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Impairment of the bradycardia response to apnoea and simulated diving in smokers

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ABSTRACT

Apnoea and diving induce autonomic cardiovascular responses of bradycardia and blood flow redistribution toward vital organs that are aimed at improving subject survival in hypoxic conditions. Among factors that influence autonomic nervous activity, and thus affect cardiovascular responses, cigarette smoking is known to reduce vagal cardiac-nerve activity and to increase sympathetic nervous activity. In this study we have assessed the bradycardia response to apnoea and to diving in human smokers. By recording electrocardiograms, heart rate (HR) was monitored on ten healthy habitual smokers (SM) and ten non-smokers (non-SM), in eupnoea, in air, and in simulated diving (facial immersion in water, 22 °C). The latter two conditions included apnoea and snorkelling sessions lasting 30 s each. Apnoea in air induced a 3% and a 4% HR reduction in SM and non-SM, respectively. Only in the latter, however, instantaneous HR decreased throughout the session, thus showing the occurrence of a weaker response in SM. During apnoea in simulated diving, a delayed and lower-amplitude bradycardia occurred in SM compared to non-SM, HR decreasing by 13% and 22%, respectively. Analogously, the cardiac response to snorkelling in simulated diving was smaller in SM with respect to non-SM, HR decreasing by 7% and 14%, respectively. These response patterns suggest that cardiac homeostatic adjustments to apnoea and diving are impaired in smokers. Besides causing a number of pathologies, cigarette smoking represents a risk factor for subjects performing these activities at an even non-competitive level.

Keywords: cardiac autonomic response, breath hold, face immersion, cigarette smoking

INTRODUCTION

Many animal species, included man, are able to tolerate periods of hypoxia or anoxia by performing homeostatic physiological adaptation of their cardiovascular function [1-3]. As well established by a number of investigations, the human response to a respiratory arrest mainly consists of bradycardia, peripheral vasoconstriction, increased blood pressure, and redirection of blood to oxygen-sensitive tissues, such as the brain and the heart [4-6]. The amplitude of these cardiovascular adaptations is augmented when apnoea is associated to face immersion in cold water, as in the case of the human diving response [7-13]. The respiratory arrest and stimulation of facial cold receptors, particularly those on the forehead and the eye region [10, 14-15], act in synergy causing an increase of cardiac parasympathetic nerve activity and an excitation of vasomotor centres, thus triggering the cardiovascular adjustments associated to the diving response [14, 16-18]. Recently, functional implications and the importance of co-activating cardiac autonomic activity for optimizing the cardiovascular performance during bradycardia have been described [19]. Among factors that influence autonomic nervous activity, cigarette smoking is known to induce a complex pattern of changes on autonomic cardiovascular control mechanisms in habitual smokers. Cigarette smoking reduces vagal cardiac-nerve activity and increases sympathetic nervous activity [20], and norepinephrine and epinephrine release [21]. In the case of heavy smokers, a long-term reduction of vagal cardiac activity has been suggested [22]. The powerful sympathetic excitatory effects of smoking on the heart, the skin and muscle blood vessels cause tachycardia and increased blood pressure [23]. These effects are related to tobacco chemical compounds, and especially to nicotine whose sympatho-excitatory role has been shown even in apneing habitual smokers [24].

In this study, we have assessed the performance of the bradycardia response to apnoea and to simulated diving in healthy, non-trained, habitual young smokers. Our findings show that cigarette smoking entails a spoilt bradycardia response in smokers during the performance of an even short-lasting, non-competitive apnoea or diving activity, represents a cardiovascular high-risk factor for the performing of an even short-lasting, non-competitive apnoea or diving activity.

MATERIALS AND METHODS

2.1. Subjects

Our study was performed on two groups of non trained, young and healthy male humans, 10 non-smokers (non-SM, control group; 25 ± 2.3 years of age) and 10 habitual cigarette-smokers since at least one year (SM; 6 to 12 cigarettes/day; 5 mg to 9 mg nicotine daily intake; 25 ± 2.6 years of age). None of the subjects had any history of chronic disease nor was taking any medication. Each subject gave informed consent to the experimental procedure, which was approved by the Ethical Committee of our Institution in accordance with the declaration of Helsinki.

