Iodine status in preschool children and evaluation of major dietary iodine sources: a German experience

Simone A. Johner · Michael Thamm ·
Ute Nöthlings · Thomas Remer

Abstract

Purpose Even mild iodine deficiency may negatively affect cognitive performance, especially at a young age. Our aim was to investigate iodine status in very young children and to assess the importance of iodized salt in processed foods of which the use has decreased during the last years in Germany.

Methods Twenty-four hours urinary iodine excretion (UIE) as a marker of iodine intake was measured in 378 24 h urine samples collected 2003–2010 by 221 3 to <6 years old participants of the DONALD Study. Parallel 3-d weighed dietary records and measurements of urinary sodium excretion provided data on the daily consumption of the most important iodine sources in the children's diet (iodized salt, milk, fish, meat and eggs). Time trends of UIE (2003–2010) and contributions of the different food groups were analyzed by using linear mixed-effects regression models.

Results Median UIE of 71 µg/d in boys and 65 µg/d in girls ($P = 0.03$), corresponding to an iodine intake of 82 and 75 µg/d, respectively (assumption: 15 % non-renal iodine losses), was below the recommended dietary allowance (RDA) of 90 µg/d. Milk, salt and egg intake were significant predictors of UIE; milk and salt together accounted for >80 % of iodine supply. Between 2003 and 2010, UIE decreased significantly by approximately 1 µg/d per year. The contribution of salt intake to UIE decreased from 2003–2006 to 2007–2010.

Conclusion In countries where salt is a major iodine source, already modest decreases in the iodized proportion of salt used in processed foods may relevantly impair iodine status even in preschool children.

Keywords Preschool children · 24 h Urines · Iodine excretion · Iodized salt · Time trend

S. A. Johner (✉) · T. Remer
IEL-Nutritional Epidemiology, DONALD Study at the Research Institute of Child Nutrition, University of Bonn, Heinstück 11, 44225 Dortmund, Germany
e-mail: johner@fke-do.de

M. Thamm
Central Epidemiology Laboratory, Department of Epidemiology and Health Reporting, Robert Koch Institute, General-Pape-Str. 62-66, 12101 Berlin, Germany

U. Nöthlings
IEL-Nutritional Epidemiology, University of Bonn, Endenicher Allee 11-13, 53115 Bonn, Germany

Introduction

In the 1920s, the USA, Switzerland and New Zealand were the first countries adding iodide to table salt to prevent goiter [1]. Meanwhile, salt iodization—mandatory as well as voluntary—is the most widely used iodine deficiency prophylaxis measure [2]. However, worldwide, it is estimated that still one-third of school children has insufficient iodine intake and is at risk of iodine deficiency. Europe has still the greatest proportion of children with inadequate iodine intakes (43.9 %) [3]. Remarkably, especially in industrialized countries (e.g., Australia, US) in the last years, a trend of decreased iodine intakes emerged [1, 4–6], making clear that iodine deficiency is not confined to low-income nations [7]. Although the most extreme manifestations of a severe iodine deficiency—goiter and cretinism—are rare by now [8], the effects of only mild iodine deficiency, like mental impairment that leads to poorer school performance and reduced intellectual ability, are nowadays probably of greater importance [9, 10]. Different

studies demonstrated that children with only mild to moderate iodine deficiency improved their cognitive performance when iodine intake was increased [9–12]. Although this effect until now has only been shown in schoolchildren, it can be assumed that positive influences on cognition should be even more pronounced in the younger, that is, preschool children [13].

In industrialized countries, the main proportion of salt (about 80 %) comes from processed foods [14]. During the last years (starting in 2004), the use of iodized salt by the food industry has decreased in Germany, and by now encompasses only <30 % of total added salt [15]. Parallel to this development, a deterioration of iodine status of schoolchildren was observed [16]. Whether this decrease in one of the most important iodine providers in the human diet [14] may already affect the iodine status of the particularly vulnerable age group of preschool children has not been examined until now.

By using 24 h urines and parallel 3-d weighed dietary records, our aim was to characterize the current iodine supply of German preschool children in detail, investigate its development during the last years and quantify the impact of different food groups on iodine nutrition in this age group.

Methods and materials

Study population

The study population for the present analysis was selected from the DONALD (Dortmund Nutritional and Anthropometric Longitudinally Designed) Study, an open cohort study, since 1985 gathering information about diet, metabolism and development from infancy to adulthood in Caucasian healthy subjects [17]. The children visit the Research Institute of Child Nutrition, Dortmund once a year for examinations and assessments. They include 3-d weighed dietary records, anthropometry, urine sampling, interviews on lifestyle, and medical assessments. All examinations are performed with parental, and later on with the children's written consent.

