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Exposure to nitrosamines in thirdhand tobacco smoke increases cancer risk in non-smokers

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ABSTRACT

In addition to passive inhalation, non-smokers, and especially children, are exposed to residual tobacco smoke gases and particles that are deposited to surfaces and dust, known as thirdhand smoke (THS). However, until now the potential cancer risks of this pathway of exposure have been highly uncertain and not considered in public health policy. In this study, we estimate for the first time the potential cancer risk by age group through non-dietary ingestion and dermal exposure to carcinogen N-nitrosamines and tobacco-specific nitrosamines (TSNAs) measured in house dust samples. Using a highly sensitive and selective analytical approach we have determined the presence of nicotine, eight N-nitrosamines and five tobacco-specific nitrosamines in forty-six settled dust samples from homes occupied by both smokers and non-smokers. Using observations of house dust composition, we have estimated the cancer risk by applying the most recent official toxicological information. Calculated cancer risks through exposure to the observed levels of TSNAs at an early life stage (1 to 6 years old) exceeded the upper-bound risk recommended by the USEPA in 77% of smokers' and 64% of non-smokers' homes. The maximum risk from exposure to all nitrosamines measured in a smoker occupied home was one excess cancer case per one thousand population exposed.

The results presented here highlight the potentially severe long-term consequences of THS exposure, particularly to children, and give strong evidence of its potential health risk and, therefore, they should be considered when developing future environmental and health policies.

1. Introduction

Each year 600,000 people die worldwide from exposure to environmental tobacco smoke (Oberg et al., 2011), also called second hand smoke (SHS). As numerous countries have introduced smoking bans in public places (WHO, 2010), domestic environments have become the main sources of passive smoking exposure (WHO, 2007). However, the risks of tobacco exposure do not end when a cigarette is extinguished and non-smokers, especially children, are also at risk through contact with surfaces and dust contaminated with residual smoke gases and particles, the so-called third hand smoke (THS) (Matt et al., 2004; Matt et al., 2011a). Over 40% of children have at least one smoking parent (Oberg et al., 2011) and numerous studies have demonstrated the association between prenatal and early stage childhood diseases and the smoking habits of their parents (Cook and Strachan, 1999). Although there is a general public awareness about the harms of SHS, the general public are more sceptical about THS, with a study in 2009 finding that 62.5% of non-smokers and 43% of smokers agreed that THS harms children (Winickoff et al., 2009). A study of parents' attitudes found that fathers and heavy smokers (>10 cigarettes per day) were less likely to believe that THS was harmful (Drehmer et al., 2012). The specific role of THS in tobacco-related illnesses has been questioned by the public health community (Matt et al., 2011a), however, a recent study demonstrated that chemical species associated with THS are genotoxic in human cell lines (Hang et al., 2013). Evidence of the chemical toxicity of THS is necessary to improve understanding of the risks of THS-polluted environments and to design educational strategies for families and the general public to allow them to make more informed decisions.

Nicotine is the most abundant organic compound emitted during smoking (IARC, 2004) and is considered a good marker of tobacco exposure. After cigarette smoking, nicotine deposits almost entirely on indoor surfaces, where it can be released again to the gas phase or react with ozone, nitrous acid and other atmospheric oxidants producing secondary pollutants, such as tobacco-specific nitrosamines (TSNAs) (Sleiman et al., 2010). Fig. 1 shows the structures and reaction pathways of formation of the main TSNAs. Of the TSNAs identified, N′-

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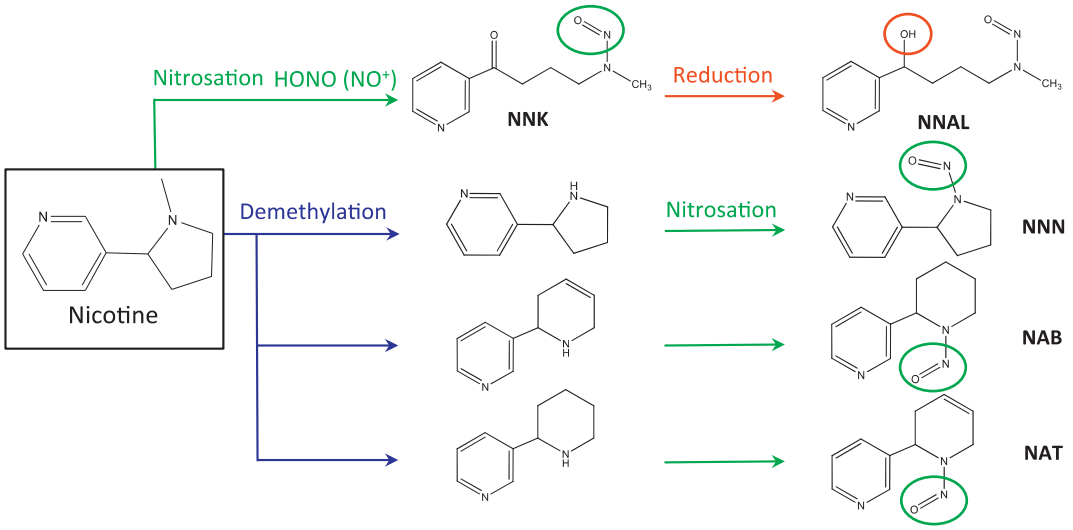

