

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Adverse Effect of Air Pollution on Odor Perception

Marco Guarneros¹, René Drucker-Colín¹,
José Esquivelzeta² and Robyn Hudson³

¹*Instituto de Fisiología Celular,*

²*Facultad de Medicina,*

³*Instituto de Investigaciones Biomédicas,*

*Universidad Nacional Autónoma de México
Mexico*

1. Introduction

The Mexico City metropolitan area has a population of more than 20 million people (Consejo Nacional de Población, 2009) which makes it one of the largest agglomerations in the world. Mexico City lies at an altitude of 2240m above sea level, and is surrounded by mountains to the south, west, and east. Air pollution driven by local emissions can affect large areas within closed valleys, where restricted air movement concentrates the suspended pollutants. Due to its altitude and latitude, Mexico City receives intense solar radiation, a condition that together with less efficient combustion promotes photochemical formation of secondary pollutants such as ground level ozone and particulate matter (Molina & Molina, 2002) which remain above the Mexican standard for many days of the year in certain city zones (Secretaría de Medio Ambiente del Distrito Federal, 2007).

A great number of studies have reported negative effects of air pollution on health, above all among the most susceptible groups of the population; children, aged persons, and asthmatic patients (review in Rosales-Castillo et al., 2001). Among the many adverse effects that have been attributed to air pollution are dermatological pathologies (Goldsmith, 1996), damage to the eyes (Versura et al., 1999), allergic manifestations (Schierhorn et al., 1999), increased levels of stress (Evans et al., 1988), possible triggering of neurodegenerative conditions such as Alzheimer's disease (Calderón-Garcidueñas et al., 2004) and others related to locomotor behavior (Rivas-Arancibia et al., 2003), as well as a list of harmful effects on the cardiovascular system including problems in the myocardium, deficiencies in the vasoconstriction system and cardiac arrest (Bhatnagar, 2006; Zanobetti & Schwartz, 2006). Consequently, air pollution is also associated with higher levels of hospitalization (Zanobetti & Schwartz, 2006) and mortality (Loomis et al., 1999). However, effects on the respiratory system have received the most clinical and epidemiological attention. For example, it has been demonstrated that air pollutants can cause inflammation and a greater susceptibility to infections in the respiratory tract, worsening of asthma, decrements in peak expiratory flow and increased mortality related to chronic exposure to photochemical pollutants and

particulate matter (Romieu et al., 1996; Gold et al., 1999; Borja-Aburto et al., 1997; Loomis et al., 1999; Tovalín et al., 2010). Chronic exposure to environmental toxicants, even below the recommended limits, also plays an important role in the outbreak of respiratory diseases (Lippmann, 1989). The damage inflicted on the respiratory system may affect the bronchia and the bronchioles, produce chronic inflammation of the lung parenchima, abnormal lung growth, delay in the maturation of the lungs and alveolar edemas. Also of concern is the possible increase in the frequency of lung diseases in populations of children exposed to Mexico City air pollution, given that these exposed populations have a higher potential risk of developing chronic respiratory diseases in their future life (Castillejos et al., 1995; Calderón-Garcidueñas et al., 2000, 2001, 2003a).

Despite the extensive literature reporting harmful effects on the sense of smell from chronic exposure to potentially harmful substances in different work environments (e.g., Cometto-Muñiz & Cain, 1991; Berglund et al., 1992; Smeets & Dalton, 2002; Smeets et al., 2002; Hastings & Miller, 2003; Chen et al., 2004; Vent et al., 2004; Zibrowski & Robertson, 2006; Heiser et al., 2010) and considerable evidence of pathological effects of chronic exposure to everyday ambient air pollution on the cellular structure of the nasal epithelium (Calderón-Garcidueñas et al., 1996, 1998, 2000, 2003b, 2009), until recently (Hudson et al., 2006), effects of big city air pollution on odor perception had remained undescribed.

2. Standardized tests

In a recent study (Guarneros et al., 2009) we compared the olfactory function of 30 young subjects from Mexico City and 30 from the neighboring but markedly less polluted state of Tlaxcala. Subjects were tested using an internationally validated olfactory test battery, the Sniffin' Sticks (Fig. 1) (Hummel et al., 1997). In a first test, we presented subjects with a series of dilutions of the odorant molecule 2 phenyl-ethanol, which has a characteristic rose smell, dissolved in an odorless solvent (propylene-glycol) to determine the minimum concentration needed for each subject to detect the presence of the odor (threshold). Subjects from Tlaxcala outperformed subjects from Mexico City on this task (Fig.1a). The results showed that the difference represented a 2- to 4-fold increase in the concentration needed by Mexico City subjects to detect the presence of the stimulus.

Tlaxcala subjects also obtained higher scores in a discrimination test than subjects from Mexico City. In this test, subjects were presented with different pairs of odorants (Table 1), and for each pair, the subjects' ability to distinguish one odor from the other was assessed. All odorants were presented at concentrations that were sufficiently high for every subject to detect. For each pair of odors, the blindfolded subjects were presented two of three times with one stimulus, and one of three times with the other (different) stimulus. The subjects' task was to indicate which stimulus was the different one. The results showed that differences between the two groups of subjects on this test were small but significant; on a scale of 1 to 16 points (correct answers), subjects from Tlaxcala scored an average of 13, more than one point above subjects from Mexico City who scored an average of 11.8 (Fig.1b).

We also evaluated odor identification, which refers to subjects' ability to correctly associate odor stimuli with their names. Subjects were presented with 16 substances that resemble odors from everyday life (Table 2) and had to correctly select each odor's name from a list of four options. It is generally accepted that higher brain functions (such as memory, speech

and thought) are implicated in tasks of odor recognition to a greater extent than in other measures of olfactory performance such as odor threshold (minimum concentration for detection) (Lötsch et al., 2008). This might account for the fact that no significant differences were found between the groups in the identification test (Fig. 1c), possibly revealing the ability of the brain to compensate the impairment observed in the threshold and discrimination tests (Hudson et al., 2006).

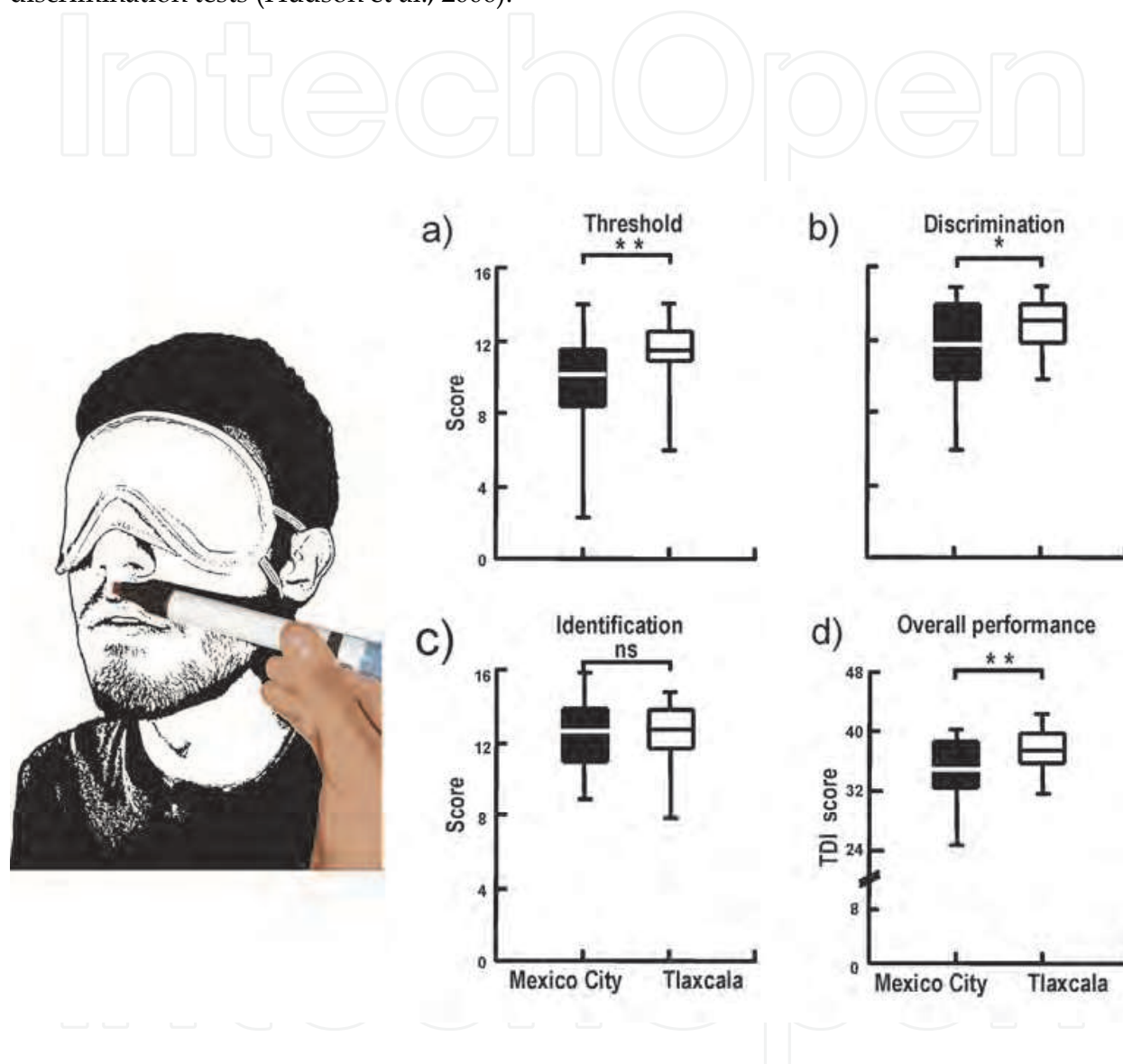


Fig. 1. Performance of subjects from Mexico City and Tlaxcala on the three tests of olfactory performance (a-c) as well as their TDI scores representing the sum of their scores on these (threshold, detection, and identification) tests (d). For each of the tests, subjects could obtain a maximum score of 16 correct responses and consequently a maximum TDI score of 48. Box plots: horizontal lines within boxes give medians, boxes' horizontal limits give the interquartile ranges, and vertical bars give the absolute ranges. * $p < 0.05$, ** $p < 0.01$, ns = not significant (Mann-Whitney U tests). (Adapted from Guarneros et al., 2009).