For the present examination, we considered only children with an age range of 3 to <6 years since especially for this vulnerable age group with extensive neuronal modeling of cognitive function data on iodine supply are lacking. Inclusion criteria were the collection of ≥1 complete 24 h urines along with ≥1 plausible 3-d weighed dietary records (encompassing the day of urine collection) during 2003–2010. For specific dietary and urinary inclusion criteria, see "urine data" and "nutritional assessment" sections. Because of the open cohort design of the DONALD Study, the number of subjects of the present subsample varied each year, with new 3 year olds entering and 6 year olds leaving the studied age range under consideration during 2003–2010. Because of the voluntary character of the DONALD Study, some children provide either only a dietary record with no urine sample or a 24 h urine sample without a dietary record. These children were not included.

A total of 222 children met the criteria, providing 383 urine samples with the corresponding number of dietary records. Urine samples and appendant dietary records were excluded in case of iodine-containing drug use, or intake of iodine-containing supplements during the time of respective urine collection. This was the case for 5 observations of 4 children (after exclusion, only one child had no remaining observation). Accordingly, 378 collected 24 h urine samples and related dietary records of 221 children remained for the present investigations.

Urine data

After children have learned to use the toilet (mostly at the age of 3–4 years), urine collections are performed each year following a standardized procedure [17]. Collections are generally carried out on the 3rd day of the 3-d weighed dietary record; 24 h urine collection starts in the morning after arising. The children are instructed to void their bladder in the morning. This micturition is completely discarded, and the time is noted as the start time of urine collection. For the next 24 h, all micturitions are collected, including the first void of the following morning. All micturition time points including the final collection on the next morning are recorded. If a micturition is lost, time is also noted, and the time span between the collected recent micturition and the lost one is subtracted from the total 24 h period. The samples are immediately stored in preservative-free, Extran-cleaned (Extran, MA03; Merck, Darmstadt, Germany) 1 L plastic containers at less than −12 °C before transfer by a dietician to the research institute. A dietician reviews the child's compliance with the family and discusses the completeness of the urine collection. At the institute, the urine samples are stored at −20 °C until analyzed [18].

In the 24 h urine samples, iodine concentration was determined by a modified Sandell–Kolthoff method after acidic wet ashing of the samples [19]. Creatinine concentration was measured by the Jaffé method using a creatinine analyser (Beckman-2; Beckman Instruments, Fullerton, CA, USA). Sodium excretion was measured by flame atomic absorption spectrometry with a Perkin Elmer 1100 Spectrometer (Perkin Elmer, Überlingen, Germany).

For data analysis, 24 h urines were considered as complete when the body weight-related 24 h creatinine excretion rate was ≥0.1 mmol·kg^{-1}·d^{-1} [18] and when urine samples were not reported to contain incomplete micturitions. Otherwise, they were excluded.

Nutritional assessment

To estimate the individual food and nutrient intake, 3-d weighed dietary records were used. On three consecutive days, the weight of all foods and beverages consumed was recorded using a digital, regularly calibrated food scale to the nearest 1 g. Out of home consumed food was estimated by semi-quantitative recording (e.g., numbers of glasses, cups). Intakes of energy, nutrients (including food fortification and nutritional supplements) and food groups were calculated as individual means of the three recorded days by using our in house nutrient database LEBTAB [20], which contains detailed data on the energy and nutrient content of all recorded food items and is continuously updated.

Plausibility of dietary records was checked by calculating the ratio of reported total energy intake to predicted individual basal metabolic rate (estimated by the method of Schofield [21]). Dietary records with a ratio below the age- and sex-specific cut-off values [22] were excluded.

The intakes of food groups which naturally relevantly contribute to iodine supply were calculated (i.e., milk and whey-based milk products, saltwater fish and saltwater fish products, eggs, and meat and meat products). Processed foods like bread can also provide notable amounts of iodine, however, only if produced with iodized salt. Therefore, total salt intake was estimated from dietary records as well as 24 h urine samples with the latter being considered to be more reliable. Since most of the salt consumed stems from processed foods, the contribution of total salt intake to overall iodine excretion mostly reflects contributions of industrially and non-industrially processed foodstuffs.

Anthropometric measurements

Anthropometric measurements of the DONALD participants were performed at each annual visit by nurses who had been trained according to standard procedures [23], with the children dressed in underwear only and barefoot. Standing height was measured with a stadiometer (Harpenden, Crymych, UK) to the nearest 0.1 cm, and weight was measured on an electronic scale (Seca 753E; Seca Weighing and Measuring System, Hamburg, Germany) to the nearest 0.1 kg. From these measurements, BMI and body surface area were calculated, the latter according to the formula of Du Bois & Du Bois. [24] Sex- and age-independent BMI-standard deviation scores were calculated by using German national reference data [25].

Statistical analysis

SAS procedures were used for data analysis (version 9.2, SAS Institute, Cary, NC, USA). Significance was defined as $P < 0.05$, a trend as $P < 0.1$

Characteristics of the study population are presented as mean $\pm$ SD for normally distributed variables or median with interquartile range for non-normally distributed variables. All observations (i.e., also repeated samples from the same individual) were included for the calculation of means and medians. Sex differences and time-related differences (2003–2006 vs. 2007–2010) were tested by repeated measures regression analyses (linear mixed-effects regression models, PROC MIXED in SAS, adjusted for age) to account for the dependency between the repeated measurements that were available for >50 % of the investigated children.