2.2. Methods and protocol

Bipolar ECG lead I configuration was continuously monitored in each subject. The respiratory frequency was roughly estimated during recordings by silently counting for the experimental duration. No equipment was used to record breathing frequency continuously. Recordings were performed at constant room temperature (22°C) and humidity (60% RH) during the morning (from 9.00 to 11.00), after 12 h of abstinence from alcohol and caffeine-containing beverages, as well as from smoking in the case of SM subjects.

The individuals were all familiar with the experimental protocol. The subject was laying down in a prone position on a bench, keeping his arms on it and his head free of bending leaning out of it. Recordings started after a 5 minutes interval from electrode positioning. The experimental protocol initiated with an eupnoea period, during which the subject spent 4 minutes at rest breathing spontaneously (I period), followed by an initial apnoea session (DA) and a successive snorkelling one (DS) “in air” (II period). In the III and last period, the subject repeated the sessions of apnoea, (IA) and snorkelling (IS) while simulated diving by immersing his face up to the temples in a water container located in front of him. The water temperature was set to 22 °C in order to induce bradycardia [25]. Each session lasted 30 s and was spaced by a 4 min recovery interval from the successive one, according to Hayashi et al [17].

2.3. Data Analysis

Tracings of ECG were displayed on an oscilloscopic screen (5111; Tektronix, Beaverton, OR, USA). Recordings were processed through an integrated system of hardware and software designed to acquire, display and analyze ECG signals (PowerLab/4S; AD Instruments, Castle Hinn, NSW, Australia). Instantaneous HR/min was obtained from each R-R interval of the ECG signal in SM and non-SM groups. Values of HR/min were averaged each second over the entire duration of experimental sessions in SM and non-SM subject groups. Results are expressed as mean values $\pm$ SE of HR/min each second of a session (HR_s), as well as mean values $\pm$ SE of HR/min during the entire duration of each session (30 s, HR_{30s}).

Comparisons were made by repeated-measures ANOVA followed by Fisher’s least-significant difference (LSD) post hoc analysis (Statistica 98; StatSoft, Tulsa, OK), with “between subjects” factor being smoking (SM vs non-SM) and “repeated measures” factor being a session experimental period (within a group). The threshold level of statistical significance was set at $P < 0.05$.

RESULTS

Respiration-synchronous HR_s fluctuations in a 0.16-0.18 Hz frequency range were monitored on eupneic SM and non-SM subjects (I period, Figure 1). Non significant HR_s changes within each group were detected, while a moderately higher HR_{30s} was measured in SM subjects (67.6 ± 0.2) with respect to non-SM ones (65.6 ± 0.3 ; $P < 0.05$).

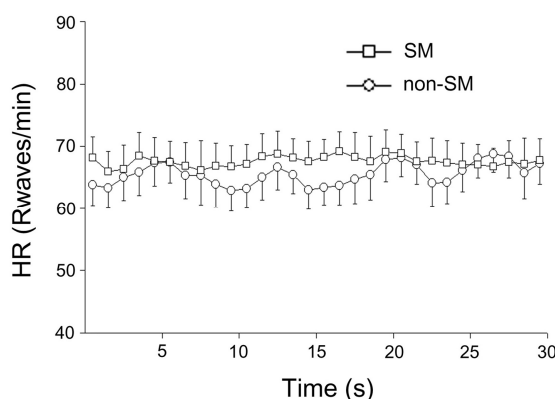


Figure 1: Heart rate recorded on 10 habitual smoking (SM) and 10 non-smoking subjects (non-SM) in an eupnoea condition lasting 4 minutes (I period). Values are mean $HR_s \pm$ SE.

