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RHINOLOGY

Nasal response to stress test in healthy subjects: an experimental pilot study

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Abstract

Purpose Stress has been suspected to play a role in rhinitis. The role of stress on nasal patency has been not yet elucidated. The aim was to evaluate the potential effects of stress on nasal patency in healthy subjects.

Methods We conducted a prospective pilot study including 12 healthy subjects. Experimental protocol was divided in three periods (pre-task, task and recovery). In the task period, subjects were exposed to the "Trier Social Stress Test" (TSST), a standardized laboratory stressor. Different parameters including Spielberger State Anxiety Inventory (SSAI) score, visual analogic scale (VAS) of nasal patency feeling, heart rate, acoustic rhinometry measurements have been compared between the three different periods. The study population was divided into two groups according to the Spielberger Trait Anxiety Inventory (STAI) score: A "non anxious" group and a "weakly anxious" group.

Results Seven subjects were in the "non anxious" group and five in the "weakly anxious" group. TSST significantly increased heart rate in all volunteers. SSAI score was significantly increased ($p = 0.04$) after the task period (36.6 ± 11.3) when compared to the SSAI score in pre-task period (31.9 ± 12.6). VAS score of nasal patency feeling significantly decreased from pre-task to task and recovery periods. Mean minimal cross-sectional areas and mean volumes of the nasal cavities were not significantly different between the three periods, except in "weakly anxious" group, but the small number of subjects does not allow to draw a definite conclusion.

Conclusion We observed that stress influenced the feeling of nasal patency in healthy subjects. However, the objective effects of stress on nasal geometry were globally non-significant except in "weakly anxious" group. This latter result of our pilot study needs to be confirmed in a larger cohort.

Keywords Trier social stress test · Autonomous nervous system · Nasal obstruction · Anxiety · Nasal patency · Stress

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Introduction

Stress is a physiological response to restore homeostasis that has been disturbed by a threat and/or an aggression. Stress activates adrenocortical and autonomous nervous system, essentially sympathetic and parasympathetic [1]. Thus, peripheral effects of stress are ubiquitous, including cardiovascular changes. Sympathetic nervous system is mainly activated during acute phase of stress and leads to vasoconstriction, increased heart rate (HR) and blood flow. During relaxation phase, when stress stops, there is an increase of parasympathetic tone as well as a decrease of sympathetic activity, leading to opposite effects on cardiovascular system [2]. These physiological mechanisms could vary and may be influenced by the anxiety trait of the subjects [3]. The autonomic nervous systems of patients with anxiety disorders exhibit an increased sympathetic tone, adapt slowly to repeated stimuli and respond excessively to moderate stimuli. Studies indicate that in anxiety disorders, the sympathetic nervous system's drive is mainly responsible for the physical symptoms [3].

Nasal cross-sectional areas and volume fluctuate in response to inflation/deflation of the vaso-erectile tissue. Nasal mucosa includes a rich vascular network, including capillaries, arterio-venous shunts and vaso-erectile tissue which is responsible for the nasal cycle [4]. Erectile properties of the nasal mucosa depend on capacitance vessels (i.e., venous sinusoid) and vascular sphincters. The regulation of the filling of the capacitance vessels varies according to autonomic nervous system tone [5]. In consequence, the autonomic nervous system is an important regulator of nasal airflow.

It may be assumed that stress could have a direct effect on nasal patency through the activation of autonomous nervous system in vaso-erectile tissue of the nasal mucosa. On the other hand, a nasal obstruction could be responsible for anxiety, at least in obstructive sleep apnea patients [6]. Potential effects of stress on nasal patency had never been studied to date. The goal of the present pilot study was to investigate whether stress has an effect on nasal patency in a sample of healthy subjects. The second objective was to look for a relationship between this potential effect and the anxiety trait of the subjects.

Subjects and methods

Subjects

Healthy subjects were recruited among undergraduate students of our Medical University through advertisements in a local announcement during 6 months. Subjects were initially screened using a general questionnaire to evaluate habits, health aspects and drug intake. The subjects included in the study were healthy non-smokers, non-alcoholic, non-allergic and had no history of nasal or sinus disease and/or surgery. Women were all tested during the first part of their (menstrual) cycle. For each subject, gender, age and body mass index (BMI) were recorded.