	Target stimuli	Non-target stimuli
1	Butanol	2-phenylethanol
2	Isoamyl acetate	Anetol
3	Anetol	Eugenol
4	Limonene	Fenchone
5	(-) Carvone	(+) Carvone
6	Eugenol	Cinnamon aldehyde
7	Dihydro rosenoxide	Menthol
8	Acetaldehyde	Isoamylacetate
9	Citronellal	Linalool
10	Pyridine	Limonene
11	Limonene	Citronellal
12	Eucalyptol	Dipiridyl
13	Dipiridyl	Cyclopentadecanoate
14	Butanol	Fenchone
15	Octylacetate	Cinnamon aldehyde
16	Carvone	Acetaldehyde

Table 1. Stimuli used in the discrimination test.

1	Orange	Blackberry	Strawberry	Pineapple
2	Smoke	Shoe-leather	Glue	Grass
3	Honey	Vanilla	Chocolate	Cinnamon
4	Garlic	Spruce	Peppermint	Onion
5	Coconut	Banana	Walnut	Cherry
6	Peach	Apple	Lemon	Grapefruit
7	Licorice	Gummy bears	Chewing-gum	Cookies
8	Mustard	Rubber	Menthol	Turpentine
9	Onion	Cabbage	Garlic	Carrot
10	Cigarette	Coffee	Wine	Candle smoke
11	Melon	Peach	Orange	Apple
12	Clove	Pepper	Cinnamon	Mustard
13	Pear	Plum	Peach	Pineapple
14	Camomile	Strawberry	Rose	Cherry
15	Anise	Rum	Honey	Pinetree
16	Bread	Fish	Cheese	Ham

Table 2. Identification test. For each of the 16 trials, the target odorant stimulus is indicated in bold to distinguish it from the three distractors showed in the same row.

3. Tests using everyday products

In tests of olfactory performance, monomolecular substances are usually preferred for reasons of stimulus control and experimental convenience. However, tests using the molecular mixtures typical of real life can be considered to provide a more ecologically relevant approximation (Ayabe-Kanamura et al., 1998; Distel et al., 1999; Hudson, 1999; Distel & Hudson, 2001).

We therefore tested a different set of subjects from Mexico City (n=82) and Tlaxcala (n=86) with ascending concentrations of an orange juice preparation and of an instant coffee preparation to determine their thresholds (minimum concentration for detection). In this study (Hudson et al., 2006) subjects were also asked to discriminate between the odors of different dilutions of commercially available powdered preparations of two popular Mexican beverages, horchata (rice-based) and atole (maize-based). The stimuli were presented in polyethylene squeeze bottles (Fig.2) previously used in a number of studies of chemosensory perception (Hudson et al., 1994; Laska et al., 1997, 2000; Laska & Teubner, 1999; Laska & Hubener, 2001). We chose these substances to maximize the ecological validity of the stimuli and the ability of subjects to describe and to accurately name them (cf. Ayabe-Kanamura et al., 1998; Distel et al., 1999; Distel & Hudson, 2001). Again, Tlaxcala residents performed significantly better than Mexico City residents on tests of odor detection and discrimination (Fig. 2 a-c), but the two groups performed equally well on description and naming. Deficits in olfactory performance among Mexico City subjects were apparent even for young, otherwise healthy adults.

In addition, further groups of subjects from Mexico City and Tlaxcala (30 subjects from each location) were compared for their ability to detect, describe and identify the smell of a milk preparation (Guarneros & Hudson, 2009). Again, subjects from Tlaxcala detected and described the odor of milk at lower concentrations than subjects from Mexico City (Fig.2 d-e) but no significant differences were found for the frequency and concentrations for correct identification between the two groups.

4. Are these findings relevant for everyday life?

Our sense of smell plays an important role in a wide range of functions. In a recent systematic review, Stevenson (2010) classified olfactory function into three main categories: 1) functions relating to ingestive behavior, 2) avoidance of environmental hazards, and 3) social communication. For example, the human sense of smell can detect (Porter et al., 2007) and identify foods suitable for eating (Fallon & Rozin, 1983). Also, smelling can modulate appetite, dietary behaviors, and nutritional status (Duffy et al., 1995; Aschenbrenner et al., 2008; Seo & Hummel, 2009). Moreover, olfaction warns of possible microbial threat (e.g., from feces, vomit, or organic decay), evoking disgust (Stevenson et al., 2010), and of nonmicrobial hazards including gas leaks, smoke, and toxic materials, eliciting fear (Cain & Turk, 1985; Cain et al., 1987; Miwa et al., 2001; Santos et al., 2004).

We therefore tested the ability of the last-mentioned subjects to detect, describe and judge the smell of dimethyl-disulfide (DMDS) (Guarneros & Hudson, 2009), a byproduct of the decomposition of various foods which has a characteristic smell of rotten cabbage and is largely responsible for the smell of different decaying or putrefying foods including milk (van Aardt et al., 2005). The subjects from Tlaxcala could detect and give a description of DMDS at lower concentrations than the Mexico City subjects. However, the concentrations at which subjects indicated the smell to be disgusting were not statistically significant

between the two groups (Fig.3a). Again, this might be explained by the additional recruitment of higher order mechanisms in the brain involved in attentional capture and enhancement (Grabenhorst et al., 2011).

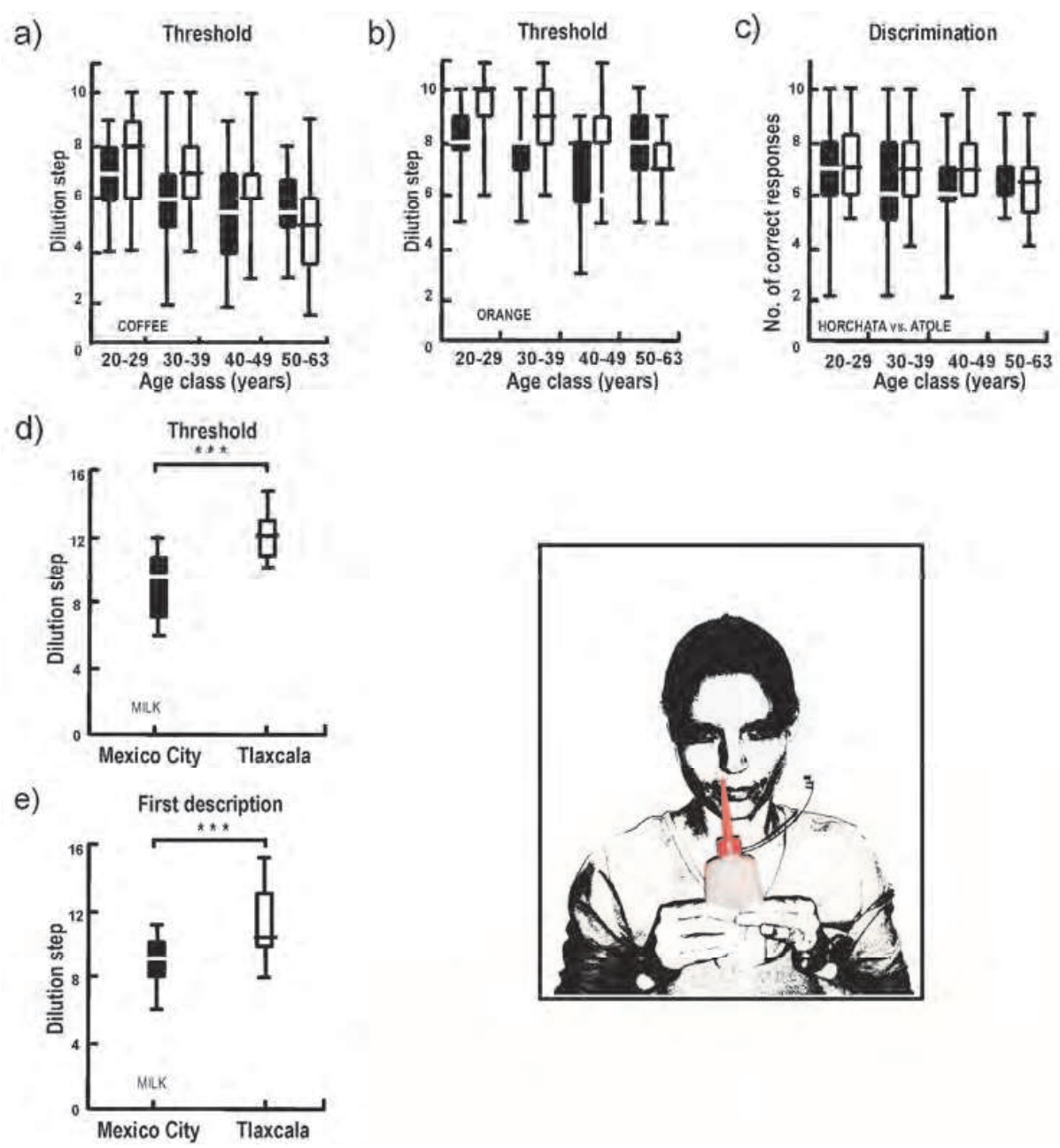


Fig. 2. Responses of subjects from Mexico City and Tlaxcala to the odor of different everyday products. The subjects from Tlaxcala outperformed the subjects from Mexico City in the following tasks a) Thresholds for detection of coffee. b) Thresholds for detection of orange. c) Discrimination task between two different Mexican beverages. d) Thresholds for detection of milk. e) First descriptions for the odor of milk. "Dilution steps" refer to the bottle numbers in the ascending order in which they were presented. Box plots: horizontal lines dividing the boxes = medians, horizontal limits of the boxes = interquartile ranges, vertical bars = percentiles 10 and 90. ***p<0.001, Mann-Whitney U tests. (Adapted from Hudson et al., 2006 and from Guarneros & Hudson, 2009).

Finally, subjects were presented with the powdered milk preparation at the concentration commercially recommended for human consumption but containing ascending concentrations of the contaminant DMDS. The concentration of DMDS at which subjects could discriminate the contaminated milk from milk without the contaminant was registered as the detection threshold for contaminated milk. Subjects from Tlaxcala not only presented lower thresholds (higher sensitivity) for DMDS in milk, but were also able to describe the odor and report it as being unpleasant (more unpleasant than milk alone) at lower concentrations than the Mexico City subjects (Fig.3). It is important to note that differences in scores were more marked for this test than for the previous one, which implies that olfactory impairment might be even more marked for complex olfactory tasks such as detecting a “target” odor when embedded in a “background” odor.

These results thus further warn of the dangers of big city air pollution by providing evidence of damage to the sense of smell and the relevance that this could have for everyday life.