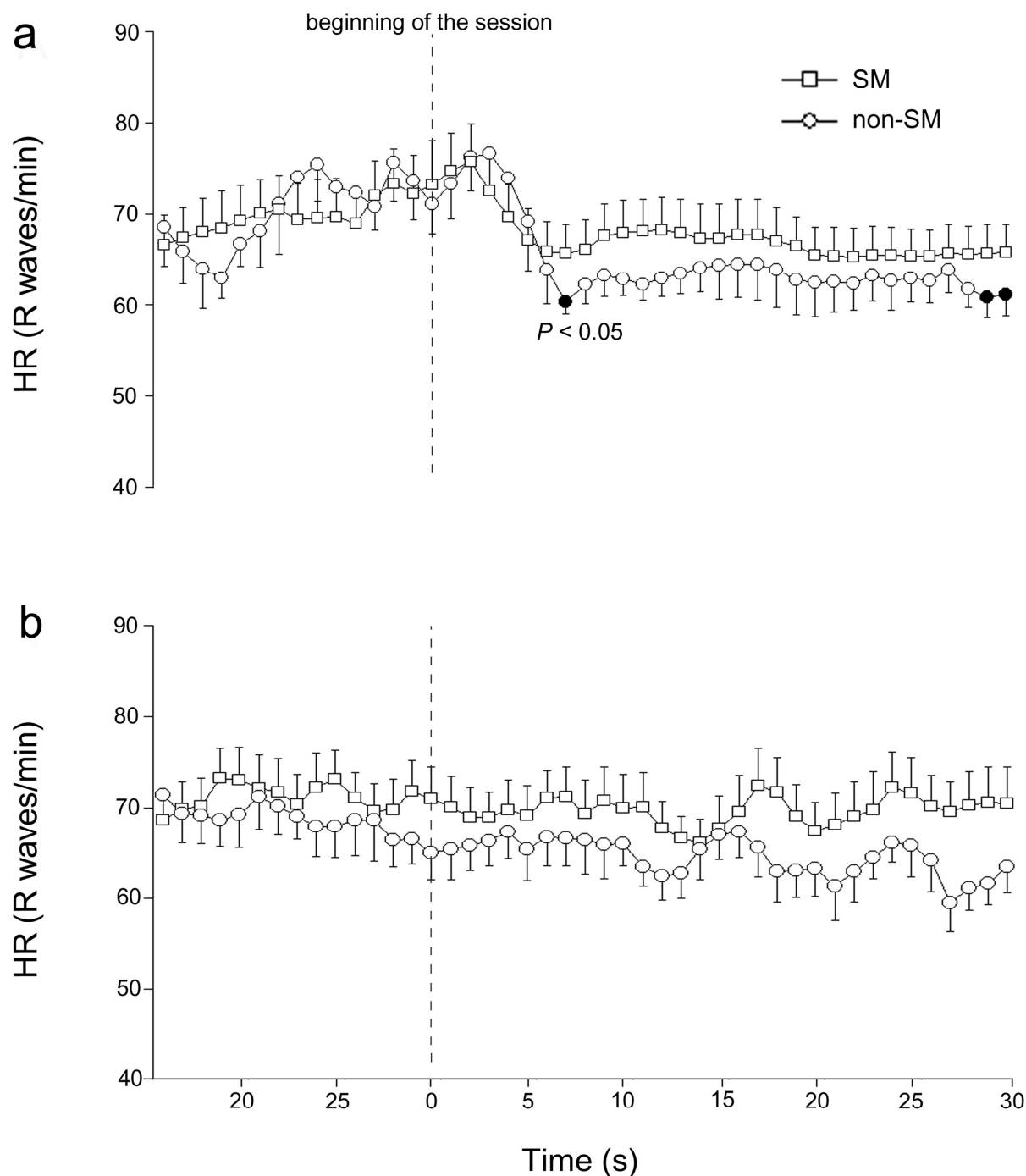


Figure 2: Heart rate recorded on 10 habitual smoking (SM) and 10 non-smoking subjects (non-SM) during experimental sessions “in air” (II period): apnoea (DA; a), breathing through snorkel (DS; b). Vertical dashed lines indicate the beginning of sessions, each one lasting 30 s. Values are mean $HR_s \pm SE$. Full symbols indicate a significant difference from the respective mean value at the beginning of the session.

