



# Effects of the exposure to ultrafine particles on heart rate in a healthy population

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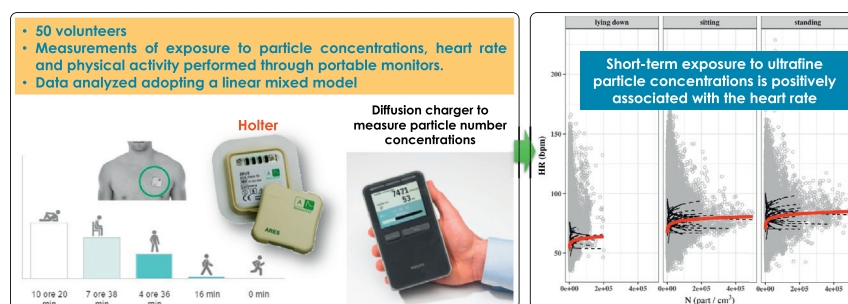
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## HIGHLIGHTS

- Evaluation of the correlation amongst ultrafine particles and heart rate
- Personal monitoring of 50 volunteers in terms of particle number concentrations
- Use of a statistical linear mixed model to fit the experimental data
- The short-term exposure to ultrafine particles is positively associated with heart.
- A logarithmic correlation amongst ultrafine particles and heart rate was estimated.

## GRAPHICAL ABSTRACT



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## ABSTRACT

The correlation amongst exposure to ultrafine particle concentrations and heart rate in a large healthy population was investigated. The study was conducted by continuously monitoring for seven days fifty volunteers in terms of exposure to particle concentrations, heart rate and physical activity performed through portable monitors. Data were analyzed adopting a linear mixed model able to manage the obtained repeated measures and to recognize a general trend resulting from the subject-specific patterns.

Results show that the short-term exposure to ultrafine particle concentrations is positively associated with the heart rate for the different physical activities of the subject investigated (laying down, sitting, standing positions). In particular, a logarithmic correlation was recognized with a sharper increase of about 4–6 bpm for a variation of the particle number concentration of  $2 \times 10^4$  part/cm<sup>3</sup> and a slighter effect for further increases of about  $0.1\text{--}0.2 \times 10^{-4}$  bpm/(part/cm).

**Capsule:** A positive correlation can be associated between the exposure to ultrafine particles and the heart rate.

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## 1. Introduction

The possible effect of the exposure to high levels of airborne particle concentration on human health represents a topic highly debated in the scientific literature (Pope and Dockery, 2006). In fact, while the previous investigations were mostly focused on the effects of short and long term-exposure to airborne particles on the respiratory system, the

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attention was recently moved to the cardiovascular issues (Chen et al., 2008; Franchini and Mannucci, 2011; Mills et al., 2008; Pope and Dockery, 2006). According to the latest research, cardiovascular health consequences of exposure to airborne particles can be even worse than those due to pulmonary ones. As an example, a recent study (Basagaña et al., 2015) examined the relationship between particulate matter constituents and daily hospital admissions in five European cities, showing that air pollution is strongly associated with hospitalization for cardiovascular diseases more than for respiratory ones. Similarly, Gold et al. (2000) observed higher rates of deaths due to cardiovascular diseases with respect to respiratory diseases (69% vs. 18%). More generally, several epidemiological studies showed increased cardiovascular mortality and morbidity in association to exposure to fine particulate matter (PM<sub>2.5</sub>, mass concentrations of particles smaller than 2.5 µm) (Bhaskaran et al., 2009; Brook, 2008; Brook et al., 2010a; Simkhovich et al., 2008) and traffic-related particles (Peters et al., 2005; Tonne et al., 2016). Specific interest was given to the correlation between heart rate variability (HRV, i.e. the specific change in time between successive heart beats, usually referred as changes of “R-R interval”) and the exposure to several air pollutants including carbon monoxide, nitrogen oxides, sulfur dioxide, ozone and particulate matter. Reduced HRV was recognized as a predictor of mortality after myocardial infarction (Mustafic et al., 2012). As an example Cárdenas et al. (2008) used the HRV as a marker to identify cardiovascular effects associated with increased PM<sub>2.5</sub> concentrations and Brook et al. (2010b) detected an association between decreased HRV and short-term exposures to PM in sensitive subjects such as eldest people and/or persons with previous illnesses. Other studies were also able to quantify the effect of PM levels on cardiovascular diseases. As an example, Pope and Dockery (2006) detected a significant growth of cardiovascular diseases in presence of PM<sub>2.5</sub> exposure estimating a 4.5% increase in coronary artery disease for a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration, whereas Gold et al. (2000) observed an increase of 0.5–1.5% for a 5–6 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>. Nonetheless, the scientific findings regarding the correlation between PM<sub>2.5</sub> and cardiovascular issues are not unanimous; indeed, Chuang et al. (2007) and Shields et al. (2013) observed negative and positive associations, respectively, amongst HRV and exposure to PM<sub>2.5</sub>, and Adar et al. (2007) found that fine particles are negatively linked with HRV.

