Analysis of Hair Trace Elements in Children with Autism Spectrum Disorders and Communication Disorders

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Abstract The primary objective of the present study is analysis of hair trace elements content in children with communication disorder (CD) and autism spectrum disorder (ASD). A total of 99 children from control, CD, and ASD groups ($n = 33$) were examined. All children were additionally divided into two subgroups according to age. Hair levels of trace elements were assessed using inductively coupled plasma mass spectrometry. The difference was considered significant at $p < 0.01$. The obtained data demonstrate that children with CD are characterized by significantly increased hair lithium (Li) (96 %; $p = 0.008$), selenium (Se) (66 %; $p < 0.001$), arsenic (As) (96 %; $p = 0.005$), beryllium (Be) (150 %; $p < 0.001$), and cadmium (Cd) (72 %; $p = 0.007$) content, being higher than the respective control values. In the ASD group, hair copper (Cu), iodine (I), and Be levels tended to be lower than the control values. In turn, the scalp hair content of Se significantly exceeded the control values (33 %; $p = 0.004$), whereas the level of iron (Fe) and aluminum (Al) tended to increase. After gradation for age, the most prominent differences in children with CD were detected in the elder group (5–8 years), whereas in the case of ASD—in the younger group (3–4 years old). Taking into account the role of hair as excretory mechanism for certain elements including the toxic ones, it can be proposed that children suffering from ASD are characterized by more profound alteration of metal handling and excretion in comparison to CD.

Keywords Metals · Neurotoxicity · Selenium · Psychiatric disorders · Developmental disorders

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by pervasive deficits in social interaction, impairment in verbal and non-verbal communication, and repetitive patterns of behavior [1]. The incidence of ASD has increased dramatically during the last years [2]. In particular, analysis of data from 1990 to 2001 detected a significant increase in ASD rate from 6.2 cases per 10,000 births to 42.5 in 2001 [2]. In general, the existing studies demonstrated an increase in ASD incidence ranging from 50 to 2000 % [3]. The results of the recent systematic review provide a median of ASD as 62/10,000 [4]. Despite significant progress in diagnostic methods and strategies, improved diagnosis of ASD cannot totally account for the observed increase in ASD rate [2]. The incidence of ASD is highly dependent on geographical location, ethnicity [5], and gender [6]. In particular, multiple studies demonstrated that boys are nearly five times more susceptible to ASD than girls [7].

Communication disorder (CD) is another group of psychiatric developmental disorder [1] with the incidence of 5–10 % in the USA [8]. In particular, the prevalence of CD in Utah was estimated to be 63.4 per 1000, being nearly two times more common in boys than girls [9]. Similar data were obtained in an Australian study [10]. At the same time, detailed

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analysis demonstrated that nearly 4 % of all CD cases are associated with ASD [9].

The etiology of the majority of psychiatric disorders is not clear. In particular, genetic [11], epigenetic [12], environmental factors, as well as gene-environment interactions [13] are considered to be the key factors in psychiatric diseases development. In particular, it has been demonstrated that exposure to organic and inorganic environmental pollutants including heavy metals significantly increase the risk of ASD [14, 15]. Multiple studies have demonstrated the association between toxic trace element content in the hair [16–18], blood compartments [19], nails [20], teeth [21], and urine [22] and ASD. Special attention was devoted to the role of mercury (Hg) in autism [23–25]. Based on the earlier findings, Bernard and the colleagues proposed autism as a novel form of Hg poisoning [26].

Moreover, certain essential trace elements like copper (Cu) may also positively influence the development of ASD [27]. In turn, zinc (Zn) has been demonstrated to play a protective role against neurodevelopmental disorders including ASD though its role in antioxidant and detoxication systems in general and metallothionein system in particular [28, 29].

At the same time, data on trace element status in children with CD are missing. Taking into account the presence of common clinical features (altered communication skills) [30], it is interesting to reveal possible similarities or differences in toxic and essential trace element status in children with CD and ASD. Therefore, the primary objective of the present study is comparative analysis of hair trace elements content in children with CD and ASD.