During the II period “in air”, HR_s fluctuations with non significant changes within each group were recorded before the DA (Figure 2a) and DS (Figure 2b) sessions. Values of HR_{30s}

measured in SM subjects before (69.9 ± 0.3) and during the DA session (67.4 ± 0.5), as well as before (71.2 ± 0.4) and during the DS session (69.6 ± 0.3), were higher compared to corresponding ones in non-SM subjects: before (67.7 ± 0.7 ; $P < 0.01$) and during the DA session (64.4 ± 0.8 ; $P < 0.003$), before (68.6 ± 0.4 $P < 0.01$) and during the DS session (64.5 ± 0.4 ; $P < 0.001$). A low-amplitude bradycardia response to breath-hold was elicited in both subjects groups, HR_{30s} decreasing by about 3% in SM subjects (from 69.8 ± 0.3 to 67.4 ± 0.5 ; $P < 0.02$) and by about 4% in non-SM ones (from 67.7 ± 0.7 to 64.5 ± 0.4 ; $P < 0.02$). Any HR_s changes with respect to the initial value were detected throughout the session in SM subjects (Figure 2a). On the other hand, HR_s measured at the beginning of the session in non-SM subjects (71.1 ± 3.3) was lower 7 s (64.4 ± 1.4) and 30 s (61.1 ± 2.3) after ($P < 0.05$).

During the III period, there were no HR_s changes before sessions within each subject group (Fig. 3a, b). In the IA session (Figure 3a), HR_{30s} was higher in SM subjects (63.9 ± 1.9) with respect to non-SM ones (57.1 ± 1.6 ; $P < 0.001$). It decreased by 22 % in non-SM subjects (before the session: 75.5 ± 0.8 ; during the session: 57.1 ± 1.6 ; $P < 0.05$), and by 13% in SM ones (before the session: 74.8 ± 1.1 ; during the session: 63.9 ± 1.9 ; $P < 0.05$). Reductions of HR_s were recorded throughout the session in SM- (from 83.3 ± 3.4 to 53.3 ± 1.9 ; $P < 0.001$) and non-SM subjects (from 80.7 ± 4.1 to 51.5 ± 2.0 ; $P < 0.001$). Compared to the value at the beginning of the session, HR_s fell faster in the non-SM group ($P < 0.05$), despite the resulting level after 30 s being the same in the two groups (Figure 3a).

In the IS session (Figure 3b), HR_{30s} was higher in SM subjects (66.0 ± 0.9) with respect to non-SM ones (61.7 ± 0.9 ; $P < 0.001$). The latter subject group showed a 14% HR_{30s} decrease (before the session: 71.9 ± 0.7 ; during the session: 61.7 ± 0.9), while only a 7% reduction was found in SM subjects (before the session: 71.0 ± 1.0 ; during the session: 66.0 ± 0.9). Decreases of HR_s were recorded in SM- (from 79.5 ± 4.5 to 63.9 ± 3.5 ; $P = 0.001$) and non-SM subjects (from 77.0 ± 4.1 to 59.9 ± 3.6 ; $P < 0.001$).

DISCUSSION

The main finding of the present study is that the bradycardia response to apnoea “in air”, or apnoea or snorkelling in simulated diving is impaired in habitual smokers, whose homeostatic adaptation of cardiac function is therefore affected.

A number of factors such as age [26], posture, respiratory pattern and stress [27-28] can influence the cardiac activity of healthy humans. The results of the present investigation are representative for the population we studied, i.e. young, healthy, non trained, smoking and non-smoking male humans in the adopted posture and breathing conditions.

During experimental sessions “in air”, SM and non-SM subjects exhibited respiration-synchronous fluctuations and rather stable HR_s associated to a regular breathing frequency (0.16-0.18 Hz). This finding is consistent with an analogous oscillation pattern and a nearly constant HR reported for subjects breathing at an equivalent frequency range (0.15-0.45 Hz) [29-30]. The higher HR_{30s} we monitored in SM- compared to non-SM subjects can be ascribed to the well known sympathetic-induced cardio-acceleration effect of cigarette smoking [20].