Fig. 1. Structures and formation pathways of the main tobacco specific N-nitrosamines (TSNAs).

nitrosonornicotine (NNN) and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK) are the most prevalent and most active carcinogens in tobacco products (Hecht, 2003; Hecht and Hoffmann, 1988), inducing tumours in the lung, liver, nasal cavities, oesophagus and exocrine pancreas, and are classified as carcinogenic for humans (Group 1 International Agency for Research on Cancer, IARC) (IARC, 2007). Whilst some TSNAs can be directly produced during tobacco smoking, several studies have suggested that airborne NNK concentrations in sidestream cigarette smoke can increase by 50–200% per hour during the first 6 h after cigarettes are extinguished (Schick and Glantz, 2007). Moreover, NNK can further degrade and its main metabolite, 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol (NNAL), is considered to have similar adverse health effects (Hecht, 2008).

Given the low volatility of TSNAs and the high levels of nicotine typically found in environments contaminated with tobacco, TSNAs can persist for weeks to months in THS. Several studies have detected nicotine in indoor dust and surfaces (Kim et al., 2008; Matt et al., 2011a) and recent studies have demonstrated a correlation between the number of cigarettes smoked and the presence of nicotine and polycyclic aromatic hydrocarbons (PAHs) (Hoh et al., 2012) in settled house dust. The health risk from THS will be substantially controlled however by the prevailing levels of TSNAs. Whilst these species have been seen directly in tobacco smoke (Mahanama and Daisey, 1996), there has been no measurement of their presence in THS.

Here we report the detailed determination of nicotine and five TSNAs (indicative of a tobacco smoking source) and eight non-specific volatile N-nitrosamines (commonly released during tobacco smoking, but likely to have additional environmental sources), in settled house dust samples from homes occupied by smoking or non-smoking occupants. The complete list of these target compounds is shown in Table 1. We have calculated the cancer risk related to exposure to observed concentrations of the carcinogen N-nitrosamines and TSNAs through non-dietary ingestion and dermal exposure by age group. For the first time, we use ambient observations to constrain risk assessment estimations of exposure to these carcinogens in THS, based on real-world measurements.

2. Material and methods

2.1. Sample collection and preparation

A total of 46 house dust samples were collected from private homes, using conventional vacuum cleaners in regular use in households between October 2011 and May 2012 in the area of Tarragona (north-eastern Spain). We have selected those samples whose residents have lived in their current home for at least one year. A questionnaire was designed to collect information about the house and any activity that might affect chemical loading (see Supplementary Material, Table S1). A summary of the collected information can be found in Table 2. Most of the samples were from flats in urban areas with low to moderate traffic intensity (up to 14,041 vehicles per day, Spanish Ministry of Public Works, personal communication). Around half (48%) of the samples were characterised as from smokers' homes, where at least one occupant was a tobacco smoker, including those whose occupants do not smoke inside the home. The mean number of cigarettes smoked per day in this group was 17 including cigarettes smoked both inside the home and at other locations outside the homes. The remainder of the samples (52%) were classified as non-smokers' homes, according to the survey information. See Table 2 for other relevant characteristics of the homes included in this study.

The collected dust was sieved with an acetone washed stainless steel sieve and the fraction under 100 μm was stored in glass vials, preserved from light and kept at 4 °C until analysis.

Table 1
IARC classification and oral slope factors of target compounds included in our study, and the source of this information.

Nitrosamine	IARC classification[a]	Oral slope factor
N-nitrosodimethylamine (NDMA)	2A	51[b]
N-nitrosomethylethylamine (NMEA)	2B	22[b]
N-nitrosodiethylamine (NDEA)	2A	150[b]
N-nitrosodi-n-propylamine (NDPA)	2B	7[b]
N-nitrosomorpholine (NMor)	2B	6.7
N-nitrosopyrrolidine (NPyr)	2B	2.1[b]
N-nitrosopiperidine (NPip)	2B	9.4[c]
N-nitrosodi-n-butylamine (NDBA)	2B	5.4[b]
Nicotine	–	–
N′-nitrosonornicotine (NNN)	1	1.4[c]
N′-nitrosoanatabine (NAT)	3	–
N′-nitrosoanabasine (NAB)	3	–
4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK)	1	49[c]
4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanol (NNAL)	–	–

[a] IARC classifications: group 1, carcinogen to humans; group 2A, possible carcinogen to humans; group 2B, probably carcinogen to humans; group 3, not classifiable as to its carcinogenicity to humans (IARC, 2013).
[b] Data from IRIS (2013).
[c] Data from OEHHA (2007).