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Mercury concentration and fatty acid composition in muscle tissue of marine fish species harvested from Liaodong Gulf: An intelligence quotient and coronary heart disease risk assessment

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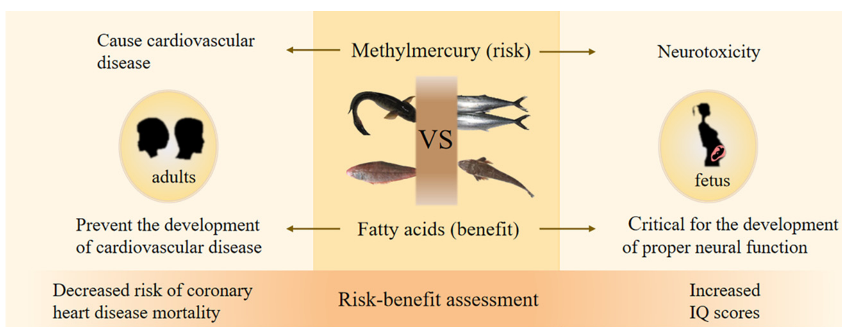
HIGHLIGHTS

- There are no differences in fatty acid concentrations among different years, nor in mercury concentrations.
- The ratio of methylmercury to total mercury is normally distributed.
- The proportion of polyunsaturated fatty acids in marine fish is not affected by dietary habits.
- Marine fish is recommended for consumption, such as Ditrema temmincki Bleeker, etc.

GRAPHICAL ABSTRACT



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ABSTRACT

Marine fish species are an important source of biologically valuable proteins, fats, fat-soluble vitamins, and n-3 polyunsaturated fatty acids, but they are also susceptible to pollutants. Mercury is liable to bioamplify in the aquatic food chain, and the health risks posed by methylmercury (MeHg) could undermine the benefits of eating fish, so risk-benefit assessments are needed for those fish species regularly consumed. The purpose of this study was to analyze the concentrations of mercury and characteristics of fatty acids in marine fish harvested from Liaodong Gulf, China, so as to better understand the risk-benefit effects of marine fish consumption. We found that the ratio of MeHg to total Hg (THg) was normally distributed. The concentrations of THg and MeHg in marine fish muscles (14 species, a total of 239) ranged from 0.920 to 0.288 μg/g and 0.050 to 0.192 μg/g, respectively. There were no significant interannual differences in the muscles' concentrations of MeHg and THg, or of their fatty acids ($p > 0.05$). The proportion of total saturated fatty acids (SFAs) and monounsaturated fatty acids (MUFAs) varied significantly among different marine fish-feeding habits (predacious, omnivorous, benthivorous and planktivorous), but the differences between polyunsaturated fatty acids (PUFAs) were not significant, which

Abbreviations: MeHg, methylmercury; THg, total mercury; SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; n-3 PUFAs, omega-3 polyunsaturated fatty acids; IQ, intelligence quotient; POPs, persistent organic pollutants; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; CHD, coronary heart disease; JECFA, Joint United Nations FAO/WHO Expert Committee on Food Additives; PTWI, provisional tolerable weekly intake; HQ, hazard quotient; DI, dose index; RBI, risk-benefit index; CVAFS, cold vapor atomic fluorescence spectrometer; GC, gas chromatography; FAME, fatty acid methyl esters; BHT, butylated hydroxytoluene; FAs, fatty acids; w.w., wet weight; d.w., dry weight.

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Chinese population

may be due to the undistinguished fatty acids ($p < 0.05$). The risk-benefit assessment using the intelligence quotient (IQ) scoring model revealed that all the studied marine fish had positive effects on child IQ under different consumption scenarios. Additionally, the integrated risk-benefit analysis for adult cardiovascular health showed that all the studied marine fish, but especially *Ditrema temmincki Bleeker*, are capable of reducing the relative cardiovascular risk posed by the MeHg in the fish. We conclude the positive effects of eating common marine fish from the Liaodong Gulf far outweigh their negative ones.

1. Introduction

In recent decades, China's coastal water environment has become severely polluted by human activities (State Oceanic Administration, China, 2015, 2016; Tong et al., 2017). Perhaps linked to this, are inevitable environmental pollutants in marine fish muscles, such as toxic heavy metals (mercury, arsenic, lead, and cadmium) (Liu et al., 2015) and persistent organic pollutants (POPs) (Hao et al., 2015). Mercury, in particular, may pose certain risks to the health of fish consumers (Wang et al., 2019), and methylmercury (MeHg) is more likely to accumulate in aquatic organisms when compared with inorganic mercury. Concentrations of MeHg increase with the age, length, and weight of aquatic organisms, and the higher the trophic level, the higher the mercury content (Laird et al., 2018). It is generally accepted that the consumption of mercury-contaminated fish is the main route of human exposure to mercury, aside from occupational mercury exposure, since MeHg can be easily absorbed into the blood from the human gastrointestinal tract (Kershaw et al., 1980; Zaza et al., 2015); hence, fish intake may pose human health risks associated with the MeHg exposure involved. MeHg is a potent neurotoxin that adversely affects the development of the brain and nervous system. It can pass through the plasma membrane, as well as through the blood-brain barrier and placenta, with studies showing that exposure to low doses of mercury in fetuses, infants, and children is associated with developmental delays, learning disabilities, and possible behavioral problems (Vejrup et al., 2018). Similarly, elevated levels of MeHg in humans' diet can increase the risk of incurring adverse health effects upon their nervous system, cardiovascular, and immune systems as adults (McSorley et al., 2018; Moreira et al., 2012).

Yet fish is also rich in high-quality protein and essential amino acids, fat-soluble vitamins, omega-3 polyunsaturated fatty acids (n-3 PUFAs), and other essential nutrients, so the consumption of fish is generally deemed good for human health (Domingo, 2016; Miklavčič et al., 2011). In particular, the n-3 PUFAs, such as docosahexaenoic acid (22:6, n-3, DHA), eicosapentaenoic acid (20:5, n-3, EPA), play a critical role in preventing the development of heart and circulatory diseases (Kris-Etherton et al., 2002). Studies have shown that the consumption of fish or fish oil can reduce the mortality rate of patients with coronary heart disease (CHD) and also reduce the risk of stroke (Bouzan et al., 2005; Roth and Harris, 2010; Song et al., 2018). Furthermore, DHA is among the most important fatty acids for the normal development of the fetal brain (Cardoso et al., 2018). It is usually transferred from the placenta to the fetus during the last trimester of pregnancy, having a key impact on how the central nervous and visual systems of the fetus develop (Gao et al., 2014b; Koletzko et al., 2008). Recently, it was found that dietary supplementation with n-3 PUFAs during the third trimester of pregnancy could significantly reduce the burden of wheezing and asthma in offspring and lessen the absolute risk of lower respiratory infections (Bisgaard et al., 2016).