To evaluate urinary iodine excretion levels (µg/d) with regard to iodine status of the preschool children, we compared the values with the iodine intake recommendations (RDA, recommended dietary allowance; EAR, estimated average requirement; DACH, recommendations of the German speaking countries in Europe) after considering a mean non-urinary iodine loss of 15 % [26, 27].

Linear mixed-effects regression models, including both fixed and random effects, were also used to analyze time trends in iodine excretion (2003–2010). The primary outcome variable was 24 h urinary iodine excretion (µg/d). The fixed effects were time (continuously in years since 2003), sex, age and urine volume [28]. Furthermore, we added creatinine excretion (standardized to body surface area) as a fixed effect to account for correlated measurement errors potentially introduced by the fact that iodine excretion and urine volume were measured in the same urine sample [29]. A random statement was included to allow for variation between the individuals, a repeated statement was included to account for the lack of independence that exists between repeated observations on the same person. An unstructured covariance for iodine excretion best specified the structure of the between-person error covariance, and a heterogeneous compound-symmetry structure best specified the structure of the within-person error covariance as they both improved the fit statistics (Akaike's Information Criterion, Bayesian Information Criterion) the most. In contrast to other models, for example, linear regression for balanced longitudinal data (PROC GLM in SAS), the linear mixed-effects regression model considers all available measurements rather than using only participants with complete follow-up data (on the assumption that any missing data are missing at random) [30]. In two separate runs of the linear mixed-effects regression model (including the same fixed effects as described above), the dependent variable iodine excretion (µg/d) was substituted by iodine concentration (µg/L) and energy-corrected 24 h iodine excretion (µg/MJ/d), respectively.

To analyze the impact of the different iodine providers on 24 h iodine excretion (µg/d), we included the dietary

iodine sources milk, fish, egg and meat intake (g/d) and sodium excretion (g/d) as a marker for salt intake as further fixed effects in the above-described basic model for time trend analysis. The final model was adjusted for the energy intake of the children.

Results

Anthropometric, urinary and dietary characteristics of the 221 children (106 boys and 115 girls) in this study are presented in Table 1. Urinary iodine concentration (μg/L)

Table 1 Anthropometric, urinary and dietary characteristics of 221 3 to <6 years old participants of the DONALD Study (2003–2010, 378 observations), stratified by sex[a]

	Total sample ($n = 221$)	Boys ($n = 106$)	Girls ($n = 115$)	P[b]
n (observations)	378	181	197	
Age (years)	4.7 ± 0.9	4.7 ± 0.9	4.6 ± 0.9	0.2
Anthropometrics				
Weight (kg)	19.1 ± 3.3	19.5 ± 3.4	18.6 ± 3.1	0.048
Height (cm)	110.3 ± 7.8	111.6 ± 7.7	109.2 ± 7.8	0.02
BMI (kg/m^2)	15.6 ± 1.3	15.6 ± 1.4	15.5 ± 1.1	0.3
BMI-SDS	−0.09 ± 0.95	−0.13 ± 1.08	−0.05 ± 0.82	0.9
24 h Urines				
24 h urine volume (mL)	582.1 (428.1; 792.0)	582.4 (416.4; 792.0)	579.1 (440.5; 790.0)	0.7
Osmolality (mosm/kg)	636.5 (483.0; 801.0)	663.0 (513.0; 867.0)	599.0 (451.0; 727.0)	0.04
24 h sodium excretion (g/d)	1.4 (1.0; 1.8)	1.4 (1.0; 1.9)	1.3 (1.0; 1.7)	0.1
24 h sodium excretion, energy-corrected (g/MJ/d)	0.25 (0.19; 0.32)	0.25 (0.19; 0.32)	0.25 (0.18; 0.33)	0.9
Iodine concentration (μg/L)	114.4 (85.6; 160.0)	124.4 (91.8; 169.2)	105.3 (76.6; 154.6)	0.02
24 h iodine excretion (μg/d)	67.2 (51.8; 87.4)	71.1 (57.0; 89.4)	65.2 (49.0; 81.7)	0.03
24 h iodine excretion, energy-corrected (μg/MJ/d)	12.3 (9.8; 15.7)	12.7 (10.3; 15.2)	11.9 (9.4; 16.1)	0.5
3-day dietary records				
Energy (MJ/d)	5.3 (4.8; 6.0)	5.5 (5.0; 6.2)	5.3 (4.7; 5.8)	0.001
Sodium intake (g/d)	1.4 (1.1; 1.7)	1.4 (1.1; 1.7)	1.4 (1.1; 1.6)	0.1
Iodine intake (μg/d)	37.4 (27.5; 50.8)	36.6 (27.3; 52.4)	37.9 (28.1; 49.7)	0.1
Milk[c] (g/d)	231.9 (131.7; 312.0)	245.9 (152.4; 327.5)	217.9 (129.1; 307.9)	0.4
Fish[d] (g/d)	0.0 (0.0; 11.6)	0.0 (0.0; 11.1)	0.0 (0.0; 11.8)	0.4
Eggs (g/d)	8.3 (0.2; 20.3)	8.4 (0.2; 19.0)	8.0 (0.2; 20.6)	0.8
Meat[e] (g/d)	47.9 (28.1; 67.8)	48.1 (29.1; 66.9)	47.7 (28.0; 70.8)	0.8

