Human mercury exposure levels and fish consumption at the French Riviera

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Abstract

Humans are exposed to methylmercury (MeHg), a bioaccumulative neurotoxin, mainly through the consumption of marine fish. Several studies showed that high MeHg exposure can lead to neurological damage. This is particularly relevant for pregnant women, because MeHg exposure negatively impacts foetal development. Populations living near the sea are generally at increased exposure risk due to higher consumption of fish and seafood. Here, we present the first study of MeHg exposure levels of the population living at the French Riviera, using mercury (Hg) concentrations in hair as a proxy for MeHg exposure. We found that older people that consume more fish presented the highest hair Hg concentrations. Compared to other Mediterranean bordering countries and other European countries, the southern France population is among those with high MeHg exposure (median for women of childbearing age is 0.56 µg g^{-1}). A global implementation of the Minamata Convention is necessary to lower MeHg exposure of the population.

Key words: *hair, methylmercury, Southern France*

1. Introduction

Methylmercury (MeHg) is a bioaccumulative neurotoxin, which is more toxic than inorganic mercury (NRC/NAS, 2000). It has been consistently observed that MeHg is biomagnifying to harmful levels along the marine food webs with increasingly greater MeHg proportion (close to 100%) in top-predators (Lavoie et al., 2013, Chen et al., 2018, Ourgaud et al., 2018).

Humans are exposed to MeHg mainly through their diet, especially through the consumption of fish and other products from aquatic environment (Schoeman et al., 2009, Castaño et al., 2015, Pérez et al., 2019, Sunderland et al., 2018). There is a global trend of increased fish consumption, which may increase the human risk of exposure to trace elements, including Hg (FAO, 2016). Worldwide, annual per capita fish consumption grew from 9.9 to over 20 kg between 1960 and 2015, respectively (FAO, 2016). In France, the consumption of fish is high (annual per capita fish consumption ranges from 30 to 60 kg, FAO, 2012, Vieira et al., 2015) and seafood has always been an important part of the Mediterranean population diet (Castaño et al., 2015; Faget, 2009; Metro et al., 2017).

The neurotoxicity of MeHg was first described for the Minamata incident, in Japan, in 1956 (Kurland et al., 1960). High-level human MeHg exposure after release of MeHg from a chemical factory led to fatalities and devastating neurological damage in Minamata (Harada, 1995). Particularly, foetuses are considered much more sensitive to MeHg exposure (NRC/NAS, 2000).

Consumption of fish contaminated with MeHg by pregnant women has resulted in serious damage of the central nervous system such as mental retardation, cerebral palsy, blindness and deafness (NRC/NAS, 2000). Since 1970, several large-scale epidemiological studies showed that even low-level chronic MeHg exposure by pregnant women leads to poor neurodevelopment of children (decreasing of fine motor-adaptive function, reduction in IQ, attention deficit disorder) later in life (Kjellstrom et al., 1986, Julshamn et al., 1987, Myers et al., 2003, Deroma et al., 2013). Several studies suggested that MeHg exposure by adults may be associated with an increased risk of cardiovascular deseases, such as hypertension and myocardial infarction (Guallar et al., 2002, Kim et al., 2014). Despite the risks of MeHg exposure, fish consumption has many benefits and should not be avoided altogether from human diets (Egeland and Middaugh, 1997, Salvo et al., 2016, Cammilleri et al., 2017, Metro et al, 2017). Fish is a valuable source of proteins, vitamin D, selenium, and other essential elements (Fox et al., 2004, Holden et al., 2008, Roos et al., 2007). Fish provide significant amounts of polyunsaturated fatty acids, which prevent cardiovascular diseases (Simopoulos, 2008, Mozaffarian and Wu, 2011). Thus it is important to balance the risks and benefits of fish consumption (Sonke et al., 2013).

Several countries and international organisations have established a reference MeHg dose estimated to be safe or without appreciable risk to health (Tab. 1). Generally, all organisations advise pregnant women, women of childbearing age and young children to limit their consumption of fish known to have high levels of Hg (high trophic level fish such as tuna, shark, swordfish) to 1-2 per week. Since October 2013, the Minamata Convention under the auspices of the United Nations Environment Program (UNEP), a global action to protect human health and environment from anthropogenic and mercury emissions, was signed (#Web1). The Minamata Convention is implemented through the control of specific human activities that contribute to widespread Hg pollution. The majority of the European countries ratified the Minamata Convention, while others countries, especially from Northern Africa, were not yet parties to the convention (#Web1).