However, obtaining the benefits of fatty acids in consumed fish may be impaired by the presence of mercury in fish muscle tissue. Therefore, the risks associated with fish consumption should be accounted for when seeking to strike a balance between the nutrient availability provided by fish versus the risks of MeHg contained in those fish. The Joint United Nations FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake (PTWI) for MeHg, of 1.6 μg/kg bw (FAO/WHO, 2011). Several risk-benefit assessments of fish consumption in specific areas have been carried out using various models/formulas, such as the hazard quotient (HQ) and dose index (DI) (Strandberg et al., 2016; Wang et al., 2019), de minimus ratios (Laird et al., 2018), risk-benefit index equation (RBI) (Dellinger et al., 2018), and quality-adjusted life years (Cohen et al., 2005). Nevertheless, there are interspecific and intraspecific differences in the mercury and fatty acids content of fish, and mercury's concentration is also greatly influenced by geographical differences (Strandberg et al., 2016). For example, the mercury levels of wild marine fish exceeded those of wild freshwater fish, which in turn were higher than those of farmed freshwater fish (Zupo et al., 2019). A high consumption of fish (131.8 g/day) is a dietary characteristic of some coastal residents in China (Wang et al., 2019), who may thus incur higher exposure to mercury. Surprisingly, however, little information is available concerning the health risk assessment of such Chinese populations.

Liaodong Gulf is one of the three major bays of Bohai Sea in China, and is the highest dimensional sea area in China, once home to the famous Liaodong Gulf fishery. Next to Liaodong Gulf in the south is the city of Huludao, where the Huludao Zinc Plant and Jinxi Petroleum Chemical Factory have inputted substantial amounts of mercury into the Gulf waters via atmospheric sedimentation and river transportation (Zheng et al., 2011). Because the exchange of mercury between the Liaodong Gulf and the high seas is limited (Men and Liu, 2015), the aquatic ecosystem of Liaodong Gulf has rapidly degraded, losing its function as a viable fishery. Indeed, in recent years, both the production and quality of fisheries have generally become impaired, threatening their long-term sustainability (Gao et al., 2014a; Guo et al., 2016), and there is evidence that the mercury released into China's coastal waters can be ingested by fish consumers through the aquatic food chain (Tong et al., 2017).

In this context then, the primary objective of this study was to quantify total mercury (THg), MeHg, and fatty acids in different marine fish species harvested from the coast of Liaodong Gulf, China. For each species, their mercury distribution and fatty acids composition were also analyzed. Considering similar studies, most have relied on just one year of measured mercury levels. Here, mercury and fatty acids concentrations were measured continuously for three years to determine their interannual variation. Specifically, we hypothesized that the composition and proportion of fatty acids and mercury varied by species, but not the year. Finally, we calculated the health effects of MeHg and fatty acids in different marine fish of Liaodong Gulf, namely the net effect of maternal marine fish consumption on fetal neural development and the relative risk of marine fish consumption on adult CHD of the Chinese population, and provided dietary recommendations for human fish consumption. This study links fetus' intelligence quotient (IQ) points associated with maternal marine fish consumption to their mothers' relative risk of CHD mortality during pregnancy.

2. Methods

2.1. Fish sample collection

During 2015–2017, a total of 14 wild-caught marine fish species were purchased directly from Huludao fishermen, in Liaoning Province, Northern China. The main characteristics of each species, including their feeding habit, body length, weight, and the ratio of dry-to-wet weights, are shown in Table S1. All samples of marine fish were collected during the end of September and beginning of October in each of 2015, 2016, and 2017; due to the randomness of sampling, the five exceptions were *Pholis fangi* (*Enedras fangi*) and tongue sole (*Cynoglossus semilaevis*) specimens, which were collected only in 2015 and 2016, the moustached thryssa (*Thryssa mystax*) in 2017, the olive flounder (*Paralichthys olivaceus*) in 2016, and the magnetic fish (*Konosirus punctatus*) in 2015. Samples were frozen and transported to the laboratory for dissection, where corresponding details of each marine fish individual, including its species name, length, and weight, were recorded. The muscle (no skin) samples (ca. 20 g each) were dissected from the dorsal part of each fish, and their wet weight recorded, after which they were separately stored in tinfoil in a refrigerator at −80 °C. The dry weight was obtained to calculate the moisture content after freeze-drying each sample. Then the samples were ground into powder using an agate mortar and passed through a 60-mesh nylon sieve. Samples used for the determination of fatty acids had to be put in sample vials and stored at −20 °C until further testing.

2.2. Measurement of total Hg concentrations

The THg concentration of each marine fish sample was determined by using an acid digestion-cold vapor atomic fluorescence spectrometer (CVAFS) (Tekran 2500, Canada) (Yan et al., 2005a; Zhao et al., 2017). Approximately 0.1000–0.2000 g of each freeze-dried sample was weighed into 25-ml color-comparison tubes to which 5 ml of nitric (guarantee reagent) acid was added. Samples were digested in a water bath at 95 °C for 3 h, after which 0.5 ml of 30% bromine chloride was added to the cooled solution and shaken well. After ca. 24 h, 2–3 drops of $NH_2OH \cdot HCl$ were added to solution to fade the pale yellow, and the digests were diluted to 25 ml with deionized water. Finally, every sample was processed for its $SnCl_2$ reduction, gold trap, and CVAFS determination.

2.3. Measurement of MeHg concentrations

Approximately 0.1000–0.2000 g of each freeze-dried sample was weighed into Teflon digestion tank, with 5 ml of 25% saturated solution of KOH added. Then the samples were digested in a water bath at 95 °C for 3 h. After cooling, the digests were diluted to 25 ml with deionized water at 60 °C. The MeHg in each digest was measured by gas chromatography (GC)-CVAFS (Yan et al., 2005b).

The respective THg and MeHg contents of marine fish samples were determined by Tort-3 (NRCC, Canada), which served as the standard reference material, while the blank and parallel samples were made with 5% for quality control. The minimum detection limit of total mercury in fish samples, by CVAFS, is 0.013 $\mu g \cdot kg^{-1}$. The recommended THg content of the reference material was 292 ± 22 $ng \cdot g^{-1}$, whose average was 284.7 ± 26.36 $ng \cdot g^{-1}$, hence the recovery rate was 98%–102%. The recommended MeHg content of the reference material was 137 ± 12 $ng \cdot g^{-1}$ and its average was 142.4 ± 3.880 $ng \cdot g^{-1}$, for a recovery rate of 101%–106%.

2.4. Fatty acid analysis

Total lipids were extracted according to the method of Folch et al. (1957). Briefly, 2-g subsamples of freeze-dried samples were accurately weighed and soaked overnight at 4 °C in 45 ml of chloroform-methanol mixture solution (2:1, v/v; containing 35 mg/L of Butylated hydroxytoluene (BHT)). After passing the solution through filter paper, the filtrate was added to a ca. 13-ml NaCl solution (0.85%). After overnight stratification at 4 °C, the lower layer of the mixed solution was treated with evaporation under reduced pressure, and the lipid material obtained and weighed.

To prepare the fatty acid methyl esters (FAME), we followed the method described by Heissenberger et al. (2010). Briefly, the lipid extract was added to 1 ml of toluene and 2 ml of H_2SO_4-methanol (1%, v/v), which was vortex shaken and then stored at 50 °C for 16 h. Then, 2 ml of $KHCO_3$ (2%, v/v) and 5 ml of BHT (0.01%) were added, the solution shaken, and the CO_2 inside released. After centrifugation, the top layer was removed. Then, 5 ml of BHT was again added to the mixture, the solution centrifuged after releasing the CO_2, its top layer removed again, and the formed FAME dried under N_2 and re-dissolved in hexane. Finally, the FAME were analyzed with GC (Shimadzu 2010 Plus, Japan).