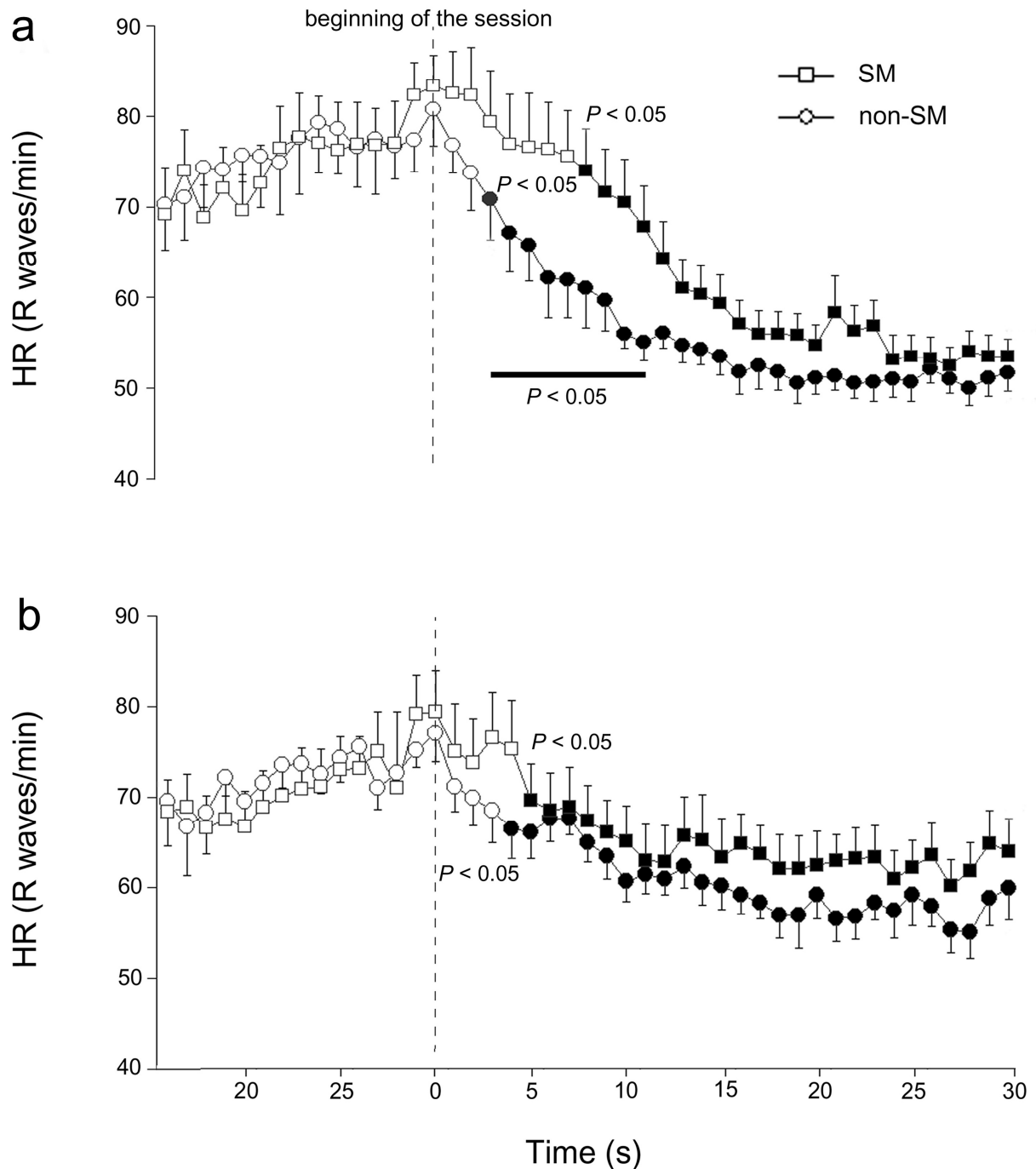


Figure 3: Heart rate recorded on 10 habitual smoking (SM) and 10 non-smoking subjects (non-SM) during experimental sessions in simulated diving conditions (III period): apnoea (IA; a), breathing through snorkel (IS; b). Vertical dashed lines indicate the beginning of sessions, each one lasting 30 s. Values are mean HR_s ± SE. Full symbols indicate a significant difference from the respective mean value at the beginning of the session; the thick line (a) marks a significant difference between mean HR_s values of the two subject groups.