Mercury (Hg) concentrations in hair, urine, tissue, toenails and blood have been widely used as biomarkers for human MeHg exposure (for example, WHO, 2008, Shao et al., 2013, Bonsignore et al., 2015). About 95% of MeHg in fish ingested by humans is absorbed in the human gut (Aberg et al., 1969, Miettinen et al., 1971). After absorption into the bloodstream, MeHg enters the red blood cells and it is distributed throughout the body within hours (Aberg et al., 1969, Clarkson, 1997). Hair incorporates MeHg present in circulating blood during hair formation in the hair follicule (Clarkson et al., 1983). Approximately 95% of measurable Hg in the blood is in methylated form (Sherlock et al., 1984), making MeHg also the dominant species in hair (80%, Cernichiari et al., 1995, Phelps et al., 1980). There are several advantages of using hair: it is non-invasive, samples are easier to obtain without medical support, to transport and store. Despite all advantages, hair analysis is suspected of having several limitations, such as: inter-individual variability in the pharmacokinetics of Hg uptake from blood to hair shaft (NRC/NAS, 2000); inter- and intra-individual variability in hair growth rate, density, colour, and waving (Sakamoto et al., 2004, Ohba et al., 2008); external contamination in the areas where ambient air Hg concentrations are elevated.

A correlation between consumption of fish or marine products and Hg levels in hair is typically observed (*e.g.,* Castaño et al., 2015, Den Hond et al., 2015). With the funding of the Consortium to Perform Human Biomonitoring on a European Scale (COPHES) and its demonstration project DEMOCOPHES (DEMOnstration of a study to COordinate and Perform Human biomonitoring on a European Scale) 17 European countries provided the baseline information on selected contaminants levels including Hg (Den Hond et al., 2015). However, France did not participate in this project. Thus, the aim of the present study was to provide a first baseline information on the Hg concentrations in human hair at the French Riviera and to complete the European assessment. The main investigations addressed are: (i) the influence of age, gender and fish consumption on Hg concentrations; (ii) a comparison of hair Hg concentrations for women of childbearing age (19 – 45 years old) in French Atlantic *vs* Mediterranean coastal areas; (iii) a comparison of Hg concentrations in hair of women of childbearing age and annual per capita fish consumption along Mediterranean and some European countries (depending if a country is party of the Minamata Convention or not); and (iv) we used this assessment to illustrate the mismatch between the MeHg exposure and a lack of commitment or political interest to sign and implement the Minamata Convention.

2. Materials and methods

2.1. Sampling design

We organized a public awareness campaign: “Arctic Mediterranean Mercury - AM^2” for societal Hg exposure in September 2017 (Fig. 3b). During the outreach events we informed the participants about Hg in the environment and exposure. The participants were then given the opportunity to join our study, and to be informed about their individual MeHg exposure level. A total 404 volunteers along the French Mediterranean coastline between Marseille and Villefranche-sur-Mer joined the study (58 % female and 42 % male with ages from 1 to 84 years old). No effort was made in selecting the volunteers according to age, gender, diet, etc.

2.2. Data collection

Hair samples were collected according to the Standard Operation Procedure (SOP) established within the framework of COPHES/DEMOCOPHES (Esteban et al., 2015). Briefly, hair strands (~10 – 30 mm) from each volunteers were collected from the nape of the neck, close to the occipital region of the scalp using titanium scissors, wearing powder free single use nitrile gloves. The grey hairs were not removed for the adult group (Pozebon et al., 2017). Given that hair is a stable material, samples were placed into polyethylene bags until chemical analysis (Pozebon et al., 2017).

A standard questionnaire was used to collect data on the age ("Adults": >18 years old and "Child": ≤ 18 years old), gender ("Female", "Male") and frequency of fish consumption (‘Almost never’: ≤ 0.5 fish meals per week, "Once": 1 meal per week, "Twice": 2 meals per week, and ‘Often’ ≥ 3 meals per week). We also subdivided all participants in smaller age groups (1 – 10; 11 – 18; 19 – 24; 25 – 29; 30 – 39; 40 – 49, ≥ 50 years old) to compare with Shao et al. (2013). Volunteers gave their consent to participate to the study.