	2003–2006	2007–2010	
n (children)	129	119	
n (observations)	189	189	
Iodine concentration (μg/L)	126.4 (91.8; 172.0)	108.5 (76.6; 144.1)	<0.0001
24 h iodine excretion (μg/d)	68.7 (54.0; 88.3)	65.2 (50.2; 83.6)	0.02
24 h iodine excretion, energy-corrected (μg/MJ/d)	12.9 (10.1; 16.0)	12.2 (9.6; 15.0)	0.09
24 h sodium excretion (g/d)	1.4 (1.0; 1.8)	1.4 (1.0; 1.8)	0.3

[a] Median (P25; P75) or arithmetic mean ± SD

[b] Differences between sex or the two time periods, respectively, were tested with linear mixed-effects regression models (PROC MIXED in SAS) to account for the dependency between repeated measurements on the same child

[c] Milk and whey-based milk products

[d] Only saltwater fish and saltwater fish products. The corresponding arithmetic mean intake (±SD) was 1.4 (±2.5) in boys and 1.4 (±2.1) in girls

[e] Meat and meat products

and absolute 24 h excretion (μg/d) were significantly higher in boys than in girls ($P < 0.05$). When corrected for the individual energy intake (MJ/d), these sex differences disappeared. The comparison of means of the different iodine parameters measured in urine between 2003–2006 and 2007–2010 revealed lower values in the second time period ($P < 0.05$, $P < 0.1$ for energy-corrected iodine excretion). Median iodine intake (μg/d) estimated from the weighed dietary records lay considerably below median iodine excretion measured in 24 h urines. With respect to the intakes of the different food groups and sodium excretion as a marker for salt intake, no changes were observed between 2003–2006 and 2007–2010 (results not shown). According to the recorded dietary intakes of foods and the information obtained from the individual interview, >90 % of the investigated children consumed iodized salt at home regularly. Correlation between sodium intake, estimated by dietary records and urinary sodium excretion was 0.53 (Spearman's correlation coefficient). Iodine excretion and sodium excretion showed a correlation of 0.43.

Median urinary iodine concentration of this study sample met the WHO recommendation of 100 μg/L that indicates an adequate iodine status. However, when translating the absolute iodine excretion per day (median 71 μg/d in boys, 65 μg/d in girls) into the estimated iodine intake by considering 15 % non-renal iodine losses (i.e., resulting in an estimated iodine intake of 82 μg/d in boys, 75 μg/d in girls), the recommendation for iodine intake (RDA) of 90 μg/d for this age group was not achieved. The comparison of the iodine excretion rates with the estimated average requirement (EAR [31], after considering 15 % non-renal iodine losses) suggests an inadequate iodine intake for 29 % of the 24 h urines (Fig. 1, shaded area); based on individuals, 26 % of the 221 children had a mean iodine excretion below the EAR. None of the children exceeded the upper limit of iodine intake (200 μg/d for 3 years old, 300 μg/d for 4 < 6 years old [31], after considering 15 % non-renal iodine losses).

Time trend analysis (i.e., the basic linear mixed-effects regression model adjusted for sex, age, urine volume and creatinine) of 24 h urinary iodine excretion showed a significant decline over the 8-year period under study (2003–2010, $\beta = -1.13$, $P = 0.03$). The same applied to the other investigated parameters of iodine status (iodine concentration (μg/L) and energy-corrected iodine excretion (μg/MJ d) (Table 2).

In a second mixed-effects regression model, the most important iodine supplying food groups were included to estimate the impact of the different dietary iodine sources on iodine status (Table 3). Except fish and meat intake, all were significant predictors of 24 h iodine excretion ($P < 0.0003$). A time-stratified run of this regression model (2003–2006 vs. 2007–2010) showed a decrease in the
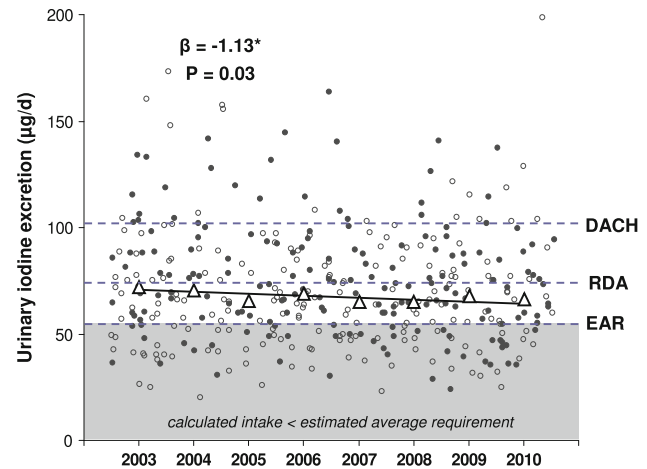
Fig. 1 Crude 24 h urinary iodine excretion (μg/d) of 3 to <6 years old preschool children in 2003–2010 ($n = 378$ urine samples, *filled circle* boys, *open circle* girls). *Results of the mixed-effects regression model estimating the impact of time (in years since 2003) on iodine excretion, adjusted for sex, age, urine volume and creatinine excretion (standardized to BSA). *Triangles* present median urinary iodine excretion (μg/d) along with corresponding regression line. All urine samples located in the gray area are suggested to reflect an insufficient iodine intake when compared to the estimated average requirement (EAR [31]; the EAR of 65 μg/d for 1- to 8-year-old children corresponds to an iodine excretion of 55 μg/d, when considering 15 % non-urinary iodine losses [26, 27]). Recommended dietary allowance (RDA, dashed line) and DACH [39] were in the same way corrected for 15 % non-urinary iodine losses