CDABB-CRM47885 was selected to serve as the fatty acid internal standard and 37 known FAME were used as reference materials. The fatty acids were qualitatively analyzed by comparing their retention times, with the undecanoic acid C11 (cdaa-256304, Shanghai Amps) used as the internal standard for this quantitative analysis. Both blank and 15% parallel samples were performed in tandem with the sample analysis, for which the standard deviation of the parallel samples was found to be within 10%.

2.5. Risk–benefit assessment of fish consumption

2.5.1. Calculation of changes in children's IQ points

To get a balanced understanding of the risks and benefits of eating different marine fish species, we used the IQ score model proposed by the FAO/WHO (FAO/WHO, 2011) to estimate changes in child IQ due to maternal marine fish consumption. In this study, however, the frequency of marine fish consumption was constant - that is, marine fish was consumed once per day - but the amount of fish consumed differed. According to the China Nutrition and Health Survey in 2002, the average daily consumption of fish of Chinese rural residents, city residents, and large-city residents was 23.7, 44.9, and 62.3 g/day, respectively (i.e., corresponding to ca. 165 g/week, 315 g/week, and 435 g/week) (Zhai and Yang, 2006), for which we assumed all the fish eaten are marine fish. Coastal residents appear to engage in a much higher consumption of fish than other people. Research showed that the average marine fish intake of local residents around the South China Sea was 131.8 g/day (i.e., ca. 920 g/week) (Wang et al., 2019). Those data values were applied in our study to represent different consumption scenarios.

The IQ point associated with DHA concentration was calculated this way:

$$\text{IQ point gain} = C_{DHA} \times s \times (x/7) \times 0.04 \qquad (1)$$

where C_{DHA} is the concentration of DHA (mg/g); s is the fish serving size (g/day); x is the number of servings of fish per week, fixed at 7, and; 0.04 is the coefficient of IQ points owing to the per mg of DHA intake per day. The maximum positive effect of DHA was estimated to occur at 5.8 points; when the calculated IQ point was >5.8, it was revised down to 5.8 according to FAO/WHO (2011).

The IQ point loss due to the concentration of MeHg was calculated as follows:

$$\text{IQ point loss} = C_{MeHg} \times s \times (x/7) \div BW \times 9.3 \times (-0.18 \,\text{or}\, -0.7) \qquad (2)$$

where C_{MeHg} is the MeHg concentration (μg/g); BW is the estimated maternal weight (60 kg); 9.3 is the correlation factor between maternal MeHg intake and the maternal hair Hg level in (μg/g); the −0.18 and −0.7 values are the central and upper-bound estimates of IQ point loss per μg/g of maternal hair Hg, respectively. The 0.7 was used here to obtain a more conservative result. So, the net IQ point gain from eating fish can be calculated as follows:

$$\text{Net IQ point gain} = \text{IQ point gain} + \text{IQ point loss} \qquad (3)$$

Combining Eqs. (1) and (2) gives the optimal weekly fish intake:

$$OWI = 5.8 \times 7/(C_{DHA} \times 0.04 - C_{MeHg} \times 0.1085) \qquad (4)$$

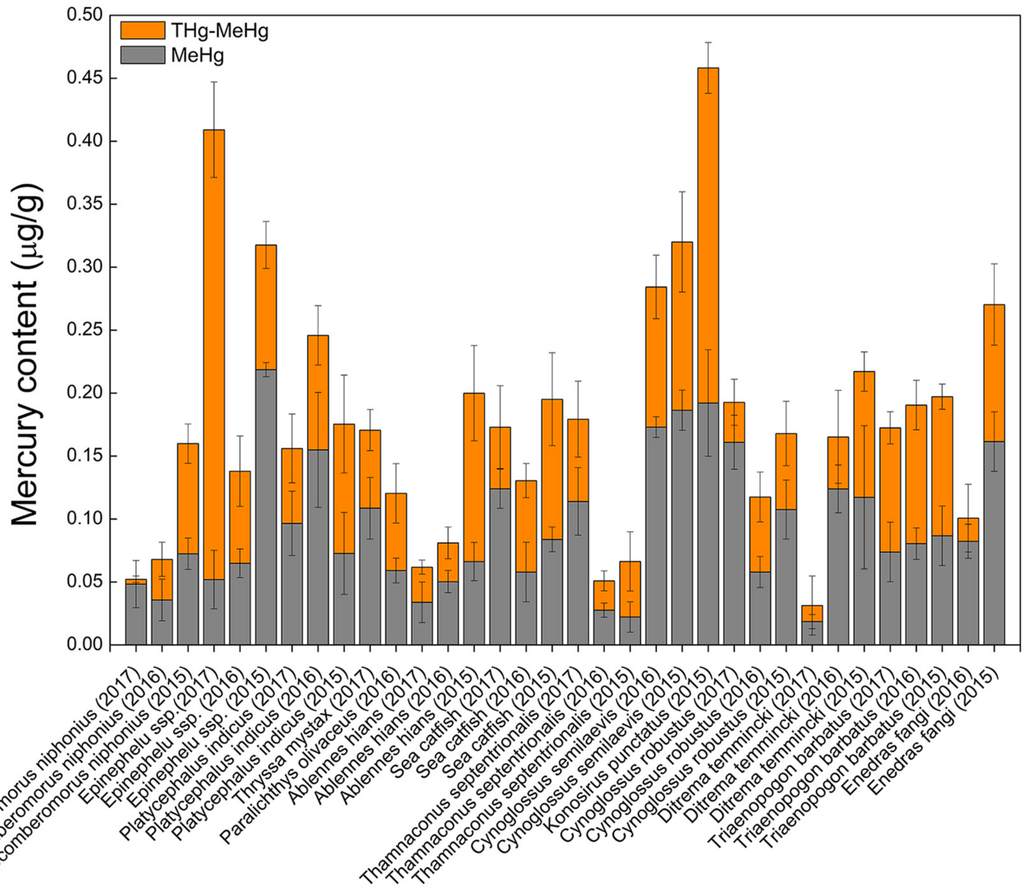

Fig. 1. The concentrations of MeHg and THg (measured in μg/g, d.w.) in marine fish harvested from Liaodong Gulf, China (2015, 2016, 2017). The error bars represent the standard deviation.

where OWI is the optimal weekly fish intake (g); the 5.8 is the maximum IQ point gain for an infant from maternal fish consumption.

2.5.2. Calculation of relative risk of CHD mortality

Ginsberg and Toal (2009) performed an integrated risk/benefit analysis for adults' cardiovascular endpoints on a species-specific basis that was supported by some earlier studies (Guallar et al., 2002; Mozaffarian and Rimm, 2006; Ohno et al., 2007). Mozaffarian and Rimm (2006) reported a 14.6% decrease in the relative risk of adult CHD mortality per 100 mg/day of n-3 PUFAs, whereas a 23% increased relative risk for adult CHD was observed per 1 ppm of hair MeHg (Guallar et al., 2002; Ohno et al., 2007). Thus, a model integrating MeHg, n-3 PUFAs, and common health endpoints for adults was developed here; i.e., the risk of CHD from the MeHg was subtracted from the n-3 PUFAs benefit. The equation for this:

$$\begin{aligned}\text{Net risk/benefit for adult CHD} = {} & [(\text{n}-3\text{PUFAs mg/meal}) \times (\text{no.meals/week}) \\ & \times (1\ \text{week}/7\ \text{days}) \times (14.6\%\text{lower risk}/100\ \text{mg n}-3\ \text{PUFAs})] \\ & -\{[\text{hair (Hg change/fish meal)} \times (\text{no.meals/week})]-0.51\ \text{ppm hair Hg}\} \\ & \times (23\%\text{higher risk}/1\ \text{ppm hair Hg})\end{aligned} \quad (5)$$