2.3. **Chemical analysis**

Mercury measurements were performed on a Hg analyser (atomic adsorption spectrometer, a Leco-AMA 254). A subsample of approximately 0.03 – 0.05 g of hair was loaded in nickel boats and placed inside a combustion tube, where the subsample was thermally decomposed (~750ºC) into a gaseous form. The evolved gases were then cleaned up from all interfering gases passing through the catalytic compounds. Mercury vapour was then transported to the amalgamator, where all Hg was trapped by gold-plated ceramics. The amalgamator was heated to ~900ºC essentially releasing all Hg vapour to the detection system of the atomic absorption spectrometer.

The method’s detection limit, estimated as three times the standard deviation of the blank samples, was 0.005 µg g^{-1}. The certified reference material (IAEA-086, human hair) was run several times per analytical batch and constantly before starting the measurements, to check the accuracy of the measurements. The measured values were on average, within ± 5% of the recommended values. Hair Hg concentrations are given on a fresh weight basis in μg g^{-1}.

2.4. Statistical analysis

Differences in hair Hg concentrations were tested with non-parametric tests (Shapiro-Wilk and Figner-Killeen tests indicated departures from normality and homogeneity of variances, respectively, except for gender). Independent 2-group Mann-Whitney U tests were used for age groups and gender. A Kruskal Wallis test One Way Anova by Ranks, followed by a Dunn's Multiple Comparisons test, was used to test for differences in hair Hg concentrations among fish consumption groups. P-values were adjusted with the Benjamini & Hochberg method for Multiple Comparisons (alpha = 0.05). Statistical analyses were performed in R version 3.5.0 (The R Foundation for Statistical Computing, 2018).

3. Results and discussion

A total of 404 hair samples from participants including children, women of childbearing and non-childbearing age and men have been analysed (Tab. 2). Hair Hg concentrations of participants ranged from 0.01 to 3.98 μg g^{-1} with a median of 0.51 μg g^{-1} (interquartile range 0.86 – 0.28 μg g^{-1}). Only one man and one woman of childbearing age exceeded the French ANSES level of 3.2 μg g^{-1}, while about 5% of women and 4% of men exceeded the US EPA level of 1.4 μg g^{-1}. None of the data exceeded the WHO level of 7 μg g^{-1}. There was no specific Hg contamination source such as gold mining, coal combustion and fluorescent light factories located around the study area, which should exclude elevation of hair Hg concentration through direct MeHg exposure. The measured hair Hg concentrations may be linked to age, gender or diet of the sampled population (Liu et al., 2008, Schoeman et al., 2009, Castaño et al., 2015, Sunderland et al., 2018).

3.1. Influence of age and gender on Hg concentration

Mean Hg concentrations increased significantly with age (Fig. 1). The highest mean concentrations of hair Hg (0.91 ± 0.62 and 0.88 ± 0.66 μg g^{-1}) were observed in the 40 – 49 and ≥ 50 age groups, respectively; the lowest hair Hg concentrations were found on the 11 – 18 age group (0.36 ± 0.34 μg g^{-1}). Adult group samples (>18 years old) had significantly higher hair Hg concentration than child group samples (≤ 18 years old) (W = 28691, P-value < 2.2e-16). It seems apparent that the body burden of Hg increased with age due to regular accumulation. A similar increase with age was observed by Liu et al. (2008), who determined that the hair Hg of a local population in Southern China increased between their twenties and forties. Shao et al. (2013) also showed increasing of mean Hg concentration for Chinese people living at the coast of up to 49 years of age. Moreover, Liu et al. (2008) and Shao et al. (2013) also noted a gradual decreasing of Hg concentrations in people > 50 years old, suggesting zero Hg content in the grey hair, which resulted from the role of sulphur-containing chemicals in the formation of hair pigment (Bou-Olayan and Al-Yakoob, 1994; Al-Majed et al., 2000). Unlike Wakisaka et al. (1990), no significant difference in Hg concentrations in hair samples between men and women was observed (W = 21429, P-value = 0.01937).

3.2. Fish consumption rate and Hg concentrations

The lowest mean hair Hg concentration (0.42 ± 0.45 μg g^{-1}, range: 0.02 – 1.41 μg g^{-1}) was observed on participants which ‘Almost never’ consume fish, corresponding to 23% of the study participants, intermediate (0.59 ± 0.42 and 0.87 ± 0.66 μg g^{-1}) concentrations were measured on participants eating fish meals ‘Once’ (46% of participants) and ‘Twice’ (22%) per week, respectively. The highest mean hair Hg concentration (1.32 ± 0.89 μg g^{-1}) was measured for participants that ‘Often’ eat fish (9%; Fig. 2a). Hair Hg concentrations were significantly different among all fish consumption groups (Kruskal-Wallis chi-squared = 73.169, df = 3, P-value = 8.941e-16; multiple comparisons P-values between 1.49e-3 to 1.34e-13).