Materials and Methods

The protocol of the present study was approved by the Local Ethics Committee of the Scientific Center for Mental Health (Russian Academy of Medical Sciences, Moscow, Russia). All procedures were performed in accordance with the principles of the Declaration of Helsinki and later amendments. Children's parents or legal representatives signed the informed consent forms. Sample collection was performed in the presence of parents or legal representatives.

A total of 99 children (boys) aged from 3 to 8 years living in Moscow were enrolled in the present study. Psychiatric diagnosis was verified in the Scientific Center for Mental Health, Russian Academy of Medical Sciences (Moscow, Russia). Thirty-three boys suffering from communication disorders (DSM-IV-TR) [1] (also classified as specific developmental disorders of speech and language (F80) in ICD-10 [31]) as well as 33 age-matched boys with ASD (DSM-IV-TR) [1] (also classified as F84 in ICD-10 [31]) were examined. The control group was presented by 33 age-matched healthy neurotypical boys. Data on the absence of psychiatric disorders in the controls were obtained from the results of

regular mandatory psychiatric examination of children. The mean age in the control, CD, and ASD group was 5.0 ± 1.7, 5.0 ± 1.8, and 5.0 ± 1.7 years old, respectively. Further, each group of children was divided into two subgroups with age limits of 3–4 (16 persons for each group) and 5–8 years old (17 persons for each group).

In order to prevent the influence of side factors on hair trace element content, the following exclusion criteria were used: the presence of neuropsychiatric disorders (except CD and ASD for the respective groups) including abnormal eating behaviors (ICD-10: F50), vegetarianism, endocrine disorders, metallic implants (including dental fillings), acute traumas and inflammatory diseases, and the use of mineral supplements.

At the day of sampling, all children washed their hair using their usual shampoos. Occipital scalp hair samples were collected using ethanol-precleaned stainless steel scissors in a quantity of 0.05–0.1 g. Only proximal parts of strands were used for analysis. In the laboratory, the obtained samples were washed with acetone, rinsed three times with double distilled water, and subsequently dried on air at 60 °C.

Microwave digestion was used for homogenization of the collected samples. In particular, 0.05 g of cleaned hair strands were introduced into Teflon tubes with concentrated HNO_3 and loaded into Berghof Speedwave 4 (Berghof Products & Instruments, Germany) system. Microwave digestion was performed for 20 min at the maximal temperature of 170–180 °C. After cooling to a room temperature, the obtained solutions were added with distilled deionized water to a total volume of 15 ml. The resulting samples were used for analysis of cobalt (Co), copper (Cu), iron (Fe), iodine (I), lithium (Li), manganese (Mn), selenium (Se), silicon (Si), zinc (Zn), aluminum (Al), arsenic (As), beryllium (Be), cadmium (Cd), mercury (Hg), nickel (Ni), lead (Pb), and tin (Sn) content by means of inductively coupled plasma mass spectrometry. The analysis was performed at NexION 300D (PerkinElmer Inc., Shelton, CT 06484, USA) equipped with ESI SC-2 DX4 autosampler (Elemental Scientific Inc., Omaha, NE 68122, USA).

Calibration of the system was performed using standard solutions of trace elements prepared from the Universal Data Acquisition Standards Kit (PerkinElmer Inc., Shelton, CT 06484, USA). Internal online standardization was performed using Yttrium (Y) Pure Single-Element Standard (PerkinElmer Inc., Shelton, CT 06484, USA). Laboratory quality control was performed using control analysis of certified reference material of human hair GBW09101 (Shanghai Institute of Nuclear Research, Shanghai, China). The recovery rates for all analyzed trace elements exceeded 90 % during the whole period of investigation.

The obtained data were processed using Statistica 10.0 (Statsoft, Tulsa, OK, USA) software. Shapiro-Wilk test demonstrated non-Gaussian distribution of the obtained data both in the general cohort of children and individual groups (control; CD; ASD). Therefore, median and the respective 25 and

75 % boundaries and Mann-Whitney *U* test were used for data expression and group comparisons, respectively. Correlation analysis was performed using Spearman rank correlation coefficient. The level of significance was set as $p < 0.01$ for all analyses.