A comparison of HR_{30s} before and during the DA session showed that apnoea “in air” was effective on both subject groups, exhibiting bradycardia of moderate amplitude as described in the case of pre-apnoeic lung ventilation with a tidal volume. However, detection of HR_s decreases in non-SM subjects and their lack in SM ones indicates that the response was weaker in the latter compared to former. In a previous study demonstrating that bradycardia to apnoea “in air” is associated to a decrease of alveolar oxygen uptake and to an increase of plasma lactate concentration, apnoea effects have been suggested to increase anaerobic metabolism and to conserve the lung oxygen store for vital organs [12]. On these bases, the weaker bradycardia detected in SM subjects may indicate that physiological effects of apnoea “in air” are decreased and the homeostatic regulatory mechanisms affected in smokers.

In both SM- and non-SM groups, apnoea associated to simulated diving induced a greater bradycardia than that to apnoea “in air”. This finding is consistent with results of previous studies demonstrating that stimulation of cutaneous cold receptors with facial immersion potentiates the response to apnoea alone according to an inverse relationship with the temperature of the water [2, 8, 31-32]. In the IA session, bradycardia amplitude was much lower in SM subjects compared to non-SM ones, HR_{30s} decreasing by 13% and 22%, respectively. Besides, the analysis of HR_s variations throughout the session showed that the response was delayed (8 s from the session beginning) in SM subjects with respect to the faster occurrence dynamics (3 s from the session beginning) in non-SM ones.

A full face contact with water was sufficient for evoking bradycardia in SM and non-SM snorkelling subjects in simulated diving. Contact of water, and particularly on the forehead, eyes and nose, induces the response [10, 15, 33], as stimulation of trigeminal nerves supplying these sensory areas excites vasomotor centres and cardiac vagal neurons [1]. Consistently with the known synergistic effects of breath hold and face immersion [2, 9], we recorded a lower bradycardia amplitude in SM and non-SM snorkelling subjects compared to that detected when face contact was associated to apnoea. Once again, SM subjects exhibited a lower response amplitude compared to non-SM ones, HR_{30s} decreasing by 7% and 14%, respectively.

This study provides evidence on an impairment of the bradycardia response in habitual smokers, showing several degrees of response reduction when apnoeing “in air”, or apnoeing or snorkelling in simulated diving. Mechanisms affecting this important homeostatic adaptation of cardiac function in smokers can only be hypothesized. It is well known that an increase of cardiac parasympathetic nerve activity and an excitation of vasomotor centres trigger the cardiovascular adjustments associated to the diving response [14, 16]. A co-activation of cardiac autonomic activity can optimize the cardiovascular performance during bradycardia [19]. However, it has been recently shown that the prompt bradycardia occurring within the initial 30 s of breath hold associated to face immersion in water has to be exclusively ascribed to an increase of vagal cardiac activity [18]. Cigarette smoking increases sympathetic nervous activity [20], norepinephrine and epinephrine release [21], and reduces vagal cardiac-nerve activity thus increasing heart rate [20, 34]. Besides, in the case of heavy smokers, a long-term reduction of vagal cardiac activity was reported [22]. Consistently with these findings, as well with the demonstration that initial HR decreases to apnoea are induced only by a vagal-activity increase, we suggest that the lower bradycardia responses we recorded in smokers are compatible only with a reduced cardiac parasympathetic control in habitual cigarette-smoking subjects.

It is well established that adverse effects of cigarette smoking on cardiovascular function are related to a mixture of chemical components in cigarette smoke [35-3], which are detectable at high concentrations in almost every tissue and in the blood of habitual smokers [37]. Future

studies on potential molecular mechanisms reducing cardiac parasympathetic activity in cigarette smokers are therefore needed.

CONCLUSIONS

In conclusion, we measured the bradycardia response to apnoea and simulated diving in healthy habitual smokers and non-smokers. We found that this autonomic homeostatic mechanism is importantly impaired in habitual smokers. Besides causing a number of pathologies, cigarette smoking represents a cardiovascular high risk-factor for habitual smokers performing an even non-competitive activity of apnoea or diving.

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