Previous studies reported that fish consumption rates affect Hg concentrations in human hair. For example, significantly higher Hg concentrations were found for people living in coastal areas from Sicily and China, who often eat fish (4-7 times per week), compared to those who eat fish less frequently (1 – 2 times per week; Giangrosso et al., 2015, Shao et al., 2013). Miklavčič et al., 2014, also noted that the highest exposure levels to Hg were found in coastal populations of Europe, which consume more fish than inland populations.

Despite a statistically significant difference between hair Hg concentration for children and adults overall (W = 28691, P-value < 2.2e-16), such a difference was not evident between children and adults who consume fish with the same frequency (Fig. 2b). Mean Hg concentrations for children and adults who consume fish ‘Almost never’ and ‘Once’ were equivalent, while for a weekly consumption of ‘Twice’ and ‘Often’, mean Hg concentrations were lower for children. Such a variation of individual mean Hg concentration has been observed even within families, where children and their mothers with the same fish consumption rate showed different Hg concentrations in hair (Den Hond, 2015). Children are generally characterized by lower Hg concentrations than their mothers, however, Castaño et al. (2015) showed that there is strong correlation between the mother and child in the same family. We are aware that questionnaire answers about individual fish consumption rates do not reflect a precise estimation but rather a "best guess", especially for children. Our broader fish consumption categories were chosen to incorporate some of those uncertainties.

4. Regional (and coastal) variations in hair Hg concentration and fish consumption in Europe

Mean Hg concentration in hair for women of childbearing age in the French Mediterranean coast was slightly lower (geometric mean 0.52 $\mu g\ g^{-1}$) than in the

French Atlantic coast (Brittany and Nantes, geometric mean 0.62 and 0.67 μg g^{-1}, respectively, Pichery et al., 2012). Previous studies have shown that fish from Mediterranean waters show higher Hg levels than Atlantic fish. For example, bluefin tuna (*Thunnus Thynnus*), which is commonly found in the Mediterranean Sea, was reported to be nearly five times as much concentrated in Hg compared with yellowfin tuna (*Thunnus albacares*), which is absent in Mediterranean Sea (Cammilleri et al., 2018). Significant higher Hg concentrations in Mediterranean fish might lead to higher MeHg exposure by population. Comparison of hair Hg concentrations of the Mediterranean and Atlantic coasts is not obvious in this study due to the absence of quantitative data about fish consumption by populations in the French Atlantic coast.

Geometric mean Hg levels in hair for women of childbearing age in the French Mediterranean coast ('Once' per week - 0.62 μg g^{-1}, and 'Often' - 1.91 μg g^{-1}) were higher than for women of childbearing age with similar fish consumption rates sampled inland (Toulouse, South-West of France; 0.44 μg g^{-1} and 1.32 μg g^{-1}, respectively; Sonke et al., 2013). The French Mediterranean coast compared to inland Toulouse may be related to higher fish consumption from the Mediterranean Sea (Vieira et al., 2015; Faget, 2009), but we cannot draw any conclusion based on our study.

There is a widespread difference in MeHg exposure in the European population and the difference is very likely related to consumption of fish and other products from marine environment (Fig. 3a, right panel). Comparing with other contries along the Mediterranean Sea, we found that the Southern France hair Hg concentrations were similar to Hg concentrations found in Italy, Croatia and Albania, but lower than in Spain, Morocco and Greece (Fig. 3c; Miklavčič et al., 2013, Babi et al., 1999, Den Hond et al., 2015, Elhamri et al., 2007, Pérez et al., 2019). According to the European Market Observatory for fisheries and aquaculture products (2017), the annual fish consumption in France is about 34 kg per capita, while it is about 45 kg in Spain. Annual fish consumption in Greece and Morocco is much lower than in France, 17.3 kg and 12.5 kg per capita, respectively. Higher MeHg exposure by Greek and Moroccan populations could be explained by Hg contamination of local fishes. For example, Elhamri et al. (2007) found up to 1.2 µg g^{-1} of Hg in hair for women of childbearing age in the Tetouan province, Morocco. This was related to Hg release into the environment from several chloralkali plants which used Hg cell technology. The released Hg contributed to contamination of local fishes and lead to higher MeHg exposure for local populations, including in women of childbearing age.