Results

The obtained data demonstrate that both essential (Fig. 1) and toxic (Fig. 2) hair trace element content in a general cohort of children is affected by both CD and ASD. In particular, children with CD are characterized by significantly increased hair Li, Se, As, Be, and Cd content, being higher than the respective control values by 96 % ($p = 0.008$), 66 % ($p < 0.001$), 96 % ($p = 0.005$), 150 % ($p < 0.001$), and 72 % ($p = 0.007$).

The level of I and Si also tended to increase in CD children. At the same time, no significant group difference was detected for hair Co, Cu, Mn, Zn, Al, Hg, Ni, Pb, and Sn levels.

Hair trace elements content in a general cohort of children with ASD was differentially related to the control values as compared to the ones with CD. Particularly, hair Cu, I, and Be levels tended to decrease in comparison to the control values, although being only nearly significant. Scalp hair content of Se was significantly elevated by 33 % ($p = 0.004$) in comparison to the control values, respectively. In turn, the levels of Fe and Al in hair of ASD children were only nearly significantly higher in comparison to the respective control values by 34 % ($p = 0.021$) and 24 % ($p = 0.034$).

Comparative analysis of hair trace elements content in children with both pathologies demonstrated that essential and toxic trace element levels in hair of the examinees with CD
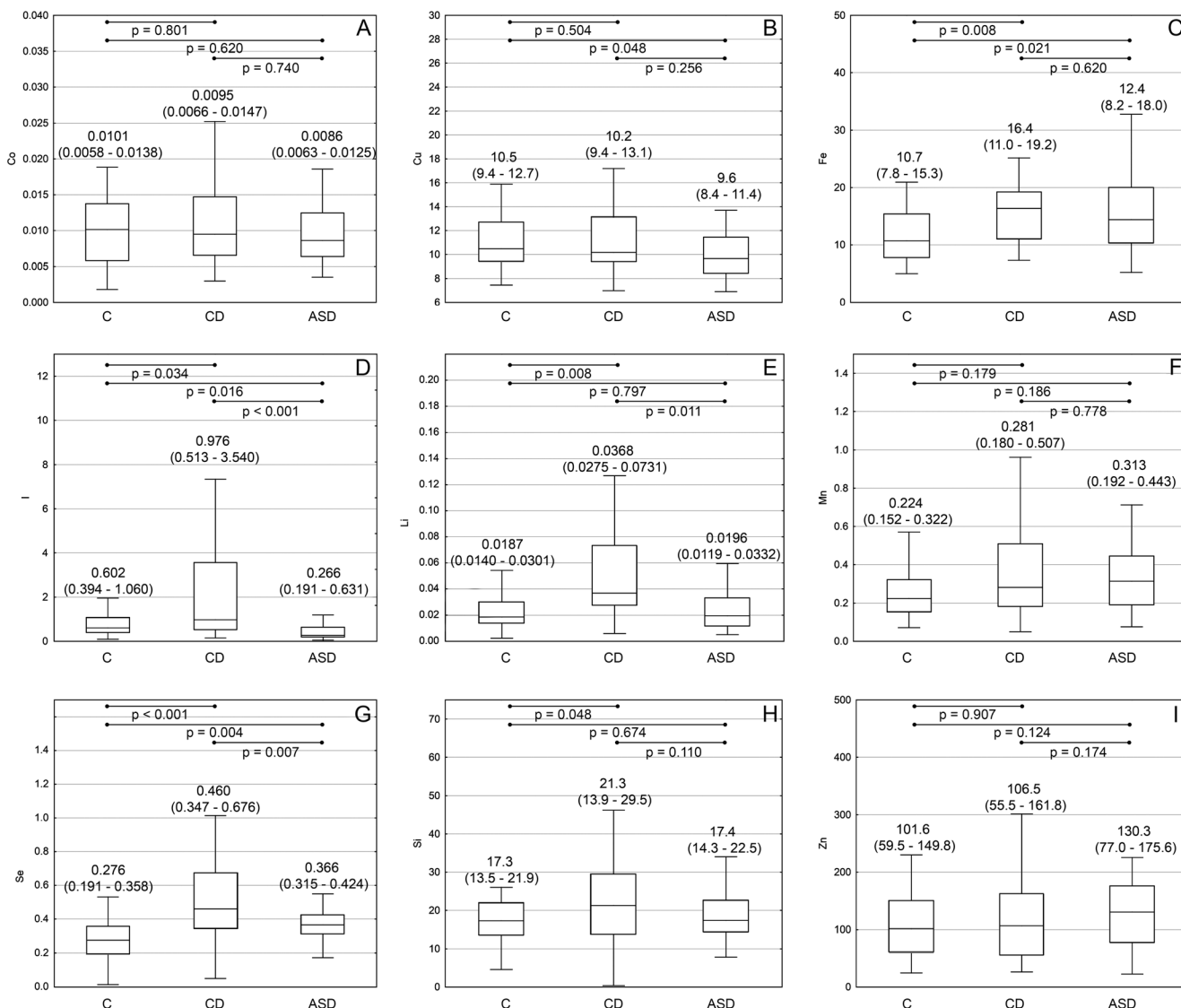
Fig. 1 Essential hair trace element content (µg/g) in children with ASD, CD, and age-matched controlsData expressed as median (line) and 25 - 75 percentile boundaries (box)