Consistent findings have been also found, in several panel studies, referred to the correlation between cardiovascular responses/diseases and UFP exposure (Laumbach et al., 2014; Peters et al., 2015; Rich et al., 2012; Samet et al., 2009; Sun et al., 2015; Vora et al., 2014; Weichenthal et al., 2011; Zareba et al., 2009). Nonetheless, a limited number of studies have been conducted. Weichenthal (2012) recently shown that UFPs (ultrafine particles, i.e. particles with a diameter smaller than 0.1 µm), which are measured in terms of number concentrations, can play a significant role in acute cardiovascular morbidity as already demonstrated for respiratory diseases (Buonanno et al., 2013) or lung cancer risk (Pacitto et al., 2018b; Stabile et al., 2017). This should not represent an unexpected finding since recent researches recognized that UFPs cause several damages through translocation into the systemic circulation (Campagnolo et al., 2017; Lee et al., 2014).

A decrease of HRV for higher exposure to particle number concentrations was recognized by Chan et al. (2004) in their study considering 9 young adults and 10 elderly patients with lung function impairments analyzed from 7 a.m. to 11 p.m. On the other hand, Samet et al. (2009) observed an increase in frequency domain markers of heart rate variability in young healthy humans and further epidemiological studies (Laumbach et al., 2014; Weichenthal et al., 2011; Zareba et al., 2009) have reported no significant association between exposure to traffic particles and HRV outcomes.

The above-mentioned contradictory results can be due to a peculiar difference in the type of monitoring system of pollutants used in the research. In a recent structured review of panel studies concerning the link between short-term exposure to air pollution, particularly fine

particulate matter (PM<sub>2.5</sub>), and adverse cardiovascular effects, Buteau and Goldberg (2016) analyzed thirty-one studies recognizing that twenty-one studies measured fine particle concentrations in one or multiple fixed-site monitoring stations positioned at different distances from participants, eight studies were performed using personal monitoring, and the remaining two studies measured fine particles through a mobile laboratory. Instead as regards the relationship between UFPs exposure and possible effects on the cardiovascular system, in a recent review, Weichenthal (2012) examined nine cases of association between controlled human exposure to ultrafine particles (assessed using personal monitors or by a mobile laboratory) and heart rate indices recognizing a significant association for six over nine studies. Indeed, personal air pollution measurements are still rare while ambient fixed-site monitors are ordinarily used for estimation of the personal exposure of the entire population (Hampel et al., 2014). Actually, fixed-site stations, in comparison to personal monitors, do not take into account for personal exposure factors, as well as for factors related to transport mode, traffic, weather conditions, and particle concentrations (Buonanno et al., 2011a; Buonanno et al., 2012; Buonanno et al., 2014) that can strongly affect the real exposure of the population. A further limitation of the mentioned researches concerns the small number of cases analyzed: they were mainly conducted for specific populations, such as elderly population or patients with particular diseases. Finally, an additional aspect to be considered is the lag time (i.e. timing of the electrocardiogram recording relative to the exposure) between the exposure period and the measurements of heart rate variability. In most of the cases analyzed, the electrocardiogram monitoring was not simultaneous but it was performed before or after to the exposure of the subjects to the airborne particle concentration.

To this end, in the present paper, a community-based study in a relatively large population of healthy individuals was conducted in order to detect possible short-term effects of ultrafine particles on cardiac autonomic function by measuring heart-rate (HR) continuously for a period of seven days. To this end, personal particle concentration monitors were adopted in order to assess the actual individual exposure of selected volunteers.

## 2. Materials and methods

### 2.1. Methodology and experimental apparatus

The study was conducted from November 2016 to November 2017, and it involved fifty volunteers aged 18–60 years. All the participants lived in Cassino (resident population of 33,000 inhabitants, surface area of 83 km<sup>2</sup>), Central Italy, and in the surrounding areas.

A self-administered questionnaire was used to collect personal data, including gender, age, weight, height, body mass index (BMI), blood pressure, breath frequency, smoking status and remote pathological history. Non-smokers, non-alcoholics and having a good health status volunteers (without a personal history of cardiovascular, pulmonary, neurological or endocrine disease) were selected. A personal monitoring system was used to detect both HRV and exposure to particles. In particular, the mobile experimental apparatus consisted of (a) a heart rate variability meter (Holter), (b) an accelerometer for physical activity tracking, (c) portable particle concentration monitors (NanoTracer or Discmini).

The Holter monitor used in the experimental analysis is the AthenaDiaX ECG recorder (ARES: 54 × 54 × 9.6 mm and ZEUS 2D: 57.4 × 57.4 × 9.6 mm) which is able to monitor the heart rate variability with an accuracy of 1 ms. The Holter was attached to the subject's chest using adhesive electrodes, bone planes were chosen for the position, in order to minimize the artefacts generated by muscle activity. The Holter is a battery-operated portable device measuring and recording the electrical activity of the heart (Electrocardiography, ECG) continuously for 24 h or longer. Data were processed by means of the Themislight software ([www.athenadiax.com](http://www.athenadiax.com)) which allows to display and assess the

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