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Sound presentation during different respiration phases alters the sound-induced vasoconstriction mediated by the sympathetic nerve

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HIGHLIGHTS

- Sound presentation causes larger vasoconstriction in inspiration than in expiration.
- A respiration derived sympathetic tone gates a sound-induced sympathetic tone.
- RVLM is suggested as the neuronal center of the gate mechanism.

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ABSTRACT

The sympathetic orienting response induced by sound has been widely studied and utilized as an index of sound-induced emotions and other mental phenomena. Since sympathetic activity has its own oscillation that is synchronized with the respiration rhythm (sympatho-respiratory coupling), it is possible that the sound-induced orienting response of sympathetic activity varies depending on the respiration phase. In this study, the sound presentations were timed to coincide with the onset of inspiration or expiration. 10 experimental sounds were presented to 12 males aged 21–35 years. Respiration was monitored with an elastic chest band. Vasoconstriction at a finger was measured with laser Doppler flowmetry as a sympathetic orienting response. We found that the sound-induced vasoconstriction was larger for sounds presented in the inspiration phase than for those presented in the expiration phase, suggesting that the respiration network-derived sympathetic tone works as a gate for the sound-induced sympathetic tone.

1. Introduction

The effects of auditory stimuli on the autonomic nervous system have been widely studied. The sounds used in these studies have ranged from environmental noise [2] to emotion-inducing sounds [8,15]. The responses of the sympathetic nervous system have been commonly used to evaluate the effect of sound stimuli on autonomic activities and have been observed by measuring, for example, the skin conductance response (SCR), electromyograms, and vasoconstriction [6,23]. On the other hand, the sympathetic nervous system has its own oscillation.

For decades coupling has been indicated between the sympathetic nervous system and the respiratory oscillator network producing a common respiratory rhythm [1,5,13]. The coupling is easily observed as a change in the heart rate, known as respiratory sinus arrhythmia (RSA), which is classically described as increases and decreases in the heart rate modulated by arterial baroreflex. However, anatomical studies have demonstrated that at least partial sympatho-respiratory coupling occurs in the medulla [18–20,26] and it is suggested that RSA partly originates in the nucleus ambiguus [19]. One of the notions that explains these relationships (the mechanisms that link respiration and sympathetic activity) is called the respiratory gate mechanism [17]. It is known that several inputs, for example, baroreceptors [9] and chemoreceptors [14], are 'gated' by the respiration phase. Some studies have showed that this gating mechanism also exists for auditory inputs [11,12]. These studies focused on cardiac responses and reported that the position of the stimulus in the respiratory cycle alters the response.

They reported that stimulation provided during the expiration phase causes the heart rate to decrease at first and then accelerate after a few seconds [12], but their reports are inconsistent regarding the response to stimulation provided in the inspiration phase [12,27,28]. Since the observations were made with respect to heart rate, it is difficult to derive its change on an autonomic level especially in such a biphasic response. They did not discuss the details

Abbreviations: ECG, electrocardiogram; LDF, laser Doppler flowmetry; RSA, respiratory sinus arrhythmia; SCR, skin conductance response; SPL, sound pressure level; RVLM, rostral ventrolateral medulla; CeA, central nucleus of the amygdala; NTS, nucleus tractus solitarius; CVLM, caudal ventrolateral medulla; MGB, medial geniculate body; LA, lateral amygdala; VRC, ventrolateral respiratory column; IE neurons, inspiratory-to-expiratory neurons.

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Table 1
List of sounds.

White noise	Pink noise	Brown noise	Blue noise	1 kHz tone
Pistol	Scratch 1	Scratch 2	Scratch 3	Scratch 4

of the neuronal link to explain the 'gate' system. They repeatedly used the same sound, which usually causes habituation [12,27,28].

In this report we try to refigure this experiment from a new point of view. We measured blood flow using the laser-Doppler technique at digit tip skin. The skin vasoconstrictor reflex revealed in the reduction of blood flow suggests the direct effect of sympathetic activity due to its sufficiency of sympathetic innervations.

2. Materials and methods

17 healthy males aged 21–35 years participated in the physiological experiments described below. Females were not selected to avoid the effects of the menstrual cycle. The participants were informed that they would hear a lot of sounds. They gave written consent, which was approved by the Ethics and Safety Committees of NTT Communication Science Laboratories. They were paid for their participation. The experiments were performed in a sound-insulated listening room. Participants sat on a sofa and were encouraged to relax. The experiments were conducted between 14:00 and 18:00 h to minimize the effect of circadian hormone rhythms.

In the current study, we chose the sounds listed in Table 1. Noise and tone sounds were produced by MATLAB (The MathWorks, USA). Others consisted of live recordings of scratching a blackboard. These sounds were presented at 40 kHz (range 20–20,000 Hz in accordance with human aural characteristics). Each sound lasted 500 ms and had a 20 ms rise time. The sound pressure level (SPL) was modulated to 70 dB by measuring the maximum A-weighted SPL of these sounds in the slow mode. The stimuli were converted to analog signals with an audio interface (EDIROL UA-5, Roland, Japan) and presented through headphones (Sennheiser HD650). Spectrograms of the sound stimuli are shown in Supplemental Fig. 1.