Fig. 2 Toxic hair trace element content (μg/g) in children with neurodevelopmental disorders and neurotypical controlsData expressed as median (line) and 25 - 75 percentile boundaries (box)
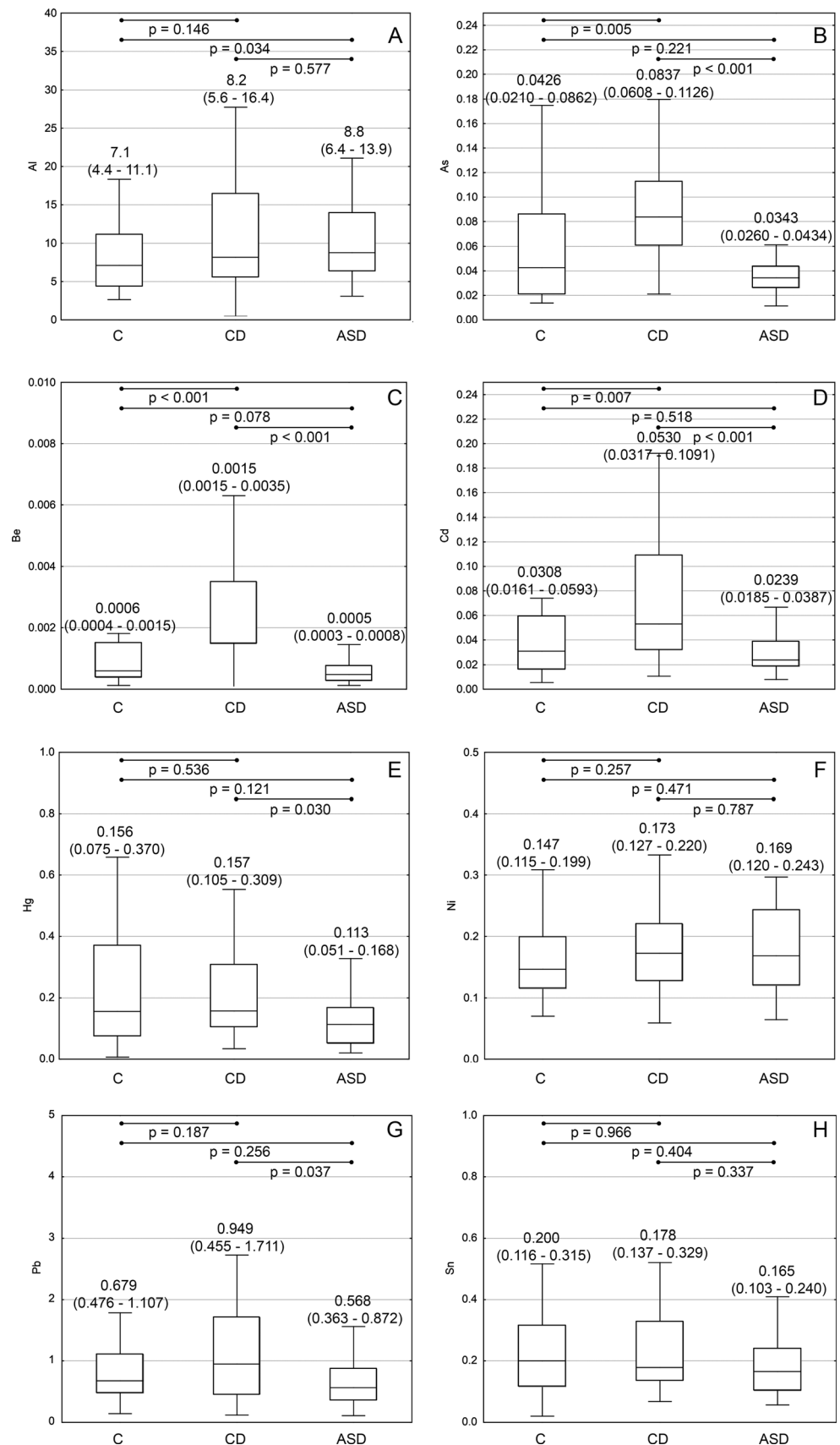
were significantly higher than those in the ASD. The most pronounced difference was detected for hair I, As, Be, and Cd, being lower in ASD children by a factor of more than three ($p < 0.001$), two ($p < 0.001$), three ($p < 0.001$), and two ($p < 0.001$), respectively. Moreover, children with ASD were characterized by significantly decreased hair Se levels (20 %, $p = 0.007$) as compared to the CD values. At the same time, scalp hair Li, Hg, and Pb content were nearly significantly lower than the values in CD children by 47 % ($p = 0.011$), 28 % ($p = 0.030$), and 40 % ($p = 0.037$), respectively.

