For the power, we used the ratio:

$$R_\rho = P_\rho(\omega)\,/\,P_{-\infty}(\omega)\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(4)$$

with $P_\rho(\omega)$ and $P_{-\infty}(\omega)$ obtained by (3) for noise intensities ρ dBSL and –∞ dBSL, respectively. R_ρ can be assumed to follows the F distribution $F(2N, 2N)$ where N is the number of epochs used in the estimates $P_\rho(\omega)$, $P_{-\infty}(\omega)$, 100 in our case, under the null hypothesis of equal power. (The rationale for this test is the hypothesis that the power is equal to the variance of the signal where ensemble average is replaced by time average.) Let $F^{\alpha/2}(2N, 2N)$ be the upper 100 α/2 % point of $F(2N, 2N)$. Then for each subject, the null hypothesis of equal power was rejected if obtained ratio R_ρ satisfied

$$R_\rho > F^{\alpha/2}(2N, 2N)\ \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(5)$$

We used 5 values of $\rho \neq -\infty$ dBSL, so the most conservative (two-tailed) test of significance level α would be obtained by using α/5 instead of α in (5).

For coherence

$$D_\rho=\frac{2}{\sqrt{3}}\frac{g(2\,|\,\hat{C}_\varphi(\rho)\,|)-g(2\,|\,\hat{C}_\varphi(-\infty)\,|)}{\sqrt{2/(N-4)}}\cdots\cdots\cdots\cdots(6)$$

was used [7]. Here $\hat{C}_\varphi(\rho)$ is the estimate of phase coherence at noise intensity ρ and $g(x)=\sin^{-1}(\sqrt{3/8x})$. When $\left|\hat{C}_\varphi(-\infty)\right| < 0.45$, D_ρ is known to be approximately normally distributed with mean 0 and variance 1 under the null hypothesis: $C_\varphi(\rho)= C_\varphi(-\infty)$ [7]. The underlying assumption is that the phase is distributed according to the Von Mises distribution, which is probably the simplest and natural distribution for the phase in our experiment. For each subject, if $D_\rho > \arg(F(x)=1-\alpha/(2K))$ where F is the cumulative normal distribution function and K (= 5) the number of levels of $\rho \neq -\infty$ dBSL used, then we decided that there was increase in the phase coherence with significance level α. Division by $2K$ was again to be on the conservative side.

E. Max value tests on group data

For each subject, the values

$$R^* = \max\{R_\rho, \rho=-6\,\text{dB},...,6\,\text{dB}\},\quad D^* = \max\{D_\rho, \rho=-6\,\text{dB},...,6\,\text{dB}\}\ \cdots\cdots\cdots\cdots\cdots(7)$$

were obtained and averaged across the subjects. R_ρ' s and D_ρ' s were assumed to be distributed according to the F-distribution and the normal distribution, respectively, as mentioned above, but the theoretical distributions of their maximum values are extremely difficult to obtain in closed forms [8]. We therefore performed 10^6 Monte Carlo simulations to obtain the distributions of the average maximum values under the null hypothesis of equal power and equal coherence. Then the averages of R^* and D^* were used as test statistics against the distributions obtained. Usual hypothesis tests were performed. We refer to this test as the Max Value Test below.

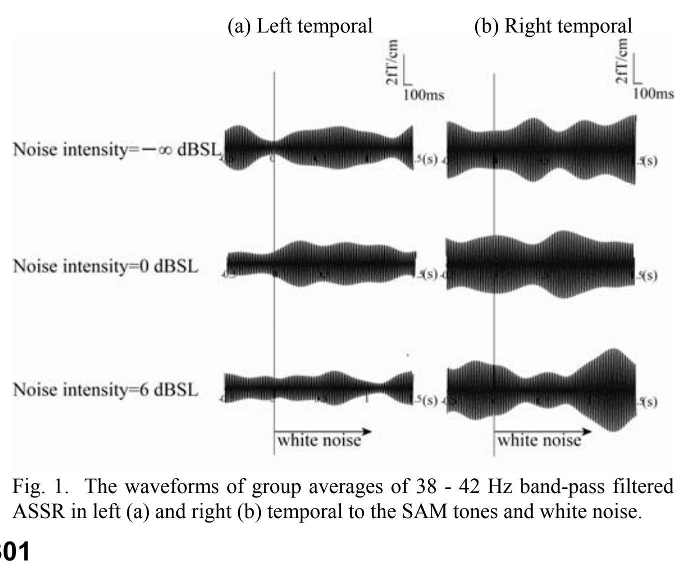

Fig. 1. The waveforms of group averages of 38 - 42 Hz band-pass filtered ASSR in left (a) and right (b) temporal to the SAM tones and white noise.