Experimental protocol

The subjects were blind to the method and the objectives prior to the study. They were told not to have physical activity 12 h prior to testing. All subjects were studied on a single day; all experimental sessions were run between 11:30 a.m. and 1:30 p.m. to minimize physiological variations of cortisol levels. Upon arrival, the subjects were told that the study was designed to investigate nasal patency using non-invasive techniques and were informed about the questionnaires they had to fill. The procedure was divided in three periods ("pre-task", "task" and "recovery" periods) and seven phases. In the pre-task period, subjects were accommodated in a first room, sound-attenuated and temperature-controlled (22 ± 2 °C), with light kept constant. In this room, heart rate was recorded and acoustic rhinometry performed. Then, the subjects completed i/ visual analogic scale (VAS) of nasal patency feeling scoring from 0 (no obstruction) to 10 (total obstruction), ii/ the Spielberger State/Trait Anxiety Inventory (SSAI and STAI in French language).

In the task period, subjects were exposed to the "Trier Social Stress Test" (TSST) which is a standardized laboratory stressor [7]. During the first 10 min, the patients rested alone without any information. Then, the subjects were called in a second room where they met a jury composed of three senior researchers. The jury delivered a short introduction to the forthcoming tasks: i/ a 5 min free talk about their future career and ii/ a mental arithmetic task (serial subtraction during 5 min) in front of the jury. They were falsy informed that the experimental session would be video- and audio-taped for later analysis. Explanations were followed by another 10 min period to prepare their talk in the first room. Then, heart rate was recorded, VAS of nasal patency feeling was collected and acoustic rhinometry measurements were performed as already described [8].

After that, subjects came back in the second room and made their talk and mental arithmetic task in front of the jury. During the recovery period, the subjects were debriefed: they were told that the aim of the study was to investigate effects of stress on nasal patency and that no video or audio were recorded. Heart rate was monitored, VAS was collected and acoustic rhinometry measurements were performed. Subjects then filled the SSAI.

Methods

SSAI and STAI are validated and widely used to score the state of anxiety of subjects in many studies [9]. Briefly, the 20-items of the SSAI deal with how the subject feels at the moment, while the 20-items of the STAI deal with how the subject feels in general. Each item is rated on a scale from 1 to 4, therefore with a range of score from 20 to 80. The more anxious the subject is, the higher the score is.

The heart rate (HR) was measured using MIROxi (medical international research, Roma, Italy).

Nasal obstruction was evaluated subjectively using the VAS and objectively using the two-microphone acoustic reflection method (i.e., acoustic rhinometry) [10, 11] which is a non-invasive and accurate method that enables to measure rapid changes in mucosal engorgement. Minimal cross-sectional area (MCA) (cm^2) and volume (cm^3) of the nasal cavities were determined at each acoustic rhinometry measurements. The experimental protocol was approved by the local research ethics committee (IRB). Written informed consent was obtained from all subjects before participating in the study.

Statistical analysis

The different parameters (visual analogic scale (VAS) of nasal patency feeling, heart rate acoustic rhinometry measurements) have been compared between the three different periods according to gender. Data were expressed as means ± SDs. Statistical analyses were performed with a statistical software package (Statistica v7.1, Stat Soft®, France). The Mann–Whitney test was used for comparing unpaired data. Friedman's ANOVA with Wilcoxon test as a post-test were used for comparing paired samples. A p value < 0.05 was considered significant. The study population was divided into two groups according to STAI score. A "non anxious" group was defined when STAI score was less than 40, while a "weakly anxious" group was defined when STAI score was more than 40 according to the literature [12].

Results

Study population characteristics

The final sample of this study was composed of 12 volunteers. Sex ratio (men/women) was 5/7. Mean age was 23.8 ± 1.8 years (extreme 19–26 years). Mean age was significantly higher ($p = 0.02$) in women (24.7 ± 0.8 years) than in men (22.4 ± 2.1 years). Mean BMI was 21.8 ± 2.6 kg/m^2. BMI was not different between women (21.9 ± 3.3 kg/m^2) and men (21.6 ± 1.2 kg/m^2). Mean STAI was 36.5 ± 7.2. Mean STAI scores were not different between women and men (38.3 ± 5.3 and 34 ± 9.4, respectively).