Children with communication disorders aged 3–4 years are characterized by a rather stable hair trace element profile (Table 1). Only hair Ni levels were significantly 48 % ($p = 0.007$) higher than compared to the respective control values, whereas Be levels only tended to increase (20 %; $p = 0.044$). The obtained data demonstrate that hair trace element content in children with ASD aged 3–4 years was more variable. Hair Be levels in children with ASD were threefold lower ($p = 0.002$) than in the neurotypical ones. At the same time, hair Fe levels exceeded the control group values by 43 % ($p = 0.009$). Nearly significant difference with respect to the control values in ASD children was detected for hair Al (+29 %; $p = 0.034$), I (−34 %; $p = 0.031$), and As (−55 %; $p = 0.038$) levels.

Comparative analysis of CD and ASD group revealed a tendency to decreased hair I (38 % ($p = 0.028$)) and Se (22 % ($p = 0.046$)) content in the latter. At the same time, hair levels of As and Be in the children suffering from ASD were

decreased by a factor of more than two ($p < 0.001$) and three ($p < 0.001$), as compared to the respective CD group values.

In children aged 5–8 years, opposite tendencies were detected (Table 2). In particular, elder children with CD without autism were characterized by nearly twofold higher hair levels of I ($p = 0.018$), Li ($p < 0.001$), Se ($p < 0.001$), As ($p = 0.003$), and Cd ($p = 0.028$). At the same time, hair content of Be in children suffering from exceeded the control levels by a factor of three ($p = 0.002$). In turn, ASD patients were characterized by a rather stable hair trace element spectrum. Only hair Se content in ASD children significantly exceeded the control values by 77 % ($p = 0.007$). At the same time, hair Cu and Pb levels were 18 % ($p = 0.011$) and 41 % ($p = 0.038$) lower than compared to the control values. Children with communication disorders were characterized by more than fourfold higher level of hair I as compared to the ASD group values ($p = 0.004$). Hair content of Li was also 82 % ($p = 0.001$) higher than that in ASD group. The level of Se and Pb was only nearly significantly higher by 11 % ($p = 0.044$) and 42 % ($p = 0.046$). The level of As ($p = 0.001$), Be ($p < 0.001$), and Cd ($p < 0.001$) in CD group exceeded the respective ASD values by a factor of more than two.