III. Results

Fig.1 shows the grand average of the band-pass filtered (38-42 Hz) ASSR in left (a) and right (b) temporal in all the six subjects. The power and phase coherence of ASSRs obtained in the left and right temporal regions were statistically compared and right temporal regions were tested by two-way (laterality × noise intensity) analysis of variance (ANOVA) which exhibited a significant main effect of the laterality for the power ($F(1,50)=13.159$, $p<0.0001$) and the phase coherence ($F(1,50)=28.827$, $p<0.0001$). The power of ASSR obtained in the right temporal was larger than that in left temporal (left: $0.622 \pm 0.283 \times 100 (fT/cm)^2$, right: $0.808 \pm 0.476 \times 100 (fT/cm)^2$). Similarly, the phase coherence of ASSR was higher in the right temporal region than in the left (left: 0.060±0.076, right: 0.149±0.106). There were no significant effects of the noise intensities nor interaction between laterality and noise intensities.

Fig.2 shows the average power of ASSRs obtained in the left temporal region for the 6 noise intensities. Table 1 shows the result of the test of equality of power by the criterion (6) for each subject. It is seen that 4 subjects showed increase in power ($R_\rho>1$) and three of them were significant ($5 \times p < 0.05/2$). However, The *max value test* did not detect a 'positive' effect either; the average of the maximum ratio R_ρ was 1.158 which gave $p=0.767>0.05/2$.

Fig.3 shows the average phase coherence of ASSRs obtained in the left temporal for the 6 noise intensities. Table 2 shows the result of the test of equality of phase coherence for each subject. Three subjects showed increase in phase synchrony ($D_\rho>0$) but none of them were significant ($5 \times p>0.05/2$). Neither the repeated measures Dunnett's multiple comparison nor the *max value test* on the group data exhibited significant 'positive' effect.

Fig.4 shows the average power of ASSRs obtained in the right temporal. Table 3 shows that all the subjects showed increase in power ($R_\rho>1$) and one of them (subject F) were significant ($5 \times p<0.05/2$). However, the multiple comparison detected no positive effect of noise on the power in the group data. In the *max value test*, the average of R_ρ was 1.276 which gave $p=0.037>0.05/2$ approaching significance.

Fig.5 shows the average phase coherence of ASSRs obtained in the right temporal. Table 4 shows that all the six subjects demonstrated increase in phase coherence ($D_\rho>0$) at some noise intensity and two of them (B and F) showed significant increase. The multiple comparison on the group data exhibited no significant 'positive' effect. On the other hand, the *max value test* detected a significant positive effect of the noise on the group data of phase coherence; the average of the maximum D_ρ values was 4.717 which gave $p<0.0001$.

IV. Discussion

The multiple comparison of Dunnet on group data showed no increase in either power or in phase coherence of ASSR in either hemisphere. However, the *max value test* revealed that in the right temporal region, there was a significant increase in phase coherence in the presence of noise. It also showed

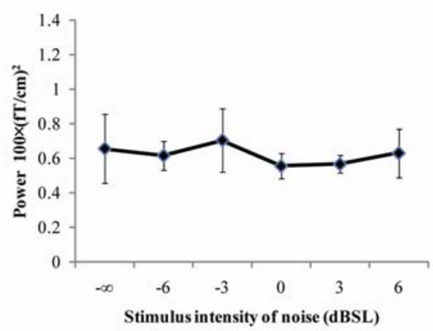

Fig. 2. The average power of ASSRs obtained in the left temporal region during the latter half of the 1 s noise burst as a function of the noise intensity (mean ±SD).

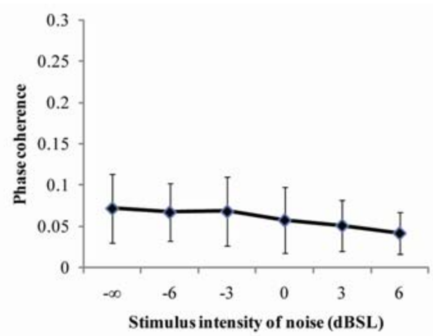

Fig. 3. The average phase coherence of ASSRs obtained in the left temporal region during the latter half of the 1 s noise burst as a function of the noise intensity (mean ± SD).

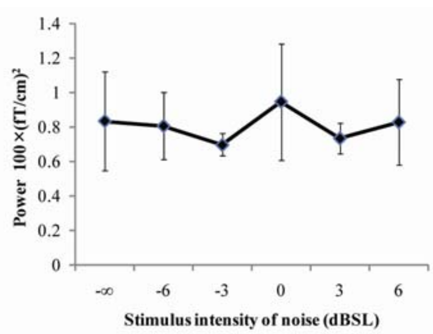

Fig. 4. The average power of ASSRs obtained in right temporal region. See the legend to Fig. 2.