where MeHg concentrations in fish are converted to hair MeHg concentrations using a one-compartment model that relates MeHg intake to the mercury detected in hair (Ginsberg and Toal, 2000):

$$\text{Hg Hair Concentration} = \frac{(S \times C_{MeHg} \times A \times (1-Ke)) \times F \times R}{V} \quad (6)$$

where S is the amount of fish per meal; C_{MeHg} is the concentration of MeHg in fish (μg/g); A is the absorption factor (95%), meaning that 95% of the fish MeHg would be absorbed by the gastrointestinal tract; Ke is the elimination constant, expressed as 1.4% per day; F is the fraction of absorbed dose taken up by blood (5%); V is the volume of blood in the body (=5 L); R is the ratio of the hair concentration (in ppb) to blood concentration (μg/L) (=250). Finally, the units were converted to ppm.

Assuming that only one fish species was consumed per week, and that all fish consumed were marine fish, we calculated the health risks from specific species consumption based on four consumption patterns.

2.6. Statistical analysis

After applying the homogeneity of variance test (Levene's test), the significance of the interspecific and interannual differences in the fatty acids and mercury contents in muscle were determined by one-way ANOVAs in SPSS software (Version 22.0). The alpha level for believing a significant difference existed was set to a priori $p < 0.05$. Spearman rank coefficients between mercury content and fatty acid contents in each and all marine fish muscles were also calculated in SPSS software, for which the significance level was set to $p < 0.05$.

3. Results and discussion

3.1. Mercury concentrations in fish from the Bohai Bay

Fig. 1 shows the THg and MeHg levels for the muscles of collected marine fish samples. These MeHg and THg concentrations respectively ranged from 0.050 μg/g (*Ablennes hians*) to 0.192 μg/g (*Konosirus punctatus*) and 0.099 μg/g (*Thamnaconus septentrionalis*) to 0.458 μg/g (*Konosirus punctatus*) μg/g (all dry weights). The Joint FAO/WHO Food

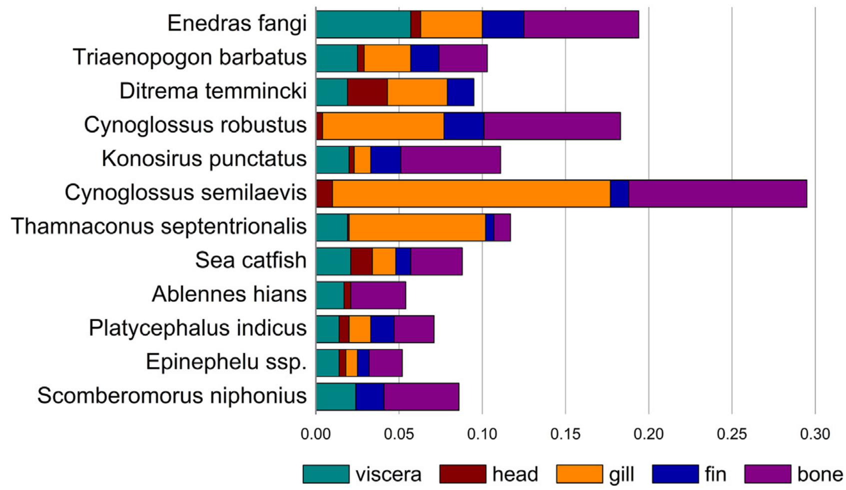

Fig. 2. Distribution of THg (μg/g, d.w.) contents in different tissues of 12 marine fish harvested from Liaodong Gulf, China.

Standards Programme Codex Committee on Contaminants in Foods recommended that the maximum level of MeHg in fish is 1.0 μg/g for predatory fish, and 0.5 μg/g for other fishery products, and both safety thresholds have been adopted in many countries (FAO/WHO, 2011). In our study, after their conversion to wet weight equivalents, the MeHg values of all fish were below the threshold dose of 0.5 μg/g, even the predacious fish. Mercury can biomagnify in aquatic food webs (Chen and Hu, 2012), and its levels in muscle tissue will depend on the age, trophic level, feeding habits and size (length and weight) of the fish (Chen and Hu, 2012; Dang and Wang, 2012; Liu et al., 2014a). We also uncovered species-specific differences in MeHg and THg concentrations ($p < 0.01$). Surprisingly, the predacious fish did not harbor higher mercury concentrations than omnivorous, benthivorous, or planktivorous fish, with no significant differences detected among the four feeding habits ($p > 0.05$). THg concentrations in other tissues of fish were also measured in this study. Overall, the highest concentrations of THg were found in muscle tissue, followed by bone, gill, viscera, fin, and head (Fig. 2). The high affinity of THg with sulfhydryl groups associated with thiol-containing amino acids in muscle likely explains the accumulation of total mercury in muscle tissue (O'Bryhim et al., 2017). Since muscle tissue is the most important fish part consumed, focusing research on it is sensible.

The interannual differences for either MeHg or THg concentrations were not significant ($p > 0.05$), indicating negligible temporal variability of mercury concentration during the studied time period. A significant positive correlation between the MeHg and THg concentrations was found in all marine fish muscle samples ($r = 0.902$, $p < 0.01$, $n = 239$), and their ratio was normally distributed with values between 40% and 70%, a result similar to those of fish harvested from the South China Sea (Liu et al., 2014b) but the mean values are divergent. The mean value of MeHg/THg in this study and that of Liu et al. (2014b) was 54.2% and 72.7%, respectively. It is generally believed that MeHg is the predominant form of mercury occurring in fish muscles, with a ratio of MeHg to THg of 95% (Driscoll et al., 2013; Swanson and Kidd, 2010). In fact, we found species-specific differences in the ratio of MeHg to THg ($p < 0.05$), which may be related to differences in the absorption and metabolism of THg and MeHg among the differing fish species. Therefore, a universal 95% MeHg content of fish muscle is likely neither tenable nor advisable, depending on the region and species, but this requires more data to properly ascertain.

The coastal water environment of China has been seriously polluted by human activities. Although Wang et al. (2018) showed the spatial distribution of mercury concentrations did not differ significantly among the four seas in China, the highest concentrations were nonetheless still observed in the Bohai Sea, which echoed the findings of Tong et al. (2017). Comparing the reported mean/median mercury concentrations in the muscle tissue of fish from China's seas from other studies, we found that the THg concentration of the Bohai Sea was higher (Table 1). This result is consistent with the mercury contents of its seawater, indicating that environmental matrix mercury concentration is a key factor affecting the mercury levels in fish organisms. Despite this, the THg concentrations in marine fish muscle tissues from the Bohai Sea were still at moderate level compared with THg concentrations of marine fish from elsewhere in the world (Table 1).

Table 1
Comparison of mercury concentrations in fish muscle tissue in this study and other regions of the world.