Correlation analysis (Table 3) revealed a significant inverse correlation between hair Al, As, Hg, Ni, Sn, and age values in a general cohort of children, whereas only hair Zn was directly interrelated with age at a significant level. At the same time, assessment of correlation between age and trace elements in

Table 1 Comparative analysis of hair trace elements content (µg/g) in the youngest group of children (3–4 years) without neuropsychiatric disorders, with communication disorders, and autism spectrum disorders

Element	Control ($n = 16$)	CD ($n = 16$)	ASD ($n = 16$)
Co	0.0090 (0.0055–0.0151)	0.0106 (0.0068–0.0171)	0.0111 (0.0086–0.0157)
Cu	10.4 (9.6–11.7)	10.2 (8.6–18.1)	10.6 (8.8–12.5)
Fe	11.2 (8.9–19.7)	16.9 (12.6–19.1)	16.0 (11.5–22.9)*
I	0.719 (0.523–1.381)	0.774 (0.489–3.269)	0.473 (0.182–0.700)
Li	0.0213 (0.0142–0.0422)	0.0480 (0.0060–0.0757)	0.0165 (0.0119–0.0470)
Mn	0.165 (0.146–0.409)	0.281 (0.145–0.920)	0.326 (0.195–0.469)
Se	0.310 (0.224–0.459)	0.468 (0.357–0.640)	0.364 (0.317–0.407)
Si	16.6 (14.2–19.7)	21.3 (16.8–32.2)	17.4 (14.9–22.8)
Zn	70.3 (55.0–119.1)	77.6 (29.9–111.7)	77.0 (63.8–141.8)
Al	6.8 (4.6–11.2)	9.6 (6.2–17.5)	8.8 (7.4–19.1)*
As	0.0787 (0.0290–0.1506)	0.0868 (0.0684–0.1308)	0.0391 (0.0284–0.0591)[†]
Be	0.0015 (0.0005–0.0015)	0.0018 (0.0015–0.0049)	0.0005 (0.0003–0.0007)[†]
Cd	0.0343 (0.0160–0.0513)	0.0554 (0.0321–0.0988)	0.0277 (0.0224–0.0617)[†]
Hg	0.166 (0.085–0.426)	0.152 (0.109–0.452)	0.116 (0.066–0.203)
Ni	0.139 (0.110–0.199)	0.206 (0.159–0.401)*	0.198 (0.138–0.270)
Pb	0.600 (0.450–1.027)	1.344 (0.435–1.516)	0.717 (0.547–1.273)
Sn	0.260 (0.193–0.339)	0.228 (0.160–0.412)	0.240 (0.133–0.464)

Data expressed as median (25–75)

CD communication disorders, *ASD* autism spectrum disorders

*Significant difference in comparison to the control group values at $p < 0.01$

[†] Significant difference in comparison to the CD group values at $p < 0.01$

Table 2 The level of hair trace elements (μg/g) in the elder neurotypical children and examinees with communication disorders and autism spectrum disorders

Element	Control (n = 17)	CD (n = 17)	ASD (n = 17)
Co	0.0115 (0.0061–0.0138)	0.0085 (0.0059–0.0123)	0.0068 (0.0048–0.0104)
Cu	10.6 (9.4–15.9)	9.9 (9.4–12.2)	8.7 (8.2–11.1)
Fe	10.6 (7.6–14.2)	14.3 (10.1–20.9)	10.5 (8.8–15.7)
I	0.477 (0.190–0.800)	1.058 (0.692–3.540)*	0.236 (0.191–0.421)[†]
Li	0.0157 (0.0110–0.0256)	0.0368 (0.0299–0.0731)*	0.0202 (0.0115–0.0290)[†]
Mn	0.266 (0.205–0.322)	0.336 (0.190–0.485)	0.241 (0.174–0.340)
Se	0.229 (0.191–0.304)	0.451 (0.347–0.676)*	0.406 (0.253–0.437)*
Si	18.9 (11.8–22.2)	21.2 (12.0–29.4)	17.3 (12.4–22.5)
Zn	118.1 (89.1–174.3)	124.1 (104.4–164.6)	153.2 (117.3–202.0)
Al	7.3 (4.4–11.0)	8.1 (5.3–11.2)	9.2 (5.3–11.8)
As	0.0291 (0.0199–0.0441)	0.0771 (0.0593–0.0913)*	0.0301 (0.0250–0.0408)†
Be	0.0005 (0.0004–0.0008)	0.0015 (0.0015–0.0015)*	0.0006 (0.0003–0.0008)†
Cd	0.0286 (0.0168–0.0593)	0.0526 (0.0317–0.1337)	0.0222 (0.0149–0.0297)†
Hg	0.149 (0.062–0.243)	0.170 (0.094–0.295)	0.097 (0.049–0.168)
Ni	0.154 (0.130–0.193)	0.168 (0.082–0.177)	0.155 (0.086–0.221)
Pb	0.791 (0.476–1.107)	0.659 (0.455–1.747)	0.463 (0.210–0.612)
Sn	0.168 (0.088–0.291)	0.164 (0.105–0.273)	0.113 (0.087–0.179)