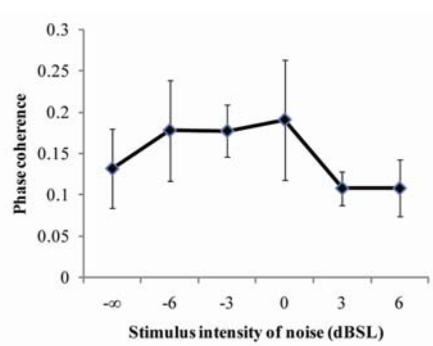

Fig. 5. The average phase coherence of ASSRs obtained in right temporal region. See the legend to Fig. 3.

TABLE I

THE RESULT OF THE TEST OF EQUALITY OF THE POWER RATIO OF ASSR OBTAINED IN LEFT TEMPORAL IN EACH SUBJECT.

Subject	A	B	C	D	E	F
ρ (maxP_ρ)	3 dBSL	-6 dBSL	-6 dBSL	3 dBSL	-3 dBSL	-3dBSL
P_ρ (100×(fT/cm)^2)	0.459	0.951	0.608	0.757	1.472	0.857
R_ρ	0.872	1.866	1.257	1.760	0.940	1.727
p	0.833	<0.001*	0.053	<0.001*	0.670	<0.001*

* indicates significant '*positive*' effect of the noise.

TABLE II

THE RESULT OF THE TEST OF EQUALITY OF THE PHASE COHERENCE OF ASSR OBTAINED IN LEFT TEMPORAL IN EACH SUBJECT.

Subject	A	B	C	D	E	F
ρ (max $\hat{C}_\varphi(\rho)$)	0 dBSL	-3 dBSL	-3 dBSL	-3 dBSL	-3 dBSL	-6 dBSL
$\hat{C}_\varphi(-\infty)$	0.055	0.021	0.260	0.051	0.020	0.024
$\hat{C}_\varphi(\rho)$	0.034	0.062	0.253	0.035	0.034	0.075
D_ρ	-0.512	1.055	-0.085	-0.387	0.425	1.242
p	0.696	0.146	0.534	0.650	0.335	0.107

TABLE III

THE RESULT OF THE TEST OF EQUALITY OF THE POWER RATIO OF ASSR OBTAINED IN RIGHT TEMPORAL IN EACH SUBJECT.

Subject	A	B	C	D	E	F
ρ (maxP_ρ)	3 dBSL	0 dBSL	-6 dBSL	-3 dBSL	0 dBSL	3 dBSL
P_ρ (100×(fT/cm)^2)	0.492	0.750	0.754	0.647	2.477	0.872
R_ρ	1.395	1.299	1.252	1.046	1.138	1.501
p	0.009	0.032	0.057	0.374	0.152	0.002*

* indicates significant '*positive*' effect of the noise.

TABLE IV

THE RESULT OF THE TEST OF EQUALITY OF THE PHASE COHERENCE OF ASSR OBTAINED IN RIGHT TEMPORAL IN EACH SUBJECT.

Subject	A	B	C	D	E	F
ρ (max $\hat{C}_\varphi(\rho)$)	-6 dBSL	-3 dBSL	0 dBSL	0 dBSL	0 dBSL	-3 dBSL
$\hat{C}_\varphi(-\infty)$	0.279	0.006	0.217	0.093	0.168	0.029
$\hat{C}_\varphi(\rho)$	0.414	0.096	0.325	0.137	0.235	0.159
D_ρ	1.630	2.378	1.327	0.710	0.877	2.407
p	0.051	0.009*	0.092	0.239	0.190	0.008*

* indicates significant '*positive*' effect of the noise.

that the increase in power also approached (but not reached) significance. Therefore we may conclude that in the group data SR was seen in the right hemisphere which was contralateral to the SAM stimulus. TABLEs I-IV show that out of the 6 subjects, 3 showed significant increase in either power or in phase coherence in either one or both of the hemispheres suggesting the occurrence of SR in these subjects.

The ascending auditory pathways from both ears meet at the level of the brainstem and send more fibers to the auditory field contralateral to their origin. Consequently each hemisphere receives signals primarily from the contralateral ear. In electroencephalographic recordings, Wolpaw and Penry found larger amplitudes of auditory responses (N1/P2) contralaterally than ipsilaterally to the stimulated ear [9]. Other studies have confirmed the dominance of contralateral responses in auditory evoked potentials and fields. Moreover, Tiihonen et al [10] found that auditory evoked 40 Hz steady-state magnetic fields and sustained fields were larger when the right hemisphere was contralateral to the stimulus than when the left hemisphere was. Our previous experiences also agree with this finding and we gave the SAM tone to the left ear to capture SR in the right hemisphere possibly more easily than in the left hemisphere; the result mentioned above was as expected.

As the SAM tone and the noise entered different ears separately, the SR observed in the present study occurred most likely in the central nervous system and not in the peripheral. We cannot totally exclude the possibility of the SR occurring in the periphery as a result of feedback via some efferent pathway although it seems unlikely.

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