To our knowledge, there is no published data of MeHg exposure levels for African Mediterranean countries, except Morocco (Elhamri et al., 2007) and Egypt (El-baz et al., 2009). These countries do not present high fish consumption rates but we found that there are potential health risks connected with the release of industrial Hg to the environment. For example, the Mercurial Complex of Azzaba, in Algeria, was an area of very active Hg mining until

2005 (200-500 t y^{-1}; Hylander and Meili, 2003). This site alone accounts for 1 million tons of Hg waste (Ministry of land planning, environment and the city, Algeria, 2012). Moreover, the cement industry potentially remains an important source for Hg emissions in Northern African countries (#Web2).

Our data showed that France exhibits greater Hg concentrations in hair for women of childbearing age than other European countries (Fig. 3c) with one exception for Portugal (where Hg concentrations are up to 1.2 µg g^{-1}, Den Hond et al.,2015). This trend is in accordance with the higher annual fish consumption per capita in Portugal (56 kg; European Market Observatory for fisheries and aquaculture products, 2017).

We noted that the highest hair Hg concentrations (related to high MeHg exposure) were found along the Mediterranean Sea on countries that are not parties to the Minamata Convention (Fig. 3c). For instance, Spain, which has among the highest annual fish consumption per capita of 45.2 kg, and the highest Hg hair concentration in this study of 1.49 µg g^{-1} (Den Hond et al., 2015), and Greece, with and annual fish consumption of 17.3 kg per capita and Hg level of 1.20 µg g^{-1} (Miklavčič et al., 2013), signed the convention on 10 October 2013 but did not ratify it. We also noted the lack of data on MeHg exposure levels for Northern African and Middle East countries surrounding the Mediterranean Sea. Taking in account that most of these countries did not ratify the Minamata Convention (Fig. 3c), we propose further research of MeHg exposure for Northern African and Middle East countries.

We hypothesize that populations of non-party countries are not informed about the potential health risks of MeHg exposure. Moreover, published data (Elhamri et al., 2007, Miklavčič et al., 2013) showed that, relatively to the Minamata Convention, non-party countries have elevated MeHg exposure even if they have a low annual fish consumption (*i.e.*, Greece and Morocco). In this case, high MeHg exposure may be explained by Hg industrial contamination of local or imported fishes. Non-party countries are characterized by relatively significant Hg emissions to the atmosphere, according to the Data Visualisation on Global Mercury Emissions by Country and Sector, (2018). For example, Greece accounts for more than 6.5 Ton y^{-1}, which is 1.5 Ton y^{-1} higher than Hg emissions in France (Fig. 3a, left panel). The implementation of the Minamata Convention can benefit party nations in terms of human health and the environment, by banning Hg from industrial processes, using the best available Hg emission-control technologies and wastewater treatment in new plants.

The implementation of the Minamata Convention may lead to some economic losses if we consider the transfer from Hg-based to less efficient or costlier industrial applications. For some of the more industrialized European countries, the impact may be more important. For instance, most of Germany’s energy demand is supplied by coal-fired power plants, which have now to be modernized to meet the standards according to the Minamata Convention (UNEP GMA, 2018). However, Germany did implement the Minamata Convention early on, since 15 September 2017. Surprisingly, some of the countries with low anthropogenic Hg emissions (lower than 1 Ton y^{-1}, *e.g.*, Albania and Cyprus, Fig. 3a) are not yet a party the Minimata Convention. The adoption of the Minamata Convention for these countries would have little impact on industry and largely be outweighed by the health benefits and associated economics gains. Pichery et al. (2012) highlighted that prenatal MeHg exposure has serious impacts on the life-time productivity and on society due to adverse cognitive and associated economic consequences.

5. Conclusion

Humans are mainly exposed to MeHg when consuming marine fish, in simple words: the more and the bigger fish we eat the more MeHg we take up. In France, in Europe and in most Western countries, protection guidelines have been developed following the Minamata Convention. However, protection guidelines are often too technical, and people tend to either avoid fish completely, at the risk of a polyunsaturated fatty acid-deficiency, or simply not respect them, at the risk of an elevated MeHg exposure.

We examined MeHg exposure of people from the French Mediterranean coast, based on Hg concentrations in their hair. We showed that older people that consumed more fish presented higher hair Hg concentrations. We highlighted that very few study participants presented values above the French reference dose and none above the WHO reference dose. Comparison with Mediterranean bordering and European countries showed that the southern France population is among those with higher MeHg exposure.

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