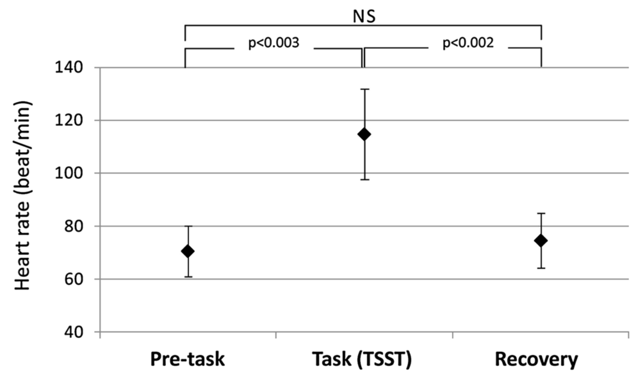

Fig. 1 Variation of the heart rate (mean ± SD) during the three periods of the experimental protocol

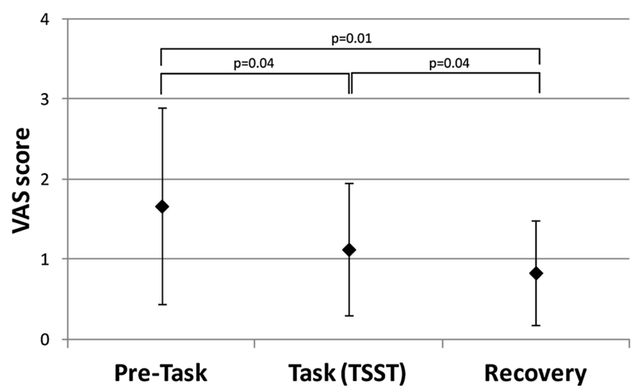

Fig. 2 Variation of the visual analogic scale (VAS) of nasal patency feeling (mean ± SD) during the three periods of the experimental protocol. VAS scores from 0 (no obstruction) to 10 (total obstruction)

Effects of TSST

TSST significantly increased HR in all volunteers (Fig. 1). SSAI score was significantly increased ($p = 0.04$) after the task period (36.6 ± 11.3) when compared to the SSAI score in pre-task period (31.9 ± 12.6). VAS score of nasal obstruction significantly decreased from pre-task to task and recovery periods (Fig. 2). Mean MCAs were not significantly different between the three periods (0.56 ± 0.14 cm^2 in pre task period, 0.60 ± 0.2 cm^2 in task period and 0.59 ± 0.24 cm^2 in recovery period). Mean volumes of the nasal cavities were also no significantly different between the three periods (9.8 ± 1.6 cm^3 in pre-task period, 9.6 ± 2.3 cm^3 in task period, and 9.3 ± 2.3 cm^3 in recovery period).

Effects of TSST according to gender

HR was significantly higher in women than in men, in pre-task period and in task period. In recovery period, HR was no longer different. SSAI, VAS score of nasal patency, MCA and volume of nasal cavity were not significantly different according to gender at all periods of the study.

Effects of TSST according to STAI score

Seven subjects were in the "non anxious" group and five in the "weakly anxious" group. BMI, age, VAS score of nasal patency feeling and HR were not significantly different between the two groups in all periods of the study. Mean MCA and volume of nasal cavity were not significantly different between "non anxious" and "weakly anxious" groups in all periods of the study. In the "weakly anxious" group, mean SSAI score in pre-task period (40.8 ± 12.3) was significantly higher ($p=0.04$) than mean SSAI in the "non anxious" group (23 ± 2.4). This difference was no longer observed in the recovery period (42.2 ± 14 and 31 ± 6.2 respectively).

The mean VAS score of nasal patency significantly decreased from pre-task (2.6 ± 1.5) to recovery (1.4 ± 0.7) only in the "non anxious" group ($p=0.04$). In this group, the mean volume of nasal cavity was not significantly different from pre-task (4 ± 1.2 cm^3) to task (4.4 ± 1.8 cm^3) and to recovery (4.2 ± 1.6 cm^3) periods. In the "weakly anxious" group, the mean volume of nasal cavity significantly decreased from pre-task (4.2 ± 0.3 cm^3) to recovery (3.8 ± 0.4 cm^3) periods and from task (4.2 ± 0.4 cm^3) to recovery periods ($p=0.04$).

Discussion

In this prospective pilot study, all healthy subjects exposed to the TSST had a VAS score of nasal patency feeling significantly decreased after TSST. Mean MCAs and mean volumes of the nasal cavities were not significantly different after TSST except in "weakly anxious" group. However, the small number of subjects does not allow to draw any definite conclusion.