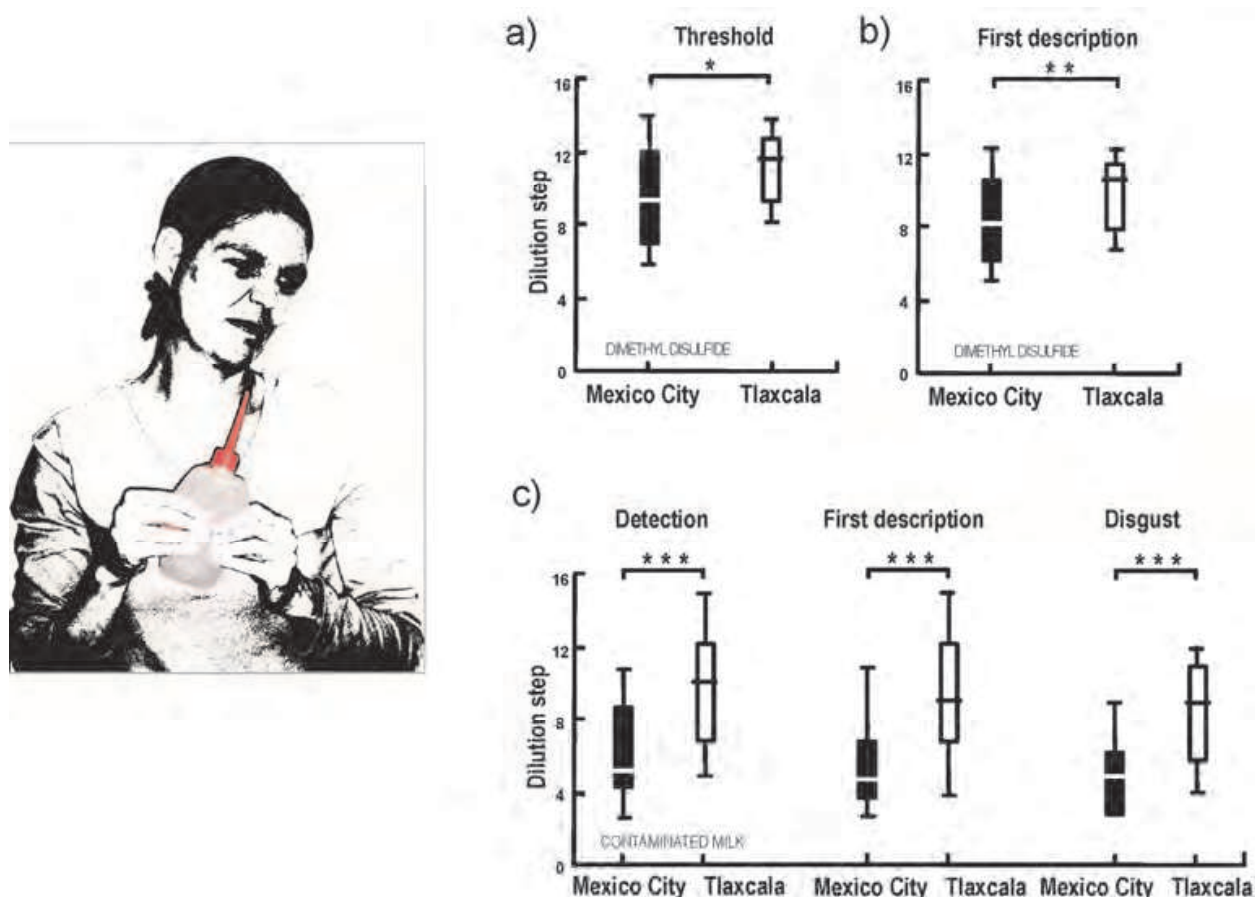


Fig. 3. Responses of subjects from Mexico City and Tlaxcala to the unpleasant stimulus dimethyl-disulfide. a) Thresholds for detection of dimethyl-disulfide. b) First description of dimethyl-disulfide. c) Thresholds for detection, first description and disgust (concentration at which subjects reported the stimulus to be disgusting) for milk with increasing concentrations of the contaminant dimethyl-disulfide. “Concentration” refers to the bottle numbers in the ascending order in which they were presented. Box plots: horizontal lines dividing the boxes = medians, limits of the boxes = interquartile ranges, vertical bars = percentiles 10 and 90. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Mann-Whitney U tests. (Adapted from Guarneros & Hudson, 2009).

5. Trigeminal sensitivity

What is commonly known as the sense of smell is composed of multiple sensations predominantly mediated by two distinct but functionally connected neural pathways, the olfactory and the trigeminal systems (Hudson et al., 1994; Laska et al., 1997). In fact, the great majority of chemosensory stimulants produce both olfactory and trigeminal activation (von Skramlik, 1925; Doty et al., 1978; Cometto-Muñiz & Cain, 1991, 1998; Hummel, 2000). Tingling, burning, pungent, prickling, cooling and fresh are common descriptors of intranasal sensations mediated by the trigeminal system. The anterior third of the nasal cavity is provided with trigeminal nerve endings sensitive to chemical substances. These project to the central nervous system including to the amygdala which processes emotional responses such as fear (Hacquemand et al., 2010).

Despite being so closely integrated, the olfactory and the intranasal trigeminal systems appear to have evolved as distinct functional adaptations. An important function of the intranasal trigeminal system is to prevent inhalation of potentially life-threatening substances by reflexively stopping inhalation (Walker et al., 2001; Scheibe et al., 2006) and triggering other protective reflexes, including sneezing, local neurogenic inflammation of the mucosa (Tizzano et al., 2010), and production of tears (Kjaergaard et al., 2004), whereas a major function of the olfactory system is to enable the learning of odors relevant to an individual's particular life experiences and environment (Hudson, 1999).

Given the contribution of both the olfactory and trigeminal systems to odor perception via the intranasal sensory surface, and notable pathological effects of air pollution on the cellular structure of the intranasal epithelium (Calderón-Garcidueñas et al., 1996, 1997, 1998, 2000, 2003b, 2009), we expected that residents of Mexico City would show significantly poorer performance than residents of Tlaxcala on a trigeminal task.

For this, the subjects tested above with Sniffin' Sticks were presented with two 250-mL polyethylene squeeze bottles with Teflon nosepieces that fit into the nostrils (Guarneros et al., 2009). The nosepieces were covered with disposable plastic caps that were replaced for each subject. Whereas the target bottle contained 30 mL of 98% eucalyptol (Fluka, Germany), a stimulus that elicits both olfactory and nasal trigeminal responses in humans (Doty et al., 1978), the odorless control bottle contained only ambient air. The headspace of the bottles was used to stimulate both sides of the nose independently but simultaneously during the same inspiration, and the subject's task was to identify the side of the nose receiving the stimulus. The side of stimulation was pseudorandomized across trials in the same manner for all subjects. Stimuli were presented using a hand-held squeeze device that simultaneously delivered a constant volume (15 mL) of air to each nostril (Fig. 4). Subjects received 40 trials (20 deliveries of eucalyptol to each nostril) from which we calculated the percent of correct responses. This previously described method (Hummel et al., 2003; Dalton et al., 2006) is based on the well-established finding that although subjects have difficulty identifying the nostril receiving a purely olfactory stimulus, they can readily do this for stimuli with a trigeminal component (Cometto-Muñiz & Cain, 1998; Hummel et al., 2003; Wysocki et al., 2003; Dalton et al., 2006).

The Tlaxcala subjects again performed significantly better than the Mexico City subjects (Fig. 4). Whereas subjects from Mexico City scored an average of 70.5% of correct answers, the subjects from Tlaxcala scored 81% of correct answers (Guarneros et al., 2009). This is potentially important given the contribution of the trigeminal system to the perception of odors (Hudson et al., 1994; Laska et al., 1997; Boyle et al., 2007; Frasnelli et al., 2009) and to

warning of the presence of toxic substances or other stimuli associated with situations that represent a threat to survival, such as smoke (Silver, 1991).

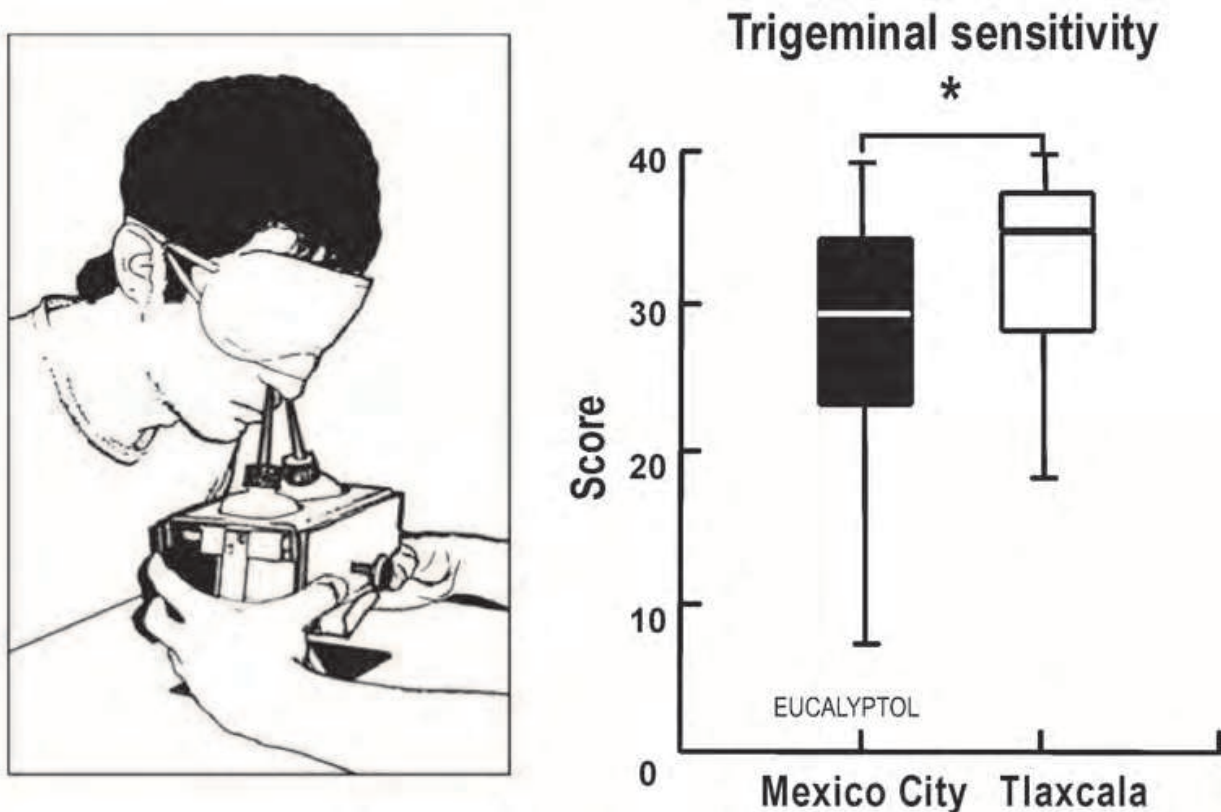


Fig. 4. Ability of subjects from Mexico City and Tlaxcala to correctly identify the nostril receiving the trigeminal stimulus eucalyptol when presented as shown in the drawing. Subjects could obtain a maximum score of 40 correct responses. Box plots: horizontal lines within boxes give medians, boxes' horizontal limits give the interquartile ranges, and vertical bars give the absolute ranges. * $p < 0.05$ (Mann-Whitney U test). (Adapted from Guarneros et al., 2009).

