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Comparison of Concentrations of Some Trace, Bulk, and Toxic Metals in the Hair of Normal and Dyslexic Children

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Hair from dyslexic children, analyzed by flameless atomic absorption spectrometry, showed significantly higher concentrations of magnesium and copper than did hair from control subjects. The hair from dyslexic children also contained significantly higher concentrations of aluminum and cadmium than that from control children; the cadmium concentration exceeded the normal acceptable range. There were no significant differences in the case of lead, calcium, selenium, or mercury. Our results indicate that excessive cadmium burden could be implicated in this form of learning disorder.

Additional Keyphrases: *magnesium · copper · aluminum · cadmium · mercury · zinc · selenium · calcium · lead