Table 2 Parameters of iodine status and predicted time trends analyzed in 378 collected 24 h urines of healthy 3 to <6 years old preschool children in 2003–2010

Outcomes	Time (2003–2010) $n = 378$ urines from 221 children	
	β^{a}	P
Iodine concentration (μg/L)	−2.86	0.006
24 h iodine excretion (μg/d)	−1.13	0.03
24 h iodine excretion energy-corrected (μg/MJ/d)	−0.24	0.02

[a] Regression coefficients of the linear mixed-effects regression model (PROC MIXED) for time trend (since 2003, in years), adjusted for sex, age, urine volume and creatinine excretion (standardized to BSA). Model was run separately for each outcome

impact of sodium excretion (i.e., salt intake) on urinary iodine excretion [$\beta = 15.4$ (2003–2006) decreased to $\beta = 12.1$ (2007–2010)].

The percentage contributions of the different food groups to estimated total iodine intake were calculated by the individual amounts of intake and the food-specific iodine contributions (β). The results are presented in Fig. 2. Milk and salt together accounted for more than 80 % of estimated dietary iodine intake from major iodine supplying foods.

Table 3 Time trend and dietary predictors of 24 h urinary iodine excretion (µg/d) in 221 preschool children (3 to <6 years old) with urine samples collected between 2003 and 2010 (378 urine samples in total)

| Predictors	Urinary iodine excretion (µg/d) $n = 378$ urines from 221 children	
	β^a	P
Time (years)	−0.98	0.02
Sodium excretion (g/d)	13.71	<0.0001
Milk (g/d)[b]	0.08	<0.0001
Fish (g/d)[c]	0.10	0.2
Eggs (g/d)	0.26	0.0003
Meat (g/d)[d]	0.06	0.08

[a] Results of the linear mixed-effects regression model (PROC MIXED) adjusted for sex, age, urine volume, creatinine excretion (standardized to BSA) and energy

[b] Milk and whey-based milk products

[c] Only saltwater fish and saltwater fish products

[d] Meat and meat products
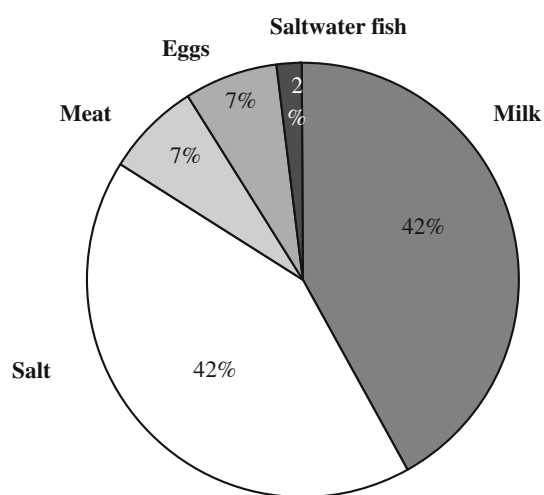
Fig. 2 Percentage contributions of the investigated food groups to estimated urinary iodine excretion of 3 to <6 years old, calculated by mean daily dietary intakes (g/d) (arithmetic means) and respective regression coefficients of the linear mixed-effects regression model (2003–2010, Table 3). The estimate for salt (derived from 24 h urinary sodium excretion) comprises salt from all kinds of processed food as well as table salt used at home

Discussion

The present investigation, for the first time, provides evidence that the use of iodized salt in processed foods is of major importance for the maintenance of adequate iodine nutrition also in preschool children. In parallel with a decrease of the percentage of iodized salt applied for industrial food production in Germany in the last years

(starting in 2004 [32]), 24 h urinary iodine excretion of preschool children significantly deteriorated, by approximately 1 µg/year between 2003 and 2010.