Data expressed as median (25–75)

CD communication disorders, ASD autism spectrum disorders

*Significant difference in comparison to the control group values at $p < 0.05$

[†] Significant difference in comparison to the CD group values at $p < 0.05$

individual groups revealed different relationships. In particular, in healthy neurotypical children, hair Cu was directly

Table 3 Correlation between hair trace elements content and age values in different groups of children

Element	Total	Control	CD	ASD
Co	−0.160	−0.065	−0.253	−0.443*
Cu	0.077	0.398*	−0.387*	−0.406*
Fe	−0.036	−0.060	0.157	−0.233
I	−0.033	−0.144	−0.148	0.327
Li	−0.037	−0.227	0.045	−0.019
Mn	−0.115	−0.105	−0.083	−0.274
Se	0.175	−0.354*	0.149	0.322
Si	−0.074	−0.125	−0.108	0.091
Zn	0.356*	0.344*	0.342*	0.433*
Al	−0.248*	−0.121	−0.286	−0.389*
As	−0.296*	−0.399*	−0.375*	−0.157
Be	0.216*	−0.413*	0.414*	0.185
Cd	0.001	−0.163	0.175	−0.142
Hg	−0.200*	−0.247	−0.258	−0.102
Ni	−0.237*	0.064	−0.465*	−0.145
Pb	−0.097	−0.059	−0.076	−0.260
Sn	−0.358*	−0.248	−0.477*	−0.357*

Data presented as correlation coefficients (r)

CD communication disorders, ASD autism spectrum disorders

*Correlation is significant at $p < 0.05$

related to age, whereas hair As, Be, and Se levels inversely correlated with age values. Oppositely, hair Be was directly related to age in children with CD, whereas hair As, Ni, and Sn were characterized by an inverse association with the parameter. In ASD children Al, Co, Cu, and Sn negatively correlated with age values. It is notable that hair Zn was directly associated with age in all groups of children.

Discussion

Generally, the obtained data demonstrate that both CD and ASD are characterized by altered trace element status as assessed by chemical analysis of scalp hair. In particular, children with ASD are characterized by a significant decrease of hair toxic trace elements content as compared to the control values. Oppositely, patients suffering from CD had significantly elevated levels of toxic trace elements in scalp hair strands. Similar trends were detected for essential trace elements. However, a significant increase in hair Se content was observed both in ASD and CD patients, being maximal in the latter.

In detail, in the present study, we detected significantly lower levels of hair Cu and I in children with ASD. The existing data demonstrate that the incidence of deficiency of all essential trace elements except Zn, Mg, and Ca is only 2 % or less [32]. At the same time, a significant association between iodine deficiency [33] and parameters of iodine status

[16, 34] and ASD has been detected. In turn, children with CD are characterized by a significant elevation of hair Fe, I, Li, and Si content. All of these trace elements were shown to have a significant impact on nervous system through modulation of neurotoxicity [35–37]. However, the role of these trace elements in pathogenesis of CD is still to be estimated.

In contrast to other essential trace elements, hair Se was significantly increased in children with both ASD and CD. The majority of the existing studies [17, 20] demonstrated a significant decrease in hair Se levels in patients with ASD. At the same time, our findings correspond to other indications of increased hair Se levels in children suffering from ASD [38, 39]. However, the role of Se in ASD is not clear. Earlier data demonstrate that Se may be neurotoxic in the case of environmental overexposure [40]. Based on these results, one can suppose that Se neurotoxicity may also play a significant role in ASD and CD development. However, Russia is not characterized by the presence of seleniferous areas [41] and, therefore, the risk of environmental Se overexposure is rather low. Moreover, earlier, we have detected a simultaneous decrease in serum Se levels in ASD patients [42]. Therefore, elevated hair Se in persons with low serum Se may be indicative of increased metalloid excretion as its incorporation into the hair is irreversible and may be considered as an excretion route [43].