Study area	n	Total Hg (μg/g)		References
		Mean or median	Range	
Dry weight				
Liaodong Gulf, Bohai	239	0.177	0.031–0.458	This study
South China Sea	166	0.152	0.011–1.772	Liu et al. (2014a)
Yellow Sea	164	0.124	0.038–0.285	Zhu et al. (2014)
Peninsular Malaysia	297	0.422	0.055–2.537	Ahmad et al. (2015)
SE Gulf of California	417	0.993	0.106–2.556	Ruelas-Inzunza et al. (2012)
Wet weight				
Liaodong Gulf, Bohai	239	0.073	0.012–0.215	This study
Mid-Atlantic Bight (adult Bluefish)	40	0.327	–	Cross et al. (2015)
Atlantic predatory fish (the Southeastern U.S.A.)	317	0.267	0.030–1.810	Sinkus et al. (2017)
Aleutians (Pacific cod)	140	0.130	0.008–0.860	Burger and Gochfeld (2007)
Persian Gulf	80	0.133	0.049–0.402	Raissy and Ansari (2014)
Southeastern United States and the Bahamas	208	0.500	0.021–3.400	Adams (2010)
Portuguese coast	739	0.031	0.004–0.204	Costa et al. (2020)

– means there is no concentration range.

3.2. Fatty acid composition

The dry weight of fatty acids in the muscle tissue of marine fish was converted to wet weight for comparison with other studies and subsequent calculations. The fatty acid profiles of different fish species in Liaodong Gulf are shown in Table 2; evidently, fatty acid profiles in terms of total and individual saturated and unsaturated fatty acids differ significantly among marine fish species ($p < 0.01$). For example, the mean n-3 PUFAs contents of all species varied widely, from 103.8 to 2511 mg/100 g, and for those with the same dietary habits, the concentration of n-3 PUFAs in *Scomberomorus niphonius* reached 7.7 times that in *Paralichthys olivaceus.* Regarding the DHA in fish samples that are critical to children's IQ improvement, the minimum and maximum concentrations were 76.7 and 689.3 mg/100 g in *Paralichthys olivaceus* and *Triaenopogon barbatus*, respectively. The major contributors to n-3 PUFAs were DHA and EPA, and all the species studied had higher levels of DHA than EPA except for the possible outliers of *Ditrema temmincki*. Similar findings have been reported for marine fish from China's southeast and France, in terms of the EPA and DHA concentrations (Gao et al., 2014b; Yamada et al., 2014), but the values obtained in our study were higher than those of marine fish purchased from markets in Kuwait (Laird et al., 2017). We found the lowest amounts of saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and PUFAs in samples from *Paralichthys olivaceus*, having contents of 452.8, 192.9, and 196.9 mg/100 g, respectively. But the highest levels of SFAs, MUFAs and PUFAs occurred among different species. Of all the fish studied, except for *Scomberomorus niphonius*, the C16:0 and C18:1 respectively were the most abundant SFAs and MUFAs in muscle tissues, consistent with the findings of Angel Rincon-Cervera et al. (2019).

Fig. 3 shows the proportion of fatty acids in muscle of marine fish differing in their feeding habits and for different years. Since four fatty acids could not be distinguished, which only counted in total fatty acids without classification, resulting in an overall lower percentage of all kinds of fatty acids, but we classify them together into one category (others). As with mercury concentrations, no significant differences in fatty acid concentrations were found among the fish taxa across years ($p > 0.05$). Previous studies indicated fatty acid contents in fish muscle were affected by seasons (e.g., Arai et al., 2015), and our sampling period was restricted to August and September of each year; so this could explain why no significant difference was found between years. According to Figs. S1 and 3, the MUFAs accounted for the highest proportion of fatty acids in all fish, followed by the SFAs, n-3 PUFAs, and n-6 PUFAs. Differences in fatty acids profiles in fish may be related to species, location, feeding habits, life stage and age of the fish (Lunn and Theobald, 2006), especially for their SFAs and MUFAs (Arai et al., 2015). In our study, there were significant differences in the proportion of total SFAs and MUFAs between different feeding habits of marine fish, but the n-6 PUFAs and n-3 PUFAs were apparently not influenced by feeding habits, perhaps due to undistinguished fatty acids. Kainz et al. (2017) showed that the contents of n-6 PUFAs and n-3 PUFAs were related to total lipids in freshwater fish, whose PUFAs were adjusted according to their total lipid status, regardless of their feeding sources and trophic positions. Omnivorous and planktivorous fish feed on phytoplankton, which contain high levels of n-3 PUFAs. Since we found no significant difference in n-3 PUFAs contents between different feeding marine fish species, our study supports the view put forth by Kainz et al. (2017).

The ratio of n-3/n-6 PUFAs in marine fish muscle tissues ranged from 0.18 to 3.06, with an average of 1.56. Compared with other studies, such as those for which the average ratio of n-3/n-6 in fish tissue from the Mediterranean was 3.2 and 4.24 for French marine fish (Prato and Biandolino, 2012; Yamada et al., 2014), our mean n-3/n-6 ratio was relatively low. Despite this, in addition to *Thryssa mystax* and *Konosirus punctatus*, the ratios of n-3/n-6 in muscle tissues of the other studied marine fish were >1; hence these species could be recommended for attaining nutritional purposes and dietary intake to reduce the risk of cardiovascular disease (HMSO, 1994; Prato and Biandolino, 2012).

In this study, significant positive Spearman rank correlations were detected between total n-3 PUFAs, n-6 PUFAs, total PUFAs, total SFAs, and total MUFAs. Except for n-3 PUFAs and n-6 PUFAs ($r = 0.626$, $p < 0.05$), and for n-3 PUFAs and total MUFAs ($r = 0.560$, $p < 0.05$), there were particularly strong positive relationships between the other fatty acids ($p < 0.01$). The significant positive correlations between fatty acids may be that fish increase or supplement fatty acids in equal proportions through food or other sources. Studies have also shown that the concentration of fatty acids in fish muscle tissue is correlated with the concentration of mercury. The study of Strandberg et al. (2016) showed that the mercury content in European perch was negatively correlated with EPA + DHA content (Strandberg et al., 2016). Laird et al. (2018) also observed negative correlations between Hg and some, but not all, fatty acid groupings in certain freshwater fish samples (Laird et al., 2018). All the studied fish samples above were harvested from lakes, yet no significant relationships between mercury and fatty acid profiles were detected in our study. It is speculated that this may be due to differences in living environment.

3.3. Human health risk assessment

3.3.1. Calculation of IQ points in children

Research has shown that the positive effects from n-3 PUFAs upon children's IQ are more dependent on DHA than other fatty acids (Cardoso et al., 2018). In our study, the presumed IQ changes due to the MeHg content and DHA content for each species are presented in Fig. 4 (as calculated following the methods of FAO/WHO (2011)). In

Table 2
Fatty acids composition (mg/100 g edible part, w.w.) in muscle of different fish species harvested from the coastal waters of Liaodong Gulf, China (2015, 2016, 2017).