Milk and salt were the main iodine sources in the children's diet, together accounting for more than 80 % of estimated iodine supply. Intake levels of the latter did not change in the investigated time period, therefore, possible reasons for the declining iodine status of preschool children are very likely related to changes of iodine content of the respective food groups. In Germany, the level laid down by law for voluntary salt iodization ranges from 15 to 25 mg iodine per kg salt. Today, most households (>80 %) consume iodized salt (in the present study sample >90 %), however, salt used by food manufacturers is only partially iodized—and informal data by the major German salt producers suggest a decreasing trend from 35 % to <30 % by now [15]. The fact that in industrialized countries about 80 % of total salt intake is provided by processed foods [14] underlines that the decreased use of iodized salt by food industry is probably the primary reason for the observed decline in iodine status of preschool children. The observed lower β-values for the contribution of sodium excretion to iodine supply during 2007–2010 versus 2003–2006 provide further support for the latter conclusion. Definitely, these time-stratified β-values should be interpreted carefully because of the rather small sample size of the subgroups ($n = 129$ and $n = 119$ children, with 189 observations each); however, a similar decrease in the contribution of sodium excretion to 24 h iodine excretion has already been reflected in our former analysis of iodine status in school children 2004–2009 [16]. Our findings emphasize the importance of a consistent appropriate salt iodization to ensure a save and sufficient iodine supply of children and other population groups and underline the responsibility of the food industry and food trade, as the main portion of salt is ingested with processed foods. However, until there is no final harmonization of trade regulations throughout highly interconnected trade regions like the European Union, which would abolish existing trade barriers for processed foods containing iodized salt, the current situation will hardly improve [33].

The second most important iodine source in our study was whey-based dairy products (i.e., mainly milk and yoghurt). Milk contributed to iodine excretion with on average 8 µg per consumed 100 g of milk. Considering 15 % non-renal iodine losses, this corresponds to an iodine intake of 9.2 µg per 100 g milk. This is in very good agreement with the current analysis of iodine content of milk in Germany. Mean iodine content of milk in 2004–2010 was 9.8 µg/100 mL [34]. In contrast to the decreased use of iodized salt in processed foods, milk iodine content slightly increased in the last years (about 13 µg/L 2004–2010 [34]). Probably, this trend antagonized

an even more pronounced deterioration of iodine status of the investigated preschool children.

Sea fish, the food group with the naturally highest iodine content, only contributed marginally to iodine supply, because of the low intake levels. Sea fish was eaten in less than 50 % of the examined records, partly explaining why no significant impact of sea fish on iodine excretion was found in our study. In our former analysis of 6–12 years old school children, sea fish significantly predicted iodine excretion of the children. Therefore, a specific encouragement in the consumption of fish could be an effective strategy to improve the children's iodine supply.

The evaluation of iodine status is rather complex. When using urinary iodine concentration (μg/L) as a marker for iodine status (a median of 100 μg/L indicates adequacy according to WHO [3]), iodine status of the present population can be classified as adequate. However, when comparing median 24 h iodine excretion of 71 μg/d in boys and 65 μg/d in girls corresponding to an iodine intake of 82 and 75 μg/d, respectively (assuming 15 % non-renal iodine losses), with the iodine intake recommendations (RDA: 90 μg/d; DACH: 120 μg/d), >50 % of our preschool children are below the recommendations. Compared to the EAR (estimated average intake, set by the IoM, 65 μg/d for 1–8 years old), still 26 % of the investigated children (29 % of 24 h urine samples) are estimated to have intakes less than the requirement (EAR). A prevalence of maximum 2 % is to be targeted [35]. These data again show the importance of 24 h urine measurements to gather a more reliable evaluation of the current iodine status. Urinary iodine concentration can be relevantly confounded by hydration status [36] and, in some cases, even can rather depend on the urinary volume than on 24 h iodine excretion [37]. In the current analysis, using only urinary iodine concentration would have masked a non-satisfying iodine nutritional status.

The comparison of absolute 24 h iodine excretion (μg/d) or iodine concentration (μg/L) between boys and girls suggests considerable sex differences in iodine supply. Iodine excretion of boys is significantly higher than of girls. However, when correcting for individual energy intake (estimated by the dietary records), these sex differences disappear. This phenomenon reflects the real physiological situation: girls have a lower iodine requirement due to a lower thyroid hormone production (that is directly associated with a lower body size and therefore lower basal metabolic rate). Therefore, different daily iodine excretions are not equitable to a different iodine status. Against this background, a revision of the current iodine intake recommendations into sex-specific reference values is preferable.

Iodine is critically involved in brain development; especially in the pre- and early-postnatal period of life, as well as during childhood, an adequate iodine intake appears to be essential for the full gain of the intellectual potential [13]. To evaluate in how far even the current—mildly insufficient—iodine status of the investigated preschool children could constitute a risk factor for a suboptimal cognitive performance, we compared our data with that of the intervention study of Gordon et al. [9] in children. These authors found that an increase in urinary iodine concentration from 66 μg/L (baseline) to 145 μg/L goes along with significantly improved results in cognitive function tests in school children. The iodine concentration at baseline (66 μg/L in 10–13 years old) corresponds to an absolute iodine excretion per day of 73 μg/d when assuming a 24 h urine volume of 900 mL [38]. We transformed this excretion value to the level that would be expected in 3–<6 years old by means of recommended energy intake (6–12 years old: 9 MJ, 3–<6: 6 MJ [39]): 73 μg/d/ 9 MJ * 6 MJ = 49 μg/d. Accordingly, an excretion rate of about 50 μg/d appears not to be sufficient to ensure development of the children's full intellectual potential [13], and this is only 28 % lower than median iodine excretion observed in the present investigated preschool children (68 μg/d).