It is also notable, that no significant group difference in hair Zn content was observed. Moreover, correlation analysis revealed similar correlation coefficients between hair Zn levels and age values for all studied groups of children, being indicative of the absence of severe alterations of Zn metabolism in both disorders. These findings are in contrast to the earlier studies demonstrating the role of Zn deficiency and altered Zn metabolism in ASD [29, 44]. However, a previous study also failed to detect a significant association between ASD and low Zn content in whole blood and erythrocytes [45]. The absence of significant alteration of Zn metabolism in the present study may be at least partially associated with the rather high Zn supply and low risk of Zn deficiency in Russia [46].

The obtained data demonstrate a significant differential alteration of hair toxic trace element content in ASD and CD patients. Despite the presence of multiple studies in this field, the results are contradictory, indicating increased, decreased, or unaffected hair heavy metal levels [47] Therefore, comparison of the current findings with the existing data is complicated. Therefore, we shall in brief review the studies being both in agreement and disagreement with the obtained results.

A significant increase in hair Al content in ASD children was observed, being in agreement with the earlier studies [17, 48] Moreover, it has been noted that a direct association between Al exposure and the incidence of ASD exist [49, 50]. At the same time, earlier study by Adams and the coauthors (2006) detected a significant decrease in hair metal levels in ASD [16].

Surprisingly, Al was the only toxic trace element being increased in hair of children suffering from ASD in the present study. In particular, the level of other toxic trace elements (As, Be, Cd, Pb) was significantly lower in ASD patients than in healthy children.

In contrast to these findings, earlier studies have demonstrated a significant accumulation of heavy metals in scalp hair in ASD [17, 47, 51, 52]. At the same time, two recent studies performed in Italy failed to detect any significant changes in hair trace elements content between ASD and control children [53, 54]. These studies confirmed the earlier findings of Adams and the colleagues (2006) who did not observe a significant difference between ASD and control levels of heavy metals [16]. Finally, certain studies demonstrated significantly decreased levels of toxic trace elements in children with autism. In particular, significantly lower Hg levels were detected in first baby haircuts of children with ASD [55, 56]. At the same time, our findings totally correspond to the earlier data obtained by Kern et al. (2007) who revealed significantly decreased hair As, Cd, and Pb levels in patients suffering from ASD when compared to the control values [57].

It is supposed that decreased hair toxic trace elements content in children with ASD aged 1–2 years may be indicative of impaired heavy metal detoxication and excretion [56], and, therefore, their sequestration in the brain as proposed in the study of children 1–6 years [57]. From this point of view, elevated hair trace elements levels in children with communication disorders without ASD may be indicative of increased heavy metal body burden but normal ability of the organism to excrete toxic trace elements and counteract their toxicity. However, further detailed analysis including assessment of trace element levels in different biological substrates (serum, urine) are required to support the hypothesis and the difference in excretory ability in children with CD and ASD.

The obtained data demonstrate that the alteration of trace elements content in both CD and ASD is age dependent. In particular, it has been noted that the most prominent difference from the control values in ASD was observed in the youngest group of children (3–4 years old), whereas in the case of CD—in the older ones (5–8 years old). These data are partially in agreement with Majewska et al. (2010) who revealed age-specific changes in hair Hg content in ASD [58]. In particular, the younger children with ASD were characterized by a significantly lower hair Hg levels and the older ones had higher hair metal content as compared to the control values [58]. Hypothetically, the observed differences may be explained by age-related differences in detoxification systems [59]. The observed difference in correlation between hair trace elements and age values also demonstrate the alteration of metal handling in children with the studied disorders.

Therefore, the obtained data demonstrate:

1. Children with CD are characterized by increased hair Li, As, Be, and Cd content with the maximal difference from the controls in the age of 5–8 years.

2. The level of Cu, I, As, Be, and Cd tended to decrease, whereas Al and Fe content tended to increase in children with ASD, being the most expressed in the youngest group (3–4 years old)

3. Hair Se levels are significantly elevated both in ASD and CD.

Compliance with Ethical Standards

Conflict of Interest   The authors declare that they have no conflict of interest.

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