6. Mechanisms of intranasal damage and defense

To avoid the olfactory neurons of the nasal mucosa coming into direct contact with toxic agents contained in inspired air, both the respiratory and olfactory systems have evolved an array of defense mechanisms. The first is formed by the trigeminal nerve endings that detect and respond to irritants transmitted by the air. If it is not possible to escape the source of danger, the rhythm of breathing is altered and sneezing and coughing may occur so as to minimize the entry of irritants to the respiratory airways. Second, in addition to the olfactory epithelium, the nasal cavity contains squamous and respiratory epithelia. Both produce antibodies and antimicrobial proteins that protect the system against damaging agents, thereby limiting the effect of these on the olfactory epithelium. A third defense consists in increased production of mucous, which retains many of the agents that could damage the system. However, the efficiency of these defense mechanisms depends to a considerable extent on an individual's local environment. Chronic exposure to atmospheric contaminants can seriously damage the respiratory and olfactory epithelia, even to the point

of causing the development of tumors (Harkema et al., 1987; Berglund et al., 1992; Calderón-Garcidueñas et al., 1994, 1998, 1999; Lewis & Dahl, 1995; Hastings & Miller, 2003).

Although cells of the nasal cavity are able to limit damage to the nasal mucosa when exposure to contaminants is brief, in the case of chronic exposure the mucosa may develop abnormal characteristics that reduce its defense capabilities, causing discomfort and disease. The most common forms of damage within the nasal cavity produced by exposure to air pollution are shortening and partial or total loss of the olfactory cilia, which arise from the dendritic knobs of the olfactory neurons and along which the olfactory receptors are located, necrosis, displasias, metaplasias and hyperplasias of the basal cells from which the olfactory receptor neurons arise during the life-long process of neuronal regeneration characteristic of the olfactory system, and loss of cohesion among cells (Calderón-Garcidueñas et al., 1998, 2001; Schierhorn et al., 1999).

When the mucociliar system is affected, the retention of toxic particles by the mucosa is reduced, thus affecting the rest of the system (Halpern, 1982). With the loss of cilia the canals of the Bowman's glands, which produce the mucous that baths the nasal cavity, cleans the cilia and is indispensable for efficient regeneration of the olfactory epithelium, are directly exposed to the environment. When these glands are affected, the epithelium regenerates more slowly and eventually may even cease to do so (Morrison & Constanzo, 1990; Hastings & Miller, 2003).

Ozone is one of the most damaging oxidative contaminants among the atmospheric toxic agents, and is probably the one that has received the most attention (Tyler et al., 1988). It is highly reactive and interacts with a great variety of organic molecules, including non-saturated fats, proteins and nucleic acids. Both in humans and laboratory animals, acute or chronic exposure to ozone produces significant damage in the epithelium and the olfactory bulbs (Harkema et al., 1987; Calderón-Garcidueñas et al., 1996, 1998, 1999, 2002, 2009; Colín-Barenque et al., 1999).

Sulfur compounds also produce pathological changes in the respiratory epithelium. Whereas at lower concentrations they cause an increase in the secretion of mucous, at high concentrations they may cause a reduction in the flow of nasal secretions (Halpern, 1982). Other toxic substances such as formaldehyde and carbon dioxide may cause an abnormal structural and functional formation of the cilia, reducing their movement and thus their capacity to eliminate toxic particles (Boat & Carson, 1990). Whereas formaldehyde and acetaldehyde may induce nasal tumors, irritants such as ammonia cause inflammation, hyperplasias, metaplasias and displasias in the nasal epithelium (Hakema et al., 1987).

7. Discussion and future directions

The olfactory system resembles a finely tuned engine. The wrong fuel, containing contaminants, will generally impair the engine's performance and eventually just shut it down. Although the system might be able to cope with toxic agents to a certain degree and remain clinically healthy for prolonged periods in the face of poor air quality, as time passes and toxicity persists, disease will manifest itself. Here it should be noted that some of the deleterious effects of air pollutants on the respiratory cells lining the nasal cavity appear as soon as 15 days after the start of exposure (arrival to the city) to pollutants such as ozone, which induces acute nasal inflammatory responses and significant epithelial lesions in humans (Calderón-Garcidueñas et al., 1994). It would not be surprising to find an associated sensory effect just as soon, although this remains to be investigated.

Conditions and the time necessary for recovery of olfactory function are also unknown, but are likely to depend on the extent of damage. The capacity of the olfactory epithelium to regenerate and recover from environmental insults might be overridden by the rate of damage caused by chronic toxic exposure leading to a loss of the equilibrium and finally a functional collapse resulting in either diminished or the complete loss of olfactory function (hyposmia and anosmia, respectively) (Crews & Hunter, 1994; Smith et al., 2009).

Functional alterations to the olfactory system caused by exposure to toxic agents constitute a problem that has only received attention quite recently despite being known for a long time. For example, at the beginning of the 20th century zinc sulfate was used to irrigate the nasal cavity, with the aim of preventing attacks by viruses and bacteria on the brain. In patients treated with this substance the development of anosmia was observed (Menco & Morrison, 2003). Also, many of the first cases of impaired olfactory function and nasal discomfort were reported in people chronically exposed to high ambient levels of substances in industrial use such as sulfur dioxide, cadmium, lead, and chromium, among others (Cone & Shusterman, 1991; Schiffman & Nagle, 1992; Hastings & Miller, 2003). Unfortunately, there are as yet no available treatments able to reverse the damage caused by the exposure to such agents, although sometimes removal of the source allows repair of the olfactory system and the recovery of normal function (Upadhyay & Holbrook, 2004).

There are very few reports regarding deficiencies in trigeminal sensitivity. However, one of the most important findings is the relation between the decline in olfactory sensitivity and a reduction of trigeminal sensitivity; there is increasing evidence that an acquired loss of the sense of smell results in a reduction in trigeminal sensitivity due to the lack of interaction centrally (Hummel & Livermore, 2002). Both the orbitofrontal cortex and the rostral insula seem to be important in the amplification of trigeminal information, and this amplification is not found in anosmic patients and is reduced in hyposmic patients (Frasnelli & Hummel, 2007). On the other hand, patients suffering from inflammatory processes such as allergic rhinitis (which is frequently worsened by chronic exposure to environmental pollutants) usually present nasal itching and sneezing after toxicant exposure, clinical correlates of the activation of trigeminal nerve endings due to local inflammatory mechanisms (Doerfler et al., 2006). Aging is also associated with impaired trigeminal sensitivity and although it is not known to what extent this reduction is due to central processes, it is known that, at least in part, a reduction in sensitivity occurs in the periphery of the system (Frasnelli & Hummel, 2007).

Many toxic agents cause inflammatory processes that can affect the epithelium of the nasal cavity, and eventually can destroy trigeminal nerve endings. Tobacco smoke and alcohol are among the substances that have been observed to affect the epithelium (Vent et al., 2003; 2004), while acrolein, which is used as a herbicide, produces inflammation and tumors in the nasal cavity (Dorman et al., 2008). However, the effect of environmental toxic agents on the trigeminal system has still been little studied.

The results of previous studies indicate that subjects who are constantly exposed to the high levels of ambient air pollution of Mexico City present a significant reduction in olfactory sensitivity but not in the ability to identify common odorant stimuli (Hudson et al., 2006; Guarneros & Hudson, 2009; Guarneros et al., 2009). The similarities in the findings of these studies and despite the differences in the test methods and stimuli employed suggest the reliability of these conclusions. Furthermore, these findings are extended by the report of an adverse effect of big city air pollution on trigeminal function. This is potentially important

given the contribution of the trigeminal system to the perception of odors and to detecting the presence of toxic substances that could inflict damage on the respiratory system (Guarneros et al., 2009).

The subjects in our studies described above were healthy non-smokers and from socio-economical backgrounds characterized by good nutrition, good hygiene and a high standard of medical care. It would not be surprising if among less favored sectors of the heterogeneous population of Mexico City, impairment of chemosensory function would be even greater. This is particularly likely given that people from less favorable socioeconomic backgrounds are typically at a higher health risk associated with often greater exposure to air pollution (O'Neill et al., 2008).

Apart from a study associating the high levels of air pollution of Mexico City with pathological changes in the appearance of the olfactory bulbs and a reduction in the perception of odors (Calderón-Garcidueñas et al., 2009), little is known about the precise nature of the damage that air pollution inflicts on the olfactory and trigeminal systems. However, evidence of notable negative effects on the tissue of the nasal cavity (e.g. Calderón-Garcidueñas et al., 1996, 1997, 1998, 2001; Valverde et al., 1997) suggests that deficits in perception are mainly due to damage in the periphery of the system. Consistent with this we repeatedly found that performance on odor identification tests was equally good for subjects from Mexico City and the control population from Tlaxcala. This may be explained by the fact that the identification of odorants presented at suprathreshold concentrations involves more central cognitive functions based on associative memory processes to a greater extent than simply detecting or discriminating between them when presented at low concentrations (Hudson et al., 2006; Lötsch et al., 2008), thereby compensating the peripheral deficiencies once the concentration of stimuli are above the threshold of perception (Hudson et al., 2006). The equally good performance of the two groups on the tests of odor identification also suggests that subjects were equally motivated and equally able to manage the test situation.

Evidence of deficits in olfactory function and trigeminal sensitivity in young subjects exposed to high levels of urban air pollution raises other questions of relevance to public health. At what age do symptoms first appear? To what extent do certain common activities such as participating in sports in the open worsen such effects, and to what extent is impairment of chemosensory function reversible?