We were able to show for the first time that stress influenced the feeling of nasal patency in healthy subjects and could affect the volume of nasal cavities in the weakly anxious patients. Thus, stress could be involved in nasal congestion state of the nasal mucosa and at least in the sensation of nasal obstruction. The role of stress on nasal patency has been not yet elucidated. In this prospective pilot study, we chose to investigate the effects of an acute and calibrated stress in a sample population of young and healthy subjects. It was therefore not surprising to observe that according to STAI, subjects had non or weakly anxious profiles. To induce stress in our study population, we chose the TSST which induces a physiological response and activates the entire hypothalamus–pituitary–adrenal (HPA) axis leading to an activation of the sympathetic nervous system [7, 13].

We have found a HR increase in task period compared to the pre-task period, confirming the stress effect of the TSST in our population, which is in agreement with previous studies [14, 15]. In the recovery period, the subjects had recovered the initial HR level, as in other studies [16, 17]. The reason for a higher HR in women than in men at baseline is not clear. The effect of stress on HR according to gender shows conflicting results in the literature. According to our results, the majority of studies advocate for a higher HR reactivity to laboratory stressor in women than men [18, 19].

In our study population, TSST induced significant variation of subjective feeling of nasal patency that was not objectively confirmed by acoustic measurements. Acoustic rhinometry was chosen for its ability to detect fast and slight variations of nasal diameter [20]. Moreover, acoustic rhinometry is a simple and non-invasive method requiring minimal cooperation from the subject [8]. TSST improved the sensation of nasal patency. One hypothesis could be that stress induces vasoconstriction in nasal turbinates via sympathetic nervous system activation [21]. However, we did not observe any significant increase in MCA or volume with acoustic measurements. In the same line, the administration of menthol had no effect on nasal resistance as measured by posterior rhinomanometry but improved the subjective feeling of nasal congestion in healthy and congested subjects [22]. The effect of menthol might be due to some actions on nasal trigeminal thermoreceptors [22]. In the weakly anxious patients, TSST induced a significant decrease of nasal volume. Therefore, the hypothesis of an adrenergic effect on nasal turbinates is not pertinent. It may suggest that the improvement of nasal patency feeling could be linked mainly to anxiety in response to stress. Interestingly, it seems that anxiety scores on the Symptom Check List 90 (SCL-90) in obstructive sleep apnea patients with nasal obstruction were higher than in those without, and that surgical correction of this nasal obstruction leads to a decrease of anxiety scores [6].

Pathophysiological conditions such as anxiety traits may contribute to the feeling of nasal patency. Indeed, improvement of VAS score was only observed in non-anxious subjects who did not exhibit any reduction in nasal volume, while reduction of nasal volume was not associated with VAS score modification in weakly anxious subjects. Nasal turbinate mucosal volume is driven by the balance between sympathetic and parasympathetic systems [4]. Our results suggest that in response to stress, a parasympathetic activation may either equalize (non-anxious patients) or overcome (weakly anxious patients) the adrenergic input in the nasal turbinates. Such a paradoxical behavior (weakly anxious patients) has already been suggested in vasomotor rhinitis which is characterized by a neurovegetative nasal dysfunction [23].

Interestingly, stress and anxiety have been suspected to play a role in rhinitis [24]. A local release of neurotransmitters of the non-adrenergic non-cholinergic system, i.e., substance P and vasointestinal peptide could also directly induce vasodilation and/or enhance the parasympathetic effects [25]. This latter hypothesis is further supported by the fact that an increased concentration of substance P has been demonstrated in chronic rhinitis such as allergic and vasomotor rhinitis [26]. The relationship between stress and neuropeptides remains to be studied.

Conclusion

In this pilot study, we were able to show for the first time that stress has an impact on the feeling of nasal patency in young and healthy subjects. However, the objective effects of stress on nasal geometry were globally non-significant, except in the weakly anxious subjects. This latter result of our pilot study needs to be confirmed in a larger cohort. Taken altogether, these results illustrate the complex mechanisms that determine the sensation of nasal patency/obstruction which variably depends on anatomical, physiological and emotional factors, as well as the complex regulation of nasal turbinate volume. This study is a prerequisite for further experiments dealing with the influence of acute and chronic stress in patients suffering from chronic rhinosinusitis, especially in neurovegetative nasal dysfunction.

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Compliance with ethical standards

Conflict of interest All authors have no conflict of interest in connection to this study.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The experimental protocol was approved by the local research ethics committee (IRB).

Research involving human participants Experimental protocol was approved by the local research ethics committee (IRB).

Informed consent Informed consent was obtained from all individual participants included in the study.

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