Blood flow was measured by laser Doppler flowmetry (LDF), using an LDF100C with a TSD143 probe (both from BIOPAC Systems, USA). The probe was attached to the participant's left middle finger. A decrease in blood flow indicated sympathetic-nervous-system-induced vasoconstriction. Respiration was observed with an elastic chest band TR651-T (Nihon-Kohden, Japan), which measured the changes in rib cage diameter caused by respiration. An electrocardiogram was also obtained with an ECG100C (BIOPAC Systems, USA) to calculate interbeat intervals (R–R intervals). R-wave detection was performed with MATLAB, and the result was visually screened to eliminate any inappropriate R-wave detection related to artifacts such as movement. All the analog outputs were digitized with a USB-6259 (National Instruments, USA). The sampling rate was 1000 Hz.

Participants were given general information about the experiment, and their written consent was obtained in advance. They sat on a sofa wearing headphones and with a rubber band around the waist to measure respiration. They were adapted to the experimental atmosphere for 5 min prior to the listening session. They were presented with 10 types of experimental sounds and 10 dummy silences as a control. The timings of the sound presentations were set to coincide with the onset of inspiration or expiration. Every sound was presented once for each respiration phase in random order. The initial presentation of each sound was evened out for each respiration phase. The intervals between sound presentations were set at random lengths ranging from 25 s to 50 s. The participants undertook the same experiment with the sounds presented in a different order after a short rest.

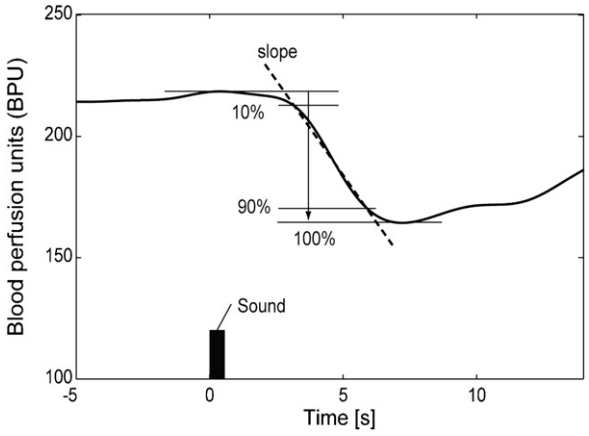

Fig. 1. Example of blood flow showing slope analysis.

The detection of the onset of inspiration and expiration and the timing of the sound presentation were programmed with Labview (National Instruments, USA). The times when the temporal differentiation of the respiratory trace exceeded the threshold were defined as the onset of inspiration and expiration. We checked carefully that the onset of the sound stimuli coincided with the beginning of the inspiration and expiration. Data that did not meet this requirement due to the detection error of the respiration phase were excluded. If these errors were found in more than half of the sound presentations for a given participant, all that participant's data were removed (4 participants). The data of participants who exhibited arrhythmia were also excluded (1 participant), thus the total number of participants used for analysis was 12. The time-series LDF data were obtained by averaging the data for inspiration and expiration both with and without sound stimuli.

Heart rate was also calculated using the R–R interval. It was interpolated at 100 Hz to form a continuous data series, which was resampled second by second. The results for each participant were averaged for each of the four conditions. To minimize the effect of RSA, the averaged data obtained for inspiration with sound presentation was subtracted from the averaged data obtained for inspiration without sound (insp*s − insp). The same procedure was used for the expiration data (exp*s − exp).

3. Results

Reductions in blood flow caused by vasoconstriction were observed when the sound stimuli were presented. The sound-induced alteration of the blood flow was determined by calculating the negative slope of the flow change. The maximum flow point found at around $t = 0$ to $t = 2$ s and the minimum point found at between $t = 3$ and $t = 12$ s were obtained and their slopes between 10% and 90% were estimated (Fig. 1). Fig. 2 shows the individual response of vasoconstriction level.

The influence of the sound presentation connected with the cycle phase of respiration was analyzed with a two-way repeated measures ANOVA ['phase of respiration' (2) × 'presence of sound' (2)]. Huynh–Feldt corrections were applied when sphericity violations were detected with the Mendoza test. The ANOVA yielded a 'phase of respiration' × 'presence of sound' interaction [$F(1, 11) = 7.649$, $\eta_G^2 = 0.0276$, $p < 0.05$] and a main effect of 'presence of sound' [$F(1, 11) = 46.252$, $\eta_G^2 = 0.523$, $p < 0.001$]. The degree of the reduction in the blood flow caused by sound stimuli was significantly larger in inspiration phase than in expiration phase (Fig. 3). A simple main effect test revealed a significant difference between sound with the inspiration phase and sound with the expiration phase [$F(1, 11) = 6.568$, $p < 0.05$].