In addition, we do not know to what extent the impairment in olfactory sensitivity could be due to chronic inflammatory disorders of the mucosa and of the paranasal sinuses. These forms of chronic disease can cause nasal obstruction and are a common cause of diminished olfactory function (Doty, 1999; Cullen & Leopold, 1999; Seiden & Duncan, 2001; Welge-Lüssen, 2009). The possibility that, at least in part, olfactory impairment caused by air pollution is due to chronic inflammation seems plausible given that the incidence of inflammatory disorders is especially high in cities with air pollution problems (Arnedo-Peña et al., 2009; Liao et al., 2009; Lindgren et al., 2009; Wichmann et al., 2009), including Mexico City (Meza-Morales et al., 1998).

Although in the last years there has been a reduction in air pollution in Mexico City, air quality standards are still being exceeded for ozone and for particulate matter with an aerodynamic diameter of less than 10 micrometers (PM_{10}) (Instituto Nacional de Ecología, 2007). It is interesting that the authorities have given particular importance to particles less than 2.5 micrometers in diameter ($PM_{2.5}$) that according to various studies have considerable negative

effects on health (Borja-Aburto et al., 1997, 1998) because they can reach the periphery of the lungs, the bronchial tubes and the alveoli. On the other hand, the larger PM₁₀ particles principally affect the upper airways of the head and neck and only rarely reach the lungs. For this reason, they have been considered comparatively less damaging than finer particles (revision in Molina & Molina, 2002). However, it is very likely that the olfactory epithelium is directly affected by high concentrations of PM₁₀. Consistent with this, there have been several studies of the relation between high atmospheric levels of PM₁₀ and health. These studies reveal that the levels of these larger particles are associated with daily mortality and indeed also represent a health risk (Rosales-Castillo et al., 2001; O'Neill et al., 2004).

A more complete view of the risk to public health might be obtained in future studies by investigating the relation between subjects' performance on olfactory and trigeminal tests and levels of air pollution at different study sites on the days that tests are actually conducted. Also, the historical record of air pollution in the areas of study and the degree of individual subjects' exposure could provide additional information resulting in a better understanding of how air pollution affects the olfactory and trigeminal systems, including to what extent effects are due to acute or to chronic exposure to contaminants, and with what possible implications for behavior and treatment.

Notably, while the development of neurodegenerative diseases has also been related to exposure to high levels of air pollution (e.g. Campbell, 2004; Villarreal-Calderon et al., 2010) and to diminished olfactory capabilities (Doty et al., 1991; Fernández-Ruiz et al., 2003; Velazquez-Pérez et al., 2006; Haehner et al., 2007), the relation between these seemingly intertwined elements has only started to be investigated recently (Calderón-Garcidueñas et al., 2009). Thus, further research in this respect might also shed light on the origins and early diagnosis of neurodegenerative diseases that represent important public health issues such as Parkinson's disease.

8. Concluding summary

Mexico City air pollution is associated with impaired olfactory function. Different aspects of odor perception are altered to varying degrees, olfactory sensitivity being the most affected. This is shown by the higher detection thresholds both for monomolecular substances and complex mixtures common in everyday life observed for Mexico City subjects compared to subjects from cleaner-air environments, but equally good performance in describing and naming odor stimuli. Also, air pollution seems to be related to an impaired ability in assessing food edibility. The adverse effects of air pollution on olfactory function appear to result mainly from peripheral damage to this system rather than from effects on more central, cognitive processes. This is supported by an extensive literature reporting the harmful effects of airborne contaminants on the nasal cavity, including to the respiratory and olfactory epithelia. People from air-polluted areas also showed poorer performance in a test of intranasal trigeminal function, which mediates the sensations of freshness, spiciness and pungency via free nerve endings that innervate the nasal cavity, and warns of the presence of potentially dangerous substances in the environment. Important topics for future research include how early in life such impairments are manifested, how they relate to different life circumstances, when and under what conditions they might be reversible, and of particular importance, to what extent they are related to the appearance of neurodegenerative diseases in the increasingly aging populations characteristic of many large urban areas.

9. Acknowledgement

MG gratefully acknowledges the Posgrado en Ciencias Biológicas, UNAM and CONACYT for a doctoral fellowship (CVU 228879).

10. References

- Arnedo-Peña, A.; Gacía-Marcos, L.; Carvajal-Ureña, I.; Busquets-Monge, R.; Morales-Suárez-Varela, M.; Miner-Canflanca, I.; Batlles-Garrido, J.; Blanco-Quirós, A.; López-Silvarrey-Varela, A.; García-Hernández, G.; Aguinaga-Ontoso, I. & González-Díaz, C. (2009). Air pollution and recent symptoms of asthma, allergic rhinitis, and atopic eczema in school children aged between 6 and 7 years. *Archivos de Bronconeumología*, Vol.45, No.5, pp. 224-229, ISSN 0300-2896
- Aschenbrenner, K.; Hummel, C.; Teszmer, K.; Krone, F.; Ishimaru, T.; Seo, H-S. & Hummel, T. (2008). The influence of olfactory loss on dietary behaviors. *Laryngoscope*, Vol.118, No.1, pp. 135-144, ISSN 0023-852X.
- Ayabe-Kanamura, S.; Schicker, I.; Laska, M.; Hudson, R.; Distel, H.; Kobayakawa, T. & Saito, S. (1998). Differences in perception of everyday odors: a Japanese-German cross-cultural study. *Chemical Senses*, Vol.23, No.1, pp. 31-38, ISSN 0379-864X.
- Berglund, B.; Lindvall, T. & Nordin, S. (1992). Environmentally induced changes in sensory sensitivities. *Annals of the New York Academy of Sciences*, Vol.64, pp. 304-321, ISSN 0077-8923.
- Bhatnagar, A. (2006). Environmental cardiology: studying mechanistic links between pollution and heart disease. *Circulation Research*, Vol.99, No.7, pp. 692-705, ISSN 0009-7330.
- Boat, T. & Carson, J. (1990). Ciliary dysmorphology and dysfunction - primary or acquired? *The New England Journal of Medicine*, Vol.323, No. 24, pp.1700-1702, ISSN 0028-4793.
- Borja-Aburto, V.H.; Loomis, D.P.; Bangdiwala, S.I.; Shy, C.M. & Rascon-Pacheco, R.A. (1997). Ozone, suspended particles, and daily mortality in Mexico City. *American Journal of Epidemiology*, Vol.145, No.3, pp. 258-268, ISSN 0002-9262.
- Borja-Aburto, V.H.; Castillejos, M.; Gold, D.F.; Bierzwinski, S. & Loomis, D. (1998). Mortality and ambient fine particles in southwest Mexico City 1993-1995. *Environmental Health Perspectives*, Vol.106, No.12, pp. 849-855, ISSN 0091-6765.
- Boyle, J.A., Frasnelli, J.; Gerber, J.; Heinke, M. & Hummel, T. (2007). Cross-modal integration of intranasal stimuli: a functional magnetic resonance imaging study. *Neuroscience*, Vol.149, No.1, pp. 223-231, ISSN 1873-7544.
- Cain, W.S. & Turk, A. (1985). Smell of danger: an analysis of LP-gas odorization. *American Industrial Hygiene Association Journal*, Vol.46, No.3, pp.115-126, ISSN 0002-8894.
- Cain, W.S.; Leaderer, B.P.; Cannon, L.; Tosun, T. & Ismail, H. (1987). Odorization of inert gas for occupational safety: psychophysical considerations. *American Industrial Hygiene Association Journal*, Vol.48, No.1, pp. 47-55 ISSN 0002-8894.
- Calderón-Garcidueñas, L.; Rodríguez-Alcaraz, A.; García, R.; Sánchez, G.; Barragán, G.; Camacho, R. & Ramírez, L. (1994). Human nasal mucosal changes after exposure to urban pollution. *Environmental Health Perspectives*, Vol.102, No.12, pp. 1074-1080, ISSN 0091-6765.
- Calderón-Garcidueñas, L.; Osnaya, N.; Ramírez-Martínez, L. & Villarreal-Calderón A. (1996). DNA strand breaks in human nasal respiratory epithelium are induced

- upon exposure to urban pollution. *Environmental Health Perspectives*, Vol.104, No.2, pp. 160-168, ISSN 0091-6765.
- Calderón-Garcidueñas, L.; Osnaya, N.; Rodríguez-Alcaraz, A. & Villarreal-Calderón, A. (1997). DNA damage in nasal respiratory epithelium from children exposed to urban air pollution. *Environmental and Molecular Mutagenesis*, Vol.30, No.1, pp. 11-20, ISSN 0893-6692.
- Calderón-Garcidueñas, L.; Rodríguez-Alcaraz, A.; Villarreal-Calderón, A.; Lyght, O.; Janszen, D. & Morgan K. (1998). Nasal epithelium as a sentinel for airborne environmental pollution. *Toxicological Sciences*, Vol.46, No.2, pp. 352-364, ISSN 1096-6080.
- Calderón-Garcidueñas, L.; Rodríguez-Alcaraz, A.; García, R.; Barragán, G.; Villarreal-Calderón, A. & Madden, M.C. (1999). Cell proliferation in nasal respiratory epithelium of people exposed to urban pollution. *Carcinogenesis*, Vol.20, No.3, pp. 383-389, ISSN 1460-2180.
- Calderón-Garcidueñas, L.; Devlin, R.B. & Miller, F.J. (2000). Respiratory tract pathology and cytokine imbalance in clinically healthy children chronically and sequentially exposed to air pollutants. *Medical Hypotheses*, Vol.55, No.5, pp. 373-378, ISSN 0306-9877.
- Calderón-Garcidueñas, L.; Valencia-Salazar, G.; Rodríguez-Alcaraz, A.; Gambling, M.T.; García, R.; Osnaya, N.; Villareal-Calderón, A.; Devlin, R. & Carson, J. (2001). Ultrastructural nasal pathology in children chronically and sequentially exposed to air pollutants. *American Journal of Respiratory Cell and Molecular Biology*, Vol.24, No.32, pp. 132-138, ISSN 1535-4989.
- Calderón-Garcidueñas, L.; Azzarelli, B.; Acuña, H.; García, R.; Gambling, T.; Osnaya, N.; Monroy, S.; Tizapantzi, M.; Carson, J.; Villarreal-Calderón, A. & Rewcastle, B. (2002). Air pollution and brain damage. *Toxicologic Pathology*, Vol.30, No.3, pp. 373-389, ISSN 1533-1601.
- Calderón-Garcidueñas, L.; Mora-Tiscareño, A.; Fordham, L.A.; Valencia-Salazar, G.; Chung, C.J.; Rodríguez-Alcaraz, A.; Paredes, R.; Variakojis, D.; Villarreal-Calderón, A.; Flores-Camacho, L.; Antúnez-Solís, A.; Henríquez-Roldán, C. & Hazucha, M.J. (2003a). Respiratory damage in children exposed to urban pollution. *Pediatric Pulmonology*, Vol.36, No.2, pp.148-161, ISSN 8755-6863.
- Calderón-Garcidueñas, L.; Maronpot, R.R.; Torres-Jardón, R.; Henríquez-Roldán, C.; Schoonhoven, R.; Acuña-Ayala, H.; Villareal-Calderón, A.; Nakamura, J.; Fernando, R.; Reed, W.; Azzarelli, B. & Swenberg, J.A. (2003b). DNA damage in nasal and brain tissues of canines exposed to air pollutants is associated with evidence of chronic brain inflammation and neurodegeneration. *Toxicologic Pathology*, Vol.31, No.5, pp. 524-538, ISSN 0192-6233.
- Calderón-Garcidueñas, L.; Reed, W.; Maronpot, R.R.; Henríquez-Roldán, C.; Delgado-Chávez, R.; Calderón-Garcidueñas, A.; Dragustinovis, I.; Franco-Lira, M.; Aragón-Flores, M.; Solt, A.C.; Altenburg, M.; Torres-Jardón, R. & Swenberg, J.A. (2004). Brain inflammation and Alzheimer's-like pathology in individuals exposed to severe air pollution. *Toxicologic Pathology*, Vol.32, No.6, pp. 650-658, ISSN 1533-1601.
- Calderón-Garcidueñas, L.; Franco-Lira, M.; Henríquez-Roldán, C.; Osnaya, N.; González-Maciel, A.; Reynoso-Robles, R.; Villarreal-Calderón, R.; Herriot, L.; Brooks, D.; Keefe, S.; Palacios-Moreno, J.; Villarreal-Calderón, R.; Torres-Jardón, R.; Medina-Cortina,