	Name	n	EPA	DHA	Total n-3PUFAs	Total n-6PUFAs	n-3/n-6	Total PUFAs	Total SFAs	Total MUFAs	Total FAs
Predacious	*Scomberomorus niphonius*	10	305.8	439.5	895.1	715.3	1.25	1610	1826	1640	5978
	Epinephelus spp.	45	94.32	180.0	521.3	294.8	1.77	816.2	988.2	964.4	3426
	Platycephalus indicus	17	112.0	184.8	296.8	267.6	1.11	564.4	890.4	1434	3339
	Thryssa mystax	1	nd	301.4	414.7	617.1	0.67	1032	3422	3897	10,147
	Paralichthys olivaceus	2	nd	76.72	103.9	92.96	1.12	196.9	452.8	192.9	1079
Omnivorous	*Ablennes hians*	3	33.67	333.6	1105	622.1	1.78	1727	2856	1960	7765
	Sea catfish	36	49.92	183.7	283.8	223.7	1.27	507.5	626.9	472.1	2044
	Thamnaconus septentrionalis	14	178.6	238.0	560.5	182.9	3.06	743.4	689.8	742.7	3042
	Cynoglossus semilaevis	3	100.0	391.2	900.0	331.6	2.71	1232	1099	1290	4867
	Konosirus punctatus	6	285.8	682.0	1040	1833	0.57	2874	2557	3470	11,526
Benthivorous	*Cynoglossus robustus*	25	163.7	378.2	588.5	401.8	1.47	990.0	976.3	698.9	3640
	Ditrema temmincki	3	1590	662.7	2511	1228	2.04	3740	3054	4928	12,386
	Triaenopogon barbatus	62	216.5	689.3	942.2	829.4	1.14	1772	3311	8233	15,295
Planktivorous	*Enedras fangi*	12	192.2	247.9	1044	552.4	1.89	1597	2113	3327	9030

All samples of marine fish were collected during the end of September and beginning of October in each of 2015, 2016, and 2017; the five exceptions were *Enedras fangi* and *Cynoglossus semilaevis* specimens, which were collected only in 2015 and 2016, the *Thryssa mystax* in 2017, the *Paralichthys olivaceus* in 2016, and the *Konosirus punctatus* in 2015. nd means the data was not detected.

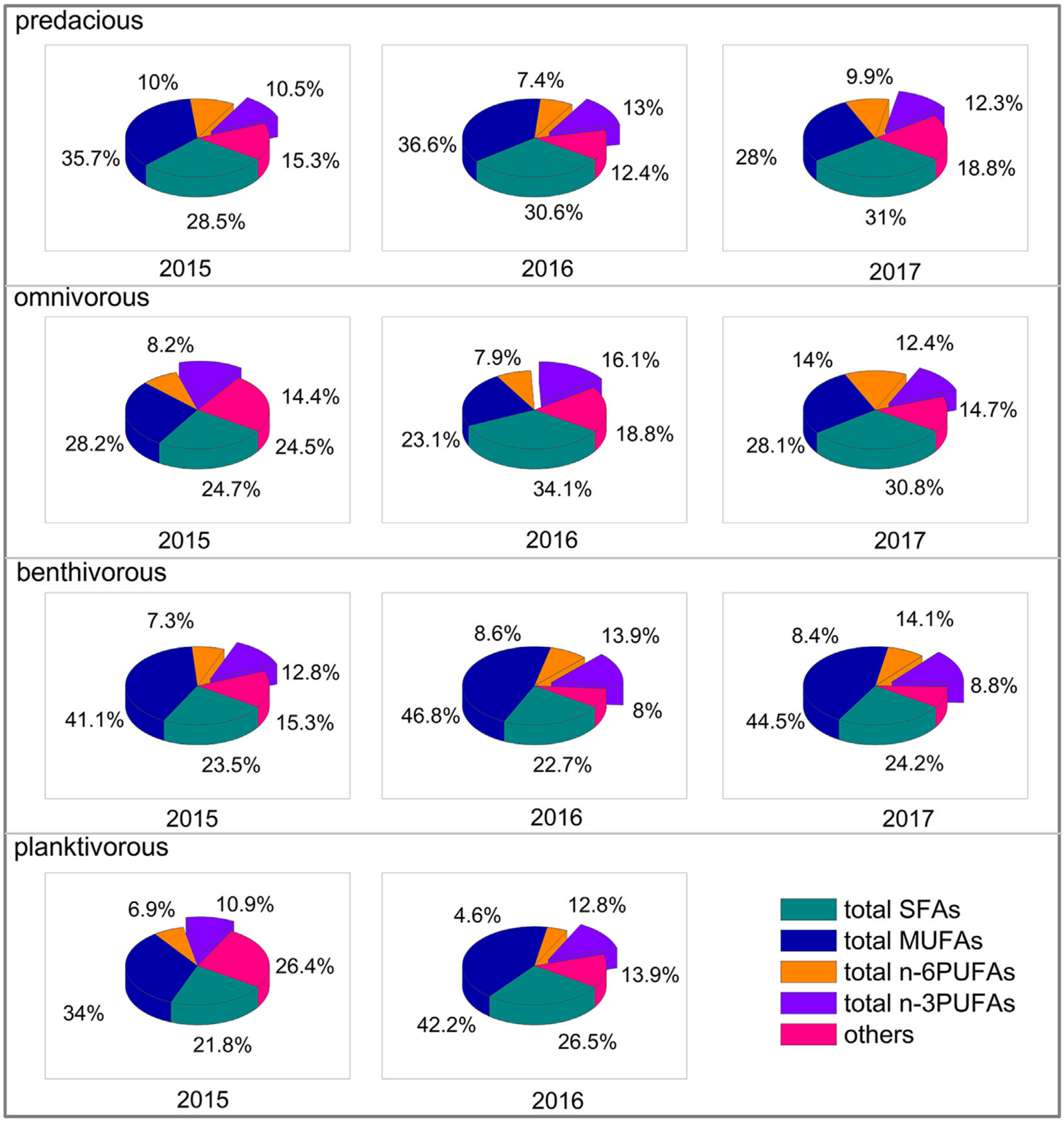

Fig. 3. Fatty acids contents in muscle of marine fish harvested from the Liaodong Gulf (percentage of total fatty acids). Data on planktivorous (*Enedras fangi*) in 2017 were not available because samples were not collected that year. There are four kinds of fatty acids (C22:0 and C20:3, C20:3 and C22:1) whose peaks cannot be distinguished, and they are named "undistinguished fatty acids". They are only counted in total fatty acids without classification, but we classify them together into one category (others).

all consumption scenarios, the DHA contents of all studied marine fish were enough to offset the negative impacts of MeHg on IQ, showing a positive net effect on children's IQ. For marine fish species having a higher DHA, such as *Konosirus punctatus*, *Ditrema temmincki,* and *Triaenopogon barbatus*, a nearly 5.8 points of net IQ gain - the maximum possible IQ benefit from consuming DHA - can be achieved under extremely low consumption scenarios (23.7 g/day). The *Paralichthys olivaceus* had the lowest net IQ point gain because it had the lowest DHA content among all fish species examined. Given the maximum limitation of IQ points (5.8) associated with DHA, the net IQ benefits of all studied fish improved except for the *Konosirus punctatus*, *Ditrema temmincki* and *Triaenopogon barbatus* when the fish were consumed at 44.9 g/day. Considering now those people with a high consumption rate, such as those living in large cities (62.3 g/day), the IQ benefit upper limit value of 5.8 points was reached or nearly so by most of the studied fish. Because of maximum limit exists for benefits, the net effect on IQ of consuming fish at 131.8 g/day actually decreased when compared with their consumption at 62.3 g/day except for *Epinephelus* spp., *Platycephalus indicus*, *Paralichthys olivaceus*, and Sea catfish; still, the negative IQ effects of MeHg were always outweighed by the positive IQ effects of DHA. The *Scoliodonsorrakowah* fish in the study of Gao et al. (2014b) were not recommended for maternal consumption because of its low EPA + DHA and higher MeHg, but other marine fish were deemed beneficial for neurodevelopment, which is consistent with our results. Thus, based on our quantitative risk-benefit analysis of effects on neurodevelopment in infants, the results suggest maternal marine fish consumption is beneficial to her fetus in all scenarios. In addition to marine fish rich in DHA, high marine fish consumption can also contribute to greater net IQ points even the species eaten have a low DHA content. Most marine fish evaluated in this study should offer significant IQ benefits when consumed at 62.3 g/day.