The main advantage of the present analysis was the availability of 24 h urine samples for the estimation of iodine status and salt intake in combination with dietary intake data assessed by weighed dietary records. Comparison of iodine intake estimates from dietary records with those from 24 h iodine excretion shows a considerable underestimation for the dietary data which is mainly due to a relevant number of processed foods containing iodized salt (bread, meat products, etc.) of which dietary information is lacking in food tables. However, at the same time, the elaborate design of the DONALD Study results in a study sample with a relatively high socioeconomic status representing a limitation of the study. Further limitations were the low number of samples collected per year and the fact that not for all preschool children repeated measurements were available and therefore not all individuals could be included in both time periods (2003–2006 vs. 2007–2010). Nevertheless, the only representative investigation concerning iodine status of German children in the last years was the KiGGS study (2003–2006) in which more that 10,000 spot urine samples were collected. Median iodine concentration that was found in 3–6 years old was 127 μg/L in boys and 113 μg/L in girls [40]. These values are in a good agreement with our findings of a median iodine concentration of 124 μg/L in boys and 105 μg/L in girls [9] confirming the nationwide relevance of our data.

Conclusion

Even if nearly all table salt used at home is iodized (as in DONALD children), only one-third of total salt added in

processed food being iodized (as in Germany) seems insufficient to ensure an adequate iodine supply of children in countries where the main iodine supplier is salt and consumption of processed foods is high. If in Germany the trend toward a decreased use of iodized salt in processed foods continues, iodine status will continue to impair and the risk of a re-emerging iodine deficiency increases. Here, the main responsibility rests with the food industry and food trade as they are the key players regarding salt fortification.

References

1. Charlton K, Skeaff S (2011) Iodine fortification: why, when, what, how, and who? Curr Opin Clin Nutr Metab Care 14:618–624
2. World Health Organisation (2007) Assessment of iodine deficiency disorders and monitoring their elimination. World Health Organisation, Geneva
3. Andersson M, Karumbunathan V, Zimmermann MB (2012) Global iodine status in 2011 and trends over the past decade. J Nutr 142:744–750
4. Vanderpump MP, Lazarus JH, Smyth PP, Laurberg P, Holder RL, Boelaert K et al (2011) Iodine status of UK schoolgirls: a cross-sectional survey. Lancet 377:2007–2012
5. Li M, Eastman CJ, Waite KV, Ma G, Zacharin MR, Topliss DJ et al (2006) Are Australian children iodine deficient? Results of the Australian national iodine nutrition study. Med J Aust 184:165–169
6. Zimmermann MB (2011) Iodine deficiency in industrialized countries. Clin Endocrinol (Oxf) 75:287–288
7. van der Haar F, Gerasimov G, Haxton DP, Zimmermann MB (2011) Iodine deficiency in UK schoolgirls. Lancet 378:1623 author reply 1624
8. de Benoist B, McLean E, Andersson M, Rogers L (2008) Iodine deficiency in 2007: global progress since 2003. Food Nutr Bull 29:195–202
9. Gordon RC, Rose MC, Skeaff SA, Gray AR, Morgan KM, Ruffman T (2009) Iodine supplementation improves cognition in mildly iodine-deficient children. Am J Clin Nutr 90:1264–1271
10. Santiago-Fernandez P, Torres-Barahona R, Muela-Martinez JA, Rojo-Martinez G, Garcia-Fuentes E, Garriga MJ et al (2004) Intelligence quotient and iodine intake: a cross-sectional study in children. J Clin Endocrinol Metab 89:3851–3857
11. Zimmermann MB, Connolly K, Bozo M, Bridson J, Rohner F, Grimci L (2006) Iodine supplementation improves cognition in iodine-deficient schoolchildren in Albania: a randomized, controlled, double-blind study. Am J Clin Nutr 83:108–114
12. Shrestha RM (1994) Effect of iodine and iron supplementation on physical, psychomotor and mental development in primary school children in Malawi. Agricultural University, Wageningen, Wageningen
13. Melse-Boonstra A, Jaiswal N (2011) Iodine deficiency in pregnancy, infancy and childhood and its consequences for brain development. Best Pract Res Clin Endocrinol Metab 24:29–38
14. Andersson M, de Benoist B, Darnton-Hill I, Delange F (eds) (2007) Iodine deficiency in Europe: a continuing public health problem. WHO Press, Geneva
15. Gärtner R (2009) Jodversorgung in Deutschland—Was ist noch zu tun? http://www.jodmangel.de/newsletter/newsletter_2009.pdf Accessed 13.09.2012
16. Johner SA, Gunther AL, Remer T (2011) Current trends of 24-h urinary iodine excretion in German schoolchildren and the importance of iodised salt in processed foods. Br J Nutr 106:1749–1756
17. Buyken AE, Alexy U, Kersting M, Remer T (2012) The DONALD cohort: an updated overview on 25 years of research based on the DOrtmund nutritional and anthropometric longitudinally designed study. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 55:875–884
18. Remer T, Neubert A, Maser-Gluth C (2002) Anthropometry-based reference values for 24-h urinary creatinine excretion during growth and their use in endocrine and nutritional research. Am J Clin Nutr 75:561–569
19. Lorenz-Wawschinek O, Tiran B, Eber O, Langsteger W (1994) Photometric determination of iodine in urine. Exp Clin Endocrinol 102:357–358
20. Sichert-Hellert W, Kersting M, Chahda C, Schaefer R, Kroke A (2007) German food composition database for dietary evaluations in children and adolescents. J Food Comp Anal 20:63–70
21. Schofield WN (1985) Predicting basal metabolic rate, new standards and review of previous work. Hum Nutr Clin Nutr 39(Suppl 1):5–41
22. Sichert-Hellert W, Kersting M, Schoch G (1998) Underreporting of energy intake in 1 to 18 year old German children and adolescents. Z Ernahrungswiss 37:242–251
23. Lohman T, Roche A, Martorell R (1988) Anthropometric standardization reference manual. Human Kinetics, Champaign
24. Du Bois D, Du Bois EF (1916) A formula to estimate the approximate surface area if height and weight be known. Arch Int Med 17:863–871
25. Neuhauser H, Schienkiewitz A, Schaffrath Rosario A, Dortschy R, Kurth B (2011) Referenzperzentile für anthropometrische Maßzahlen und Blutdruck aus der Studie zur Gesundheit von Kindern und Jugendlichen in Deutschland (KiGGS) 2003–2006. Robert Koch Institut, Berlin
26. Anke M, Groppel B, Scholz E, Bauch K (1992) Jodaufnahme, Jodausscheidung und Jodbilanz Erwachsener der neuen Bundesländer Deutschlands. In: Anke M, Groppel B, Gürtler H, Grün M, Lombeck I, Schneider H (eds) Mengen- und Spurenelemente, vol 12. Universität Jena, Arbeitstagung, pp 450–461 a
27. Nath SK, Moinier B, Thuillier F, Rongier M, Desjeux JF (1992) Urinary excretion of iodide and fluoride from supplemented food grade salt. Int J Vitam Nutr Res 62:66–72
28. Johner SA, Shi L, Remer T (2010) Higher urine volume results in additional renal iodine loss. Thyroid 20:1391–1397
29. Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham LL, Pirkle JL (2005) Urinary creatinine concentrations in the U.S. population: implications for urinary biologic monitoring measurements. Environ Health Perspect 113:192–200
30. Verbeke G, Molenberghs G (2000) PORC MIXED versus PROC GLM. In: Verbeke G, Molenberghs G (eds) Linear mixed models for longitudinal data. Springer, New York, pp 119–120
31. Food and Nutrition Board, Institute of Medicine (2001) Dietary reference intakes for vitamin A, vitamin K, arsenic, boron,

chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academy Press, Washington

32. Arbeitskreis Jodmangel (2008) Entwicklung der Marktanteile von jodiertem Speise-und Pökelsalz am gesamten Speisesalzabsatz in Großgebinden in Deutschland. http://jodmangel.de/presseinfos/bilder/grossgebinde07.jpg Accessed 13.09.2012

33. Bohac L (2011) The food industry can play an important role in correcting iodine deficiency. IDD Newsletter. p 12–15

34. Johner SA, von Nida K, Jahreis G, Remer T (2012) Aktuelle Untersuchungen zeitlicher Trends und saisonaler Effekte des Jodgehalts in Kuhmilch—Untersuchungen aus Nordrhein Westfalen. Berliner und Münchener Tierärztliche Wochenschrift 125:10–16

35. Food and Nutrition Board, Institute of Medicine (2000) Dietary reference intakes: applications in dietary assessment. National Academic Press, Washington

36. Remer T, Fonteyn N, Alexy U, Berkemeyer S (2006) Longitudinal examination of 24-h urinary iodine excretion in schoolchildren as a sensitive, hydration status-independent research tool for studying iodine status. Am J Clin Nutr 83:639–646

37. Dary O (2011) Time to refine the use of urinary iodine to assess iodine intakes in populations. Br J Nutr 106:1630–1631

38. Wudy SA, Hartmann MF, Remer T (2007) Sexual dimorphism in cortisol secretion starts after age 10 in healthy children: urinary cortisol metabolite excretion rates during growth. Am J Physiol Endocrinol Metab 293:E970–E976

39. Deutsche Gesellschaft für Ernährung (Hrsg.) (2008) Referenzwerte für die Nährstoffzufuhr. Umschau Verlag, Frankfurt a. M

40. Thamm M, Ellert U, Thierfelder W, Liesenkotter KP, Volzke H (2007) Iodine intake in Germany. Results of iodine monitoring in the German Health Interview and Examination survey for children and adolescents (KiGGS) (article in German). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 50:744–749