- H.; Delgado-Chávez, R.; Aiello-Mora, M.; Maronpot, R.R. & Doty R.L. (2009). Urban air pollution: Influences on olfactory function and pathology in exposed children and young adults. *Experimental and Toxicologic Pathology*, Vol. 62, No.1, pp. 91-102, ISSN 0940-2993.
- Campbell, A. (2004) Inflammation, neurodegenerative diseases, and environmental exposures. *Annals of the New York Academy of Sciences*, Vol.1035, pp. 117-123, ISSN 1749-6632.
- Castillejos, M.; Gold, D.R.; Damokosh, A.I.; Serrano, P.; Allen, G. & McDonnell, W.F. (1995). Acute effects of ozone on the pulmonary function of exercising schoolchildren from Mexico City. *American Journal of Respiratory and Critical Care Medicine*, Vol.152, No. 5 pt.1, pp. 1501-1507, ISSN 1073-449X.
- Chen, J.; Shi, J.; Wang, S.; Yang, S.; Lou, J. & Liu, Z. (2004). Environmental mycological study and respiratory disease investigation in tussah silk processing workers. *Journal of Occupational Health*, Vol. 46, No.5, pp. 418-422, ISSN 1341-9145.
- Colín-Barenque, L.; Ávila-Costa, M.R.; Fortoul, T.; Rugerio-Vargas, C.; Machado-Salas, J.P.; Espinosa-Villanueva, J. & Rivas-Arancibia, S. (1999). Morphologic alterations of the olfactory bulb after acute ozone exposure in rats. *Neuroscience Letters*, Vol.274, No.1, pp. 1-4, ISSN 1872-7972.
- Cometto-Muniz, J.E. & Cain, W.S. (1991). Influence of air-borne contaminants on olfaction and taste in health and disease. In: *Smell and Taste in Health and Disease*, T.V. Getchell; R.L. Doty; L.M. Bartoshuk; and J.B. Snow. (Eds.), pp. 765-785, Raven, ISBN 0881677981, New York, USA.
- Cometto-Muñiz, J.E. & Cain, W.S. (1998). Trigeminal and olfactory sensitivity: comparison of modalities and methods of measurement. *International Archives of Occupational and Environmental Health*, Vol.71, No.2, pp. 105-110, ISSN 0340-0131.
- Cone, E.J. & Shusterman, D. (1991). Health effects of indoor odorants. *Environmental Health Perspectives*, Vol. 95, pp. 53-59, ISSN 0091-6765.
- Consejo Nacional de Población. (2009). Mexico City Metropolitan Area, Government of the State of Mexico. 3.03.2011
<http://www.edomex.gob.mx/poblacion/docs/2009/PDF/ZMVM.pdf>.
- Crews, L. & Hunter, D. (1994). Neurogenesis in the olfactory epithelium. *Perspectives on Developmental Neurobiology*, Vol.2, No.2, pp. 151-161, ISSN 1064-0517.
- Cullen, M.M.; Leopold, D.A. (1999). Disorders of smell and taste. *Medical Clinics of North America*, Vol.83, No.1, pp. 57-74, ISSN 1557-9859.
- Dalton, P.; Dilks, D. & Hummel, T. (2006). Effects of long-term exposure to volatile irritants on sensory thresholds, negative mucosal potentials, and event-related potentials. *Behavioral Neuroscience*, Vol.120, No.1, pp.180-189, 0735-7044.
- Distel, H.; Ayabe-Kanamura, S.; Martínez-Gómez, M.; Schicker, I.; Kobayakawa, T.; Saito, S. & Hudson, R. (1999). Perception of everyday odors – correlation between intensity, familiarity and strength of hedonic judgement. *Chemical Senses*, Vol.24, No.2, pp. 191-199, ISSN 379-864X.
- Distel, H.; & Hudson, R. (2001). Judgement of odor intensity is influenced by subjects' knowledge of the odor source. *Chemical Senses*, Vol.26, No.3, pp. 247-251 ISSN 379-864X.

- Doerfler, H.; Hummel, T.; Klimek, L. & Kobal, G. (2006). Intranasal trigeminal sensitivity in subjects with allergic rhinitis. *European Archives of Otorhinolaryngology*, Vol.263, No.1, pp. 86-90, ISSN 1434-4726.
- Dorman, D.C.; Struve, M.F.; Wong, B.A.; Marshall, M.W.; Gross, E.A. & Willson, G.A. (2008). Respiratory tract responses in male rats following subchronic acrolein inhalation. *Inhalation Toxicology*, Vol.20, No.3, pp. 205-216, ISSN 1091-7691.
- Doty, R.L.; Brugger, W.P.E.; Jurs, P.C.; Orndorff, M.A.; Snyder, P.J. & Lowry, L.D. (1978). Intranasal trigeminal stimulation from odorous volatiles: psychometric responses from anosmic and normal humans. *Physiology and Behavior*, Vol. 20, No.2, pp. 175-185, ISSN 0031-9384
- Doty, R.L.; Perl, D.P.; Steele, J.C.; Chen, K.M.; Pierce, J.D.Jr.; Reyes, P.; Kurland, L.T. (1991). Olfactory dysfunction in three neurodegenerative diseases. *Geriatrics*, Vol. 46 (August). Suppl 1, pp. 47-51, ISSN 1936-5764.
- Doty, R.L. (1999). Olfaction. In: *Nasal polyposis: An inflammatory disease and its treatment*. N. Mygind & T. Linholdt (Eds.), pp. 153-159, Wiley Blackwell, ISBN 8716119681, Copenhagen, Denmark.
- Duffy, V.B.; Backstrand, J.R. & Ferris, A.M. (1995). Olfactory dysfunction and related nutritional risk in free-living, elderly women. *Journal of the American Dietetic Association*, Vol. 95, No.8, pp. 879-884, ISSN 0002-8223.
- Evans, G.W.; Colome, S.D. & Shearer, D.F. (1988). Psychological reactions to air pollution. *Environmental Research*, Vol.45, No.1, pp. 1-15, ISSN 0013-9351.
- Fallon, A. & Rozin, P. (1983). The psychological bases of food rejection by humans. *Ecology of Food and Nutrition*, Vol.13, No.1, pp. 15-26, ISSN 0367-0244.
- Fernández-Ruiz, J.; Díaz, R.; Hall-Haro, C.; Vergara, P.; Fiorentini, A.; Núñez, L.; Drucker-Colín, R.; Ochoa, A.; Yescas, P.; Rasmussen, A. & Alonso, M.E. (2003). Olfactory dysfunction in hereditary ataxia and basal ganglia disorders. *NeuroReport*, Vol.14, No.10, pp. 1339-1341, ISSN 1473-558X.
- Frasnelli, J. & Hummel, T. (2007). Interactions between the chemical senses: trigeminal function in patients with olfactory loss. *International Journal of Psychophysiology*, Vol.65, No.3, pp.177-181, ISSN 1872-7697.
- Frasnelli, J.; Charbonneau, G.; Collignon, O. & Lepore, F. (2009). Odor localization and sniffing. *Chemical Senses*, Vol.34, No.2, pp.139-144, ISSN 0379-864X.
- Gold, D.R.; Damokosh, A.I.; Pope, C.A. III.; Dockery, D.W.; McDonnell, W.F. & Serrano, P. (1999). Particulate and ozone pollutant effects on the respiratory function of children in southwest Mexico City. *Epidemiology*, Vol.10, No.1, pp. 8-16, ISSN 1044-3983.
- Goldsmith, L.A. (1996). Skin effects of air pollution. *Otolaryngology and Head and Neck Surgery*, Vol.114, No.2, pp. 217-219. ISSN 0194-5998.
- Grabenhorst, F.; Rolls, E.T. & Margot, C. (2011). A hedonically complex odor mixture produces an attentional capture effect in the brain. *Neuroimage*, Vol.55, No.2, pp. 832-843, ISSN 1053-8119.
- Guarneros, M. & Hudson, R. (2009). La contaminación del aire deteriora la función olfativa cotidiana en residentes de la Ciudad de México. *El Residente*, Vol.4 No. 3, pp. 81-86.
- Guarneros, M.; Hummel, T.; Martínez-Gómez, M. & Hudson, R. (2009). Mexico City air pollution adversely affects olfactory function and intranasal trigeminal sensitivity. *Chemical Senses*, Vol.34, No.2, pp.819-826, ISSN 379-864X

- Hacquemand, R.; Jacquot, L. & Brand, G. (2010). Comparative fear-related behaviors to predator odors (TMT and natural fox feces) before and after intranasal ZnSO₄ treatment in mice. *Frontiers in Behavioral Neuroscience*, Vol.4, (December), pp.188. ISSN 1662-5153.
- Haehner, A.; Hummel, T.; Hummel, C.; Sommer, U.; Junghanns, S. & Reichmann, H. (2007). Olfactory loss may be a first sign of idiopathic Parkinson's disease. *Movement Disorders*, Vol.22, No.6, pp. 839-842.
- Halpern, P.B. (1982). Environmental factors affecting chemoreceptors: an overview. *Environmental Health Perspectives*, Vol.44, pp.101-105, ISSN 0885-3185.
- Harkema, R.J.; Plopper, C.; Hyde, D.; George, J.; Wilson, D. & Dungworth, D. (1987). Response of the macaque nasal epithelium to ambient levels of ozone. *The American Journal of Pathology*, Vol.128, No.1, pp. 29-44, ISSN 1525-2191.
- Hastings, L. & Miller, M.L. (2003). Influence of environmental toxicants on olfactory function, In: *Handbook of olfaction and gustation*, Second Edition, R.L. Doty (Ed.), pp. 575-592, ISBN 978-0-8247-0719-4, Marcel Dekker, Philadelphia, USA.
- Heiser, C.; Grupp, K.; Hörmann, K. & Stuck, B.A. (2010). Loss of olfactory function after exposure to barbituric acid. *Auris Nasus Larynx*, Vol.37, No.1, pp. 103-105, ISSN 0385-8146.
- Hudson, R. (1999). From molecule to mind: the role of experience in shaping olfactory function. *Journal of Comparative Physiology A*. Vol.185, No.4, pp. 297-304, ISSN 0340-7594.
- Hudson, R.; Laska, M.; Berger, T.; Heye, B.; Schopohl, J. & Danek, A. (1994). Olfactory function in patients with hypogonadotropic hypogonadism: an all-or-none phenomenon? *Chemical Senses*, Vol.19, No.1, pp. 57-69, ISSN 379-864X.
- Hudson, R.; Arriola, A.; Martínez-Gómez, M. & Distel, H. (2006). Effect of air pollution on olfactory function in residents of Mexico City. *Chemical Senses*, Vol.31, No.1, pp. 79-85, ISSN 379-864X.
- Hummel, T.; Sekinger, B.; Wolf, S.; Pauli, E. & Kobal, G. (1997). 'Sniffin' Sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chemical Senses*, Vol.22, No.1, pp. 39-52, ISSN 379-864X.
- Hummel, T. (2000). Assessment of intranasal trigeminal function. *International Journal of Psychophysiology*, Vol.36, No.2, pp.147-155, ISSN 0167-8760.
- Hummel, T. & Livermore, A. (2002). Intranasal chemosensory function of the trigeminal nerve and aspects of its relation to olfaction. *International Archives of Occupational and Environmental Health*, Vol.75, No.5, pp.305-313, ISSN 1432-1246.
- Hummel, T.; Futschik, T.; Frasnelli, J. & Hüttenbrink, K.B. (2003). Effects of olfactory function, age, and gender on trigeminally mediated sensations: a study based on the lateralization of chemosensory stimuli. *Toxicology Letters*, Vol.140-141, pp. 273-280, ISSN 378-4274.
- Kjaergaard, S.K.; Hempel-Jørgensen, A.; Mølhave, L.; Andersson, K.; Juto, J.E. & Stridh, G. (2004). Eye trigeminal sensitivity, tear film stability and conjunctival epithelium damage in 182 non-allergic, non-smoking Danes. *Indoor Air*, Vol.14, No.3, pp.200-207, ISSN 0905-69-47.

- Laska, M.; Distel, H. & Hudson, R. (1997). Trigeminal perception of odorant quality in congenitally anosmic subjects. *Chemical Senses*, Vol.22, No.4, pp. 447-456, ISSN 379-864X.
- Laska, M. & Teubner, P. (1999). Olfactory discrimination ability for homologous series of aliphatic alcohols and aldehydes. *Chemical Senses*, Vol.24, No.3, pp. 447-456. ISSN 379-864X.
- Laska, M.; Ayabe-Kanamura, S.; Hubener, F. & Saito, S. (2000). Olfactory discrimination ability for aliphatic odorants as a function of oxygen moiety. *Chemical Senses*, Vol. 25, No.2, pp. 189-197. ISSN 379-864X.
- Laska, M. & Hubener, F. (2001). Olfactory discrimination ability for homologous series of aliphatic ketones and acetic esters. *Behavioural Brain Research*, Vol.119, No.2, pp. 193-201. ISSN 379-864X.
- Lewis, J.L. & Dahl, A.R. (1995). Olfactory mucosa: composition, enzymatic localization, and metabolism. In: *Handbook of olfaction and gustation*, Second Edition, R.L. Doty (Ed.), pp. 33, ISBN 978-0-8247-0719-4, Marcel Dekker, Philadelphia, USA.
- Liao, M.F.; Liao, M.N.; Lin, S.N.; Chen, J.Y. & Huang, J.L. (2009). Prevalence of allergic diseases of school children in central Taiwan: From ISAAC surveys 5 years apart. *Journal of Asthma*, Vol.46, No.6, pp. 541-545, ISSN 0277-0903.
- Lindgren, A.; Stroh, E.; Nihlén, U.; Montn  mery, P.; Axmon, A. & Jakobsson, K. (2009). Traffic exposure associated with allergic asthma and allergic rhinitis in adults: A cross-sectional study in southern Sweden. *International Journal of Health Geographics*, Vol.8, pp.25, ISSN 1476-072X.
- Lippmann, M. (1989). Effective strategies for population studies of acute air pollution health effects. *Environmental Health Perspectives*, Vol.81, pp. 115-119, ISSN 0091-6765.
- Loomis, D.; Castillejos, M.; Gold, D.R.; McDonnell, W. & Borja-Aburto, V.H. (1999). Air pollution and infant mortality in Mexico City. *Epidemiology*, Vol.10, No.2, pp. 118-123, ISSN 1044-3983.
- L  tsch, J.; Reichmann, H. & Hummel, T. (2008). Different odor tests contribute differently to the diagnostics of olfactory loss. *Chemical Senses*, Vol.33, No.1, pp. 17-21, ISSN 379-864X.
- Menco, B.P. & Morrison, E.E. (2003). Morphology of the mammalian olfactory epithelium: form, fine structure, function and pathology. In: *Handbook of olfaction and gustation*, Second Edition, R.L. Doty (Ed.), pp. 17-49, ISBN 978-0-8247-0719-4, Marcel Dekker, Philadelphia, USA.
- Meza-Morales, A.; Arregu  n-Osuna, L.; Navarrete, F.; Huerta-L  pez, J.G. & Medina, G. (1998). Morphological features of the nasal mucosa in healthy children exposed to different concentrations of atmospheric pollution. *Revista Alergia M  xico*, Vol.45, No.1, pp. 22-26, ISSN 0002-5151.
- Miwa, T.; Furukawa, M.; Tsukatani, T.; Costanzo, R.M.; DiNardo, L.J. & Reiter, E.R. (2001). Impact of olfactory impairment on quality of life and disability. *Archives of Otolaryngology - Head and Neck Surgery*, Vol.127, No.5, pp. 497-503, ISSN 0886-4470.
- Molina, L.T. & Molina, M.J. (2002). Air quality impacts: local and global concern. In: *Air quality in the Mexico megacity. An integrated assessment*, L.T. Molina & M.J. Molina (Eds.), pp. 1-19, Kluwer Academic Publishers, ISBN 978-1-4020-0452-0, Dordrecht, Netherlands.

- Morrison, E.E. & Costanzo, R.M. (1990). Morphology of the human olfactory epithelium. *The Journal of Comparative Neurology*, Vol.297, No.1, pp. 1-13, ISSN 0021-9967.
- O'Neill, M.S.; Loomis, D.; Borja-Aburto, V.H.; Gold, D.; Hertz, Piccioto, I. & Castillejos, M. (2004). Do associations between airborne particles and daily mortality in Mexico City differ by measurement method, region, or modeling strategy? *Journal of Exposure Analysis and Environmental Epidemiology*, Vol.14, No.6, pp. 429-439, ISSN 1476-5519.
- O'Neill, M.S.; Bell, M.L.; Ranjit, N.; Cifuentes, L.A.; Loomis, D.; Gouveia, N. & Borja-Aburto, V.H. (2008). Air pollution and mortality in Latin America: the role of education. *Epidemiology*, Vol.19, No.6, pp. 810-819, ISSN 1044-3983.
- Porter, J.; Craven, B.; Khan, R.; Chang, S-J.; Kang, I.; Judkewitz, B.; Volpe, J.; Settles, G. & Sobel, N. (2007). Mechanisms of scent tracking in humans. *Nature Neuroscience*, Vol.10, No.1, pp. 27-29, ISSN 1097-6256.
- Rivas-Arancibia, S.; Dorado-Martínez, C.; Colín-Barenque, L.; Kendrick, K.M.; de la Riva, C. & Guevara-Guzmán, R. (2003). Effect of acute ozone exposure on locomotor behavior and striatal function. *Pharmacology, Biochemistry and Behavior*, Vol.74, No.4, pp. 891-900, ISSN 0091-3057.
- Romieu, I.; Meneses, F.; Ruiz, S.; Sierra, J.J.; Huerta, J.; White, M.C. & Etzel, R.A. (1996). Effects of air pollution on the respiratory health of asthmatic children living in Mexico City. *American Journal of Respiratory and Critical Care Medicine*, Vol.154, No.2, pt.1, pp. 300-307, ISSN 1073-449X.
- Rosales-Castillo, J.A.; Torres-Meza, V.M.; Olaiz-Fernández, G. & Borja-Aburto, V.H. (2001). Los efectos agudos de la contaminación del aire en la salud de la población: evidencias de estudios epidemiológicos. *Salud Pública de México*, Vol.43, No.6, pp. 544-555, ISSN 0036-3634.
- Santos, D.V.; Reiter, E.R.; DiNardo, L.J. & Costanzo, R.M. (2004). Hazardous events associated with impaired olfactory function. *Archives of Otolaryngology Head and Neck Surgery*, Vol.130, No.3, pp. 317-319, ISSN 0886-4470.
- Scheibe, M.; Zahnert, T. & Hummel, T. (2006). Topographical differences in the trigeminal sensitivity of the human nasal mucosa. *NeuroReport*, Vol.17, No.1, pp.1417-1420, ISSN 0959-4965.
- Schierhorn, K.; Zhang, M.; Matthias, C. & Kunkel, G. (1999). Influences of ozone and nitrogen dioxide on histamine and interleukin formation in a human nasal mucosa culture system. *American Journal of Respiratory Cell and Molecular Biology*, Vol.20, No.5, pp. 1013-1019, ISSN 1044-1549.
- Schiffman, S. & Nagle, T. (1992). Effect of environmental pollutants on taste and smell. *Otolaryngology and Head and Neck Surgery*, Vol.106, No.6, pp. 693-700, ISSN 0194-5998.
- Secretaría del Medio Ambiente del DF. (2007). La calidad del aire en la Zona Metropolitana del Valle de México 1986-2006. Informe del estado y tendencias de la contaminación atmosférica. Gobierno del Distrito Federal, México DF.
- Seiden, A.M. & Duncan, H.J. (2001). The diagnosis of a conductive olfactory loss. *Laryngoscope*, Vol.111, No.1, pp. 9-14, ISSN 1531-4995.
- Seo, H-S. & Hummel, T. (2009). Effects of olfactory dysfunction on sensory evaluation and preparation of foods. *Appetite*, Vol.53, No.3, pp. 314-321, ISSN 0195-6663.

- Silver, W.L. (1991). Physiological factors in nasal trigeminal chemoreception. In : *Chemical senses, vol. 2, Irritation*. B.G. Green; J.R. Mason & M.R. Kare (Eds.), pp. 21-37, Marcel Dekker. ISBN 0-8247-8323-9, New York.
- Smeets, M. & Dalton, P. (2002). Perceived odor and irritation of isopropanol: a comparison between naïve controls and occupationally exposed workers. *International Archives of Occupational and Environmental Health*, Vol.75, No.8, pp.541-548, ISSN 0340-0131.
- Smeets, M.; Mauté, C. & Dalton, P. (2002). Acute sensory irritation from exposure to isopropanol (2-propanol) at TLV in workers and controls: objective versus subjective effects. *Annals of Occupational Hygiene*, Vol.46, No.4, pp.359-373, ISSN 0003-4878.
- Smith, W.M.; Davidson, T.M. & Murphy, C. (2009). Toxin-induced chemosensory dysfunction: A case series and review. *American Journal of Rhinology and Allergy*, Vol.23, No.6 (Nov-Dec), pp. 578-581, ISSN 1945-8924.
- Stevenson, R.J. (2010). An initial evaluation of the function of human olfaction. *Chemical Senses*, Vol. 35, No.1, pp.3-20, ISSN 379-864X.
- Stevenson, R.J.; Oaten, M.; Case, T.I.; Repacholi, B.M. & Wagland, P. (2010). Children's response to adult disgust elicitors: development and acquisition. *Developmental Psychology*, Vol.46, No.1, pp.165-177, ISSN 0012-1649.
- Tizzano, M.; Gulbransen, B.D.; Vandenbeuch, A.; Clapp, T.R.; Herman, J.P.; Sibhatu, H.M.; Churchill, M.E.; Silver, W.L.; Kinnamon, S.C. & Finger, T.E. (2010). Nasal chemosensory cells use bitter taste signaling to detect irritants and bacterial signals. *Proceedings of the National Academy of Sciences*, Vol.107, No.7, pp.3210-3215. ISSN 027-8424.
- Tovalín, H.; Herbarth, O.; Sierra-Vargas, M.; Strandberg, B.; Blanco, S.; Vega, L.; Sioutas, C.; Hicks, J.J.; Marroquín, R.; Acosta, G.; Guarneros, M.; Hernández, V.; Estrada-Muñiz, E.; Olivares, I.; Pérez, D.; Torres-Ramos, Y.; Ulrich, F.; Hudson, R.; Reyes, E.; Rodríguez, T.; Elizondo, G. & Cantellano, E. (2010) Air pollutants exposure and health effects during the MILAGRO-MCMA 2006 Campaign. In: *Air pollution: health and environmental impacts*, B. Gurjar; L.T. Molina & C.S.P. Ojha, (Eds.), pp. 203-227, CRC Press, Taylor & Francis Group, ISBN 978-1-4398-0962-4, Boca Raton, Florida, USA.
- Tyler, W.S.; Tyler, N.K.; Last, J.A.; Gillespe, M.J. & Barstow, T.J. (1988). Comparison of daily and seasonal exposures of young monkeys to ozone. *Toxicology*, Vol.50, No.2, pp. 131-144, ISSN 1879-3185.
- Upadhyay, U.D. & Holbrook, E.H. (2004). Olfactory loss as a result of a toxic exposure. *Otolaryngologic Clinics of North America*, Vol.37, No.6, pp. 1185-1207, ISSN 0030-6665.
- Valverde, M.; López, M.C.; López, I.; Sánchez, I.; Fortoul, T.I.; Ostrosky-Wegman, P. & Rojas, E. (1997). DNA damage in leukocytes and bucal and nasal epithelial cells of individuals exposed to air pollution in Mexico City. *Environmental and Molecular Mutagenesis*, Vol.30, No.2, pp. 147-152, ISSN 0893-6692.
- Van Aardt, M.; Duncan, S.E.; Marcy, J.E.; Long, T.E.; O'Keefe, S.F. & Nielsen-Sims, S.R. (2005). Aroma analysis of light-exposed milk stored with and without natural and synthetic antioxidants. *Journal of Dairy Science*, Vol.88, No.3, pp.881-890, ISSN 1525-3198.
- Velázquez-Pérez, L.; Fernández-Ruiz, J.; Díaz, R.; González, R.P.; Ochoa, N.C.; Cruz, G.S.; Mederos, L.E.; Góngora, E.M.; Hudson, R. & Drucker-Colín, R. (2006).

- Spinocerebellar ataxia type 2 olfactory impairment shows a pattern similar to other major neurodegenerative diseases. *Journal of Neurology*, Vol.253, No.9, pp.1165-1169, ISSN 1432-1459.
- Vent, J.; Bartels, S.; Haynatzki, G.; Gentry-Nielsen, M.J.; Leopold, D.A. & Hallworth, R. (2003). The impact of ethanol and tobacco smoke on intranasal epithelium in rat. *American Journal of Rhinology*, Vol.17, No.4, pp. 241-247, ISSN 1050-6586.
- Vent, J.; Robinson, A.M.; Gentry-Nielsen, M.J.; Conley, D.B.; Hallworth, R.; Leopold, D.A. & Kern, R.C. (2004). Pathology of the olfactory epithelium: smoking and ethanol exposure. *Laryngoscope*, Vol.114, No.8, pp. 1383-1388, ISSN 0023-852X.
- Versura, P.; Profazio, V.; Cellini, M.; Torreggiani, A.; Caramazza, R. (1999). Eye discomfort and air pollution. *Ophthalmologica*, Vol.213, No.2, pp.103-109, ISSN 0030-3755.
- Villarreal-Calderon, R.; Torres-Jardon, R.; Palacios-Moreno, J.; Osnaya, N.; Pérez-Guille, B.; Maronpot, R.; Reed, W.; Zhu, H. & Calderón-Garcidueñas, L. (2010). Urban air pollution targets the dorsal vagal complex and dark chocolate offers neuroprotection. *International Journal of Toxicology*, Vol.29, No.6, pp. 604-615, ISSN 1091-5818.
- von Skramlik, E. (1925). Über die Lokalisation der Empfindungen bei den niederen Sinnen [On the localization of sensation in the lower senses]. *Zeitschrift für Sinnesphysiologie*, Vol.56, pp.69-140. ISSN 0233-2906.
- Walker, J.C.; Kendal-Reed, M.; Utell, M.J. & Cain, W.S. (2001). Human breathing and eye blink rate responses to airborne chemicals. *Environmental Health Perspectives*, Vol.109, Suppl.4, pp.507-512, 0091-6765.
- Welge-Lüssen, A. (2009). Psychophysical effects of nasal and oral inflammation. *Annals of the New York Academy of Sciences*, Vol.1170, pp.585-589, ISSN 1749-6632.
- Wichmann, F.A.; Müller, A.; Busi, L.E.; Cianni, N.; Massolo, L.; Schlink, U.; Porta, A. & Sly, P.D. (2009). Increased asthma and respiratory symptoms in children exposed to petrochemical pollution. *Journal of Allergy and Clinical Immunology*, Vol.123, No.3, pp. 632-638, ISSN 1097-6825.
- Wysocki, C.J.; Cowart, B.J. & Radil, T. (2003). Nasal trigeminal chemosensitivity across the adult life span. *Perception and Psychophysics*, Vol.65, No.1, pp.115-122, ISSN 0031-5117.
- Zanobetti, A. & Schwartz, J. (2006). Air pollution and emergency admissions in Boston, MA. *Journal of Epidemiology and Community Health*, Vol.60, No.10, pp. 890-895, ISSN 0143-005X.
- Zibrowski, E.M. & Robertson, J.M. (2006). Olfactory sensitivity in medical laboratory workers occupationally exposed to organic solvent mixtures. *Occupational Medicine (Lond)*, Vol.56, No.1, pp.51-54, ISSN 0962-7480.



Advanced Topics in Environmental Health and Air Pollution Case Studies

Edited by Prof. Anca Moldoveanu

ISBN 978-953-307-525-9

Hard cover, 470 pages

Publisher InTech

Published online 29, August, 2011

Published in print edition August, 2011

The book describes the effects of air pollutants, from the indoor and outdoor spaces, on the human physiology. Air pollutants can influence inflammation biomarkers, can influence the pathogenesis of chronic cough, can influence reactive oxygen species (ROS) and can induce autonomic nervous system interactions that modulate cardiac oxidative stress and cardiac electrophysiological changes, can participate in the onset and exacerbation of upper respiratory and cardio-vascular diseases, can lead to the exacerbation of asthma and allergic diseases. The book also presents how the urban environment can influence and modify the impact of various pollutants on human health.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Marco Guarneros, René Drucker-Cofin, José Esquivelzeta and Robyn Hudson (2011). Adverse Effect of Air Pollution on Odor Perception, Advanced Topics in Environmental Health and Air Pollution Case Studies, Prof. Anca Moldoveanu (Ed.), ISBN: 978-953-307-525-9, InTech, Available from:
<http://www.intechopen.com/books/advanced-topics-in-environmental-health-and-air-pollution-case-studies/adverse-effect-of-air-pollution-on-odor-perception>

INTech
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike-3.0 License](https://creativecommons.org/licenses/by-nc-sa/3.0/), which permits use, distribution and reproduction for non-commercial purposes, provided the original is properly cited and derivative works building on this content are distributed under the same license.

IntechOpen

IntechOpen