3.3.2. Calculation of CHD risk in adults

Using the model built by Ginsberg and Toal (2009), we also quantified the effects of MeHg and fatty acids in marine fish muscle tissue for the relative risk of CHD mortality in adults. This approach assumes that all n-3 PUFAs provide health benefits, not just EPA and DHA. In their work, Ginsberg and Toal (2009) modeled on the basis of eating a fish meal per week for several months, giving consumers enough time to achieve a stable MeHg concentration in the hair to simulate these effects, during which time only the designated fish were consumed without other fish. The dose-response relationships between MeHg and CHD

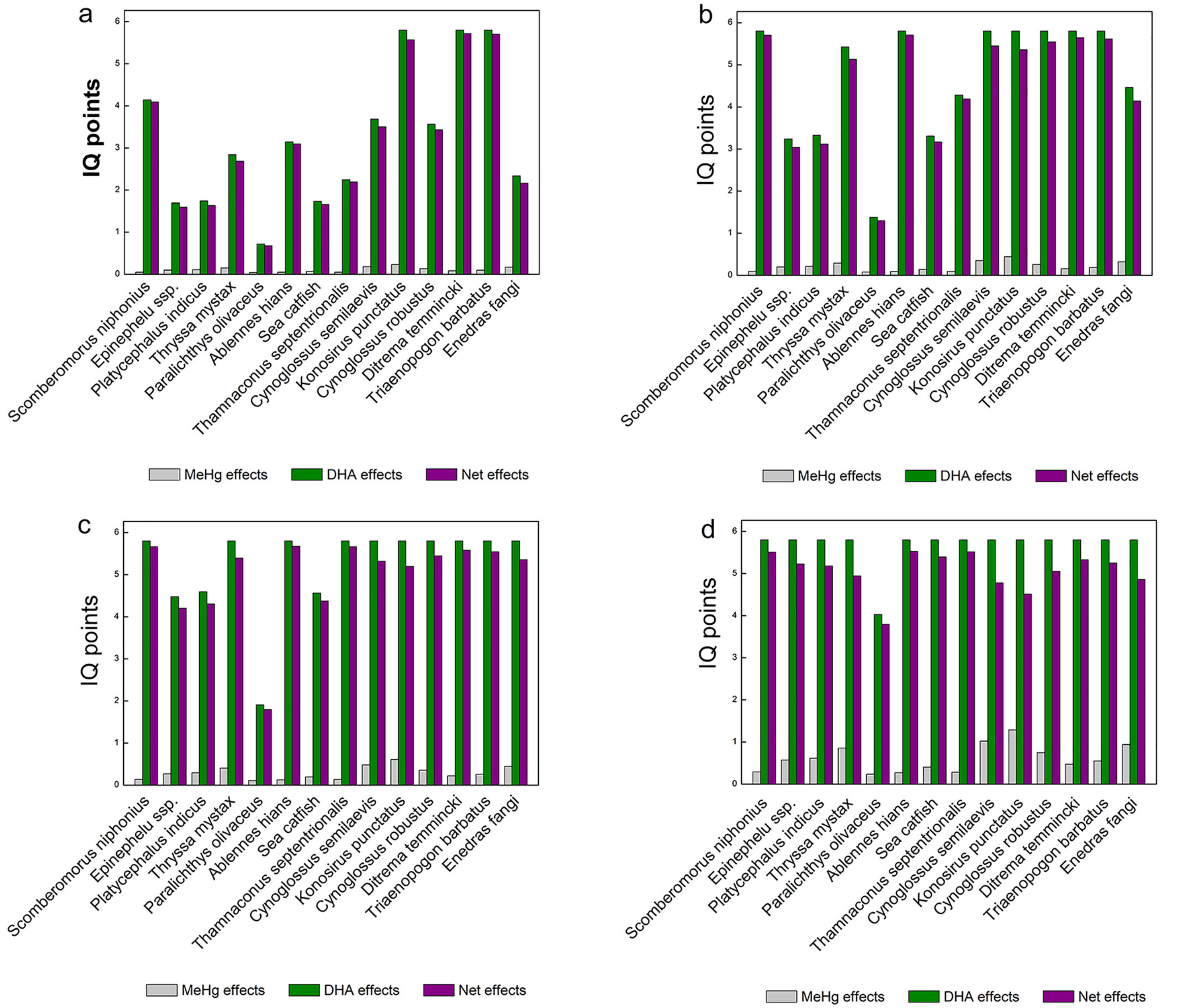

Fig. 4. Estimated changes in children's IQ points due to maternal intake of DHA and MeHg in fish species during pregnancy. (a)–(d) Consumption of fish at rates of 23.7, 44.9, 62.3, and 131.8 g/day, respectively.

mortality risks suggested a hair mercury threshold of 0.51 ppm (Ginsberg and Toal, 2009) before any adverse effects appear and a clear dose-response occurs. But this threshold is an uncertain factor that may be related to measurement errors and variability in the baseline population (Ginsberg and Toal, 2009).

Table 3 shows the net risk-benefit analysis of relative risk of CHD mortality on adults studied under different consumption scenarios. Evidently, eating any of the fish produced a positive result, indicating a net benefit for consumers. At the end point, *Ditrema temmincki* had a huge beneficial effect on cardiovascular health due to its high total n-3 PUFAs and low MeHg concentrations. It reduced the relative risk of CHD mortality by 86.6% in the scenarios of 23.7 g/day, ca, 25 times that of *Paralichthys olivaceus*. Increased consumption rates did not alter the species-specific risk-benefit patterns, and the relative risk of CHD mortality continued to decline as marine fish consumption increased. When these fish were each eaten at 131.8 g/day, the relative risk of CHD mortality was reduced by >100% except for *Platycephalus indicus*, *Thryssa mystax*, *Paralichthys olivaceus*, and Sea catfish. This surprising benefit of marine fish consumption on adult CHD mortality is consistent with the conclusions drawn recently by Dellinger et al. (2018).

Dietary supplementation with n-3 PUFAs may reduce the risk of cardiovascular disease by reducing blood triglycerides and inflammation, and by increasing high density lipoprotein cholesterol (Dias et al., 2017; Eslick et al., 2009). Relying on the model of Ginsberg and Toal (2009), which uses dose-response relationships on a common endpoint to evaluate the comprehensive effects of MeHg and n-3 PUFAs on adult CHD mortality from different fish species as their sources, has important practical value but it also has some limitations to it. Particularly, our risk assessment did not consider the role of other consumed fatty acids from fish possibly regulating blood lipid levels and lipoprotein profiles. In terms of their effects on n-3 PUFAs, some studies have demonstrated different dietary fatty acids can affect the absorption of n-3 PUFAs and the regulation of their incorporation in human plasma and tissue lipids, which may affect the net benefits of n-3 PUFAs. For example, n-6 PUFAs may compete with n-3 PUFAs in the metabolic pathway, whereas a diet enriched with SFAs can improve the incorporation of n-3 PUFAs into tissues, which may potentially reduce other cardiovascular risk factors,

Table 3
Net effects of MeHg (μg/g, w.w.) and n-3 PUFAs (mg/100 g, w.w.) in edible fish on the relative risk of adult CHD mortality (%) under different consumption scenarios (g/day). A positive result indicates decreased risk of CHD mortality.

Name	MeHg	Total n-3 PUFAs	Decreased CHD risk			
			23.7 (g/d)	44.9 (g/d)	62.3 (g/d)	131.8 (g/d)
Scomberomorus niphonius	0.020	895.1	30.8	58.3	80.9	279
Epinephelus spp.	0.040	521.3	17.7	33.5	46.5	161
Platycephalus indicus	0.043	296.8	9.88	18.7	26.0	90.6
Thryssa mystax	0.060	414.7	13.8	26.2	36.3	127
Paralichthys olivaceus	0.017	103.9	3.45	6.53	9.06	31.6
Ablennes hians	0.019	1105	38.1	72.1	100	344
Sea catfish	0.028	283.8	9.57	18.1	25.1	87.2
Thamnaconus septentrionalis	0.020	560.5	19.2	36.4	50.5	174
Cynoglossus semilaevis	0.072	900.0	30.5	57.8	80.2	278
Konosirus punctatus	0.090	1040	35.2	66.7	92.5	321
Cynoglossus robustus	0.052	588.5	19.9	37.7	52.3	181
Ditrema temmincki	0.033	2511	86.6	164	228	783
Triaenopogon barbatus	0.038	942.2	32.3	61.1	84.8	292
Enedras fangi	0.066	1044	35.6	67.4	93.5	323

such as inflammation and clotting tendencies (Dias et al., 2016, 2017). Furthermore, other fatty acids may also respectively affect plasma cholesterol levels (Dias et al., 2014, 2015, 2017). In any case, however, supplementation by n-3 PUFAs can significantly reduce plasma triglyceride concentration, thereby reducing the overall risk of cardiovascular disease (Dias et al., 2016).

3.3.3. Consumption recommendations

In China, the incidence of CHD is on the rise and tends to be younger. Pregnant women with CHD may have adverse effects on the fetus. We calculated the optimal weekly consumption of pregnant women based on the IQ points analysis of before, and then calculated the relative risk of reducing CHD mortality (Table 4). With the maximum IQ point (5.8), the optimal weekly intake of all species will not result in MeHg exposure exceeding the PTWI (1.6 μg/kg bw/week): both *Ditrema temmincki* and *Enedras fangi* can reduce the risk of CHD mortality to pregnant women by >80%, with *Ablennes hians* also suitable for fish consumption by pregnant women. To achieve the maximum IQ points, the amount of consumption required for *Paralichthys olivaceus* is much larger than other marine fish species. We also calculated the maximum consumption of adult men and women under the restriction of PTWI. Due to the difference in average body weight (male: 66.2 kg versus female: 57.3 kg; "*Report on Nutrition and Chronic Diseases of Chinese Residents* 2015"), the maximum consumption required of men is higher than for women. However, for both men and women, none of the studied marine fish exceeded the PTWI under the maximum consumption scenario. But coastal residents should still pay attention to their consumption of *Konosirus punctatus*. Considering the beneficial effects of long-chain fatty acids on cardiovascular disease, it is recommended that as much marine fish as possible ought to be consumed without exceeding the maximum consumption for a given species.

4. Conclusion

In this study, the mercury and fatty acid concentrations in 14 common marine fish species were analyzed, and the effects of fish consumption on IQ points in children and relative risk of CHD mortality in adults were calculated using an IQ scoring model and a comprehensive risk-benefit model, respectively. The results showed that the concentration of mercury in the marine fish muscle tissue of Liaodong Gulf was generally low and their fatty acid concentration was satisfactory. Mercury and fatty acid concentrations were similar between years. The results of the model estimation showed that the marine fish examined have a positive impact on children's IQ and adult CHD, so the benefits of eating fish far outweigh its health risks. This study supports the consumption of marine fish. Mothers would need to eat marine fish according to consumption recommendations if they wish to obtain the maximum IQ score for their fetus; in this respect, *Ditrema temmincki* and *Enedras fangi* are recommended. Adults should consume as much marine fish as possible to reduce their risk of CHD mortality without exceeding the maximum consumption.

Nonetheless, this study had some limitations worth discussing briefly. Firstly, the human health risk-benefit assessments were conducted based on the contents of contaminants and nutrients in fish tissue, leaving other contributing factors unaccounted for - such as the effects of other dietary fatty acids on the absorption of n-3 PUFAs and their incorporation in human plasma and tissue lipids - which may result in possible bias. Secondly, the raw contents of contaminants and nutrients were used in this study, but culinary treatments may change the actual concentrations consumed by people. Finally, the risk assessment would have been more realistic if the impact of both bioaccessibility and culinary treatment were explicitly considered. Accordingly, more comprehensive and in-depth research studies this topic are needed.

CRediT authorship contribution statement

Sujing Wang: Data curation, Writing - original draft.**Deming Dong:** Conceptualization, Methodology.**Ping Li:**Resources.**Xiuyi Hua:**Conceptualization, Methodology.**Na Zheng:**Writing - review & editing, Supervision.**Siyu Sun:**Formal analysis.**Shengnan Hou:**Validation.**Qirui An:**

Table 4
Optimal weekly (daily) maternal consumption (g) and weekly MeHg exposure (μg/kg bw/week) and decreased risk of CHD mortality (%) for mothers at the maximum IQ point. Maximum consumption (g) indicates the maximum consumption of marine fish by adults without exceeding the provisional tolerable weekly intake (PTWI).

Latin name	Optimal weekly (daily) consumption	MeHg exposure	Decrease in risk of CHD	Maximum consumption (male)	Maximum consumption (female)
Scomberomorus niphonius	233.9 (33.4)	0.08	43.4	5222.9	4520.7
Epinephelus spp.	600.4 (85.8)	0.40	64.0	2627.0	2273.8
Platycephalus indicus	586.4 (83.8)	0.42	34.9	2451.9	2122.2
Thryssa mystax	356.0 (50.9)	0.36	29.6	1766.8	1529.3
Paralichthys olivaceus	1405 (201)	0.39	29.2	6411.6	5549.6
Ablennes hians	309.0 (44.1)	0.10	70.9	5574.7	4825.3
Sea catfish	576.9 (82.4)	0.27	33.3	3719.1	3219.1
Thamnaconus septentrionalis	436.4 (62.3)	0.14	50.6	5349.5	4630.3
Cynoglossus semilaevis	273.0 (39.0)	0.33	50.2	1479.3	1280.4
Konosirus punctatus	154.4 (22.1)	0.23	32.8	1173.1	1015.4
Cynoglossus robustus	278.8 (39.8)	0.24	33.4	2024.5	1752.3
Ditrema temmincki	155.3 (22.2)	0.09	81.1	3203.9	2773.1
Triaenopogon barbatus	149.5 (21.4)	0.10	29.1	2758.3	2387.5
Enedras fangi	441.3 (63.1)	0.48	94.6	1607.8	1391.6

Formal analysis.**Pengyang Li:**Formal analysis.**Yunyang Li:**Investigation. **Xue Song:**Investigation.**Xiaoqian Li:**Formal analysis.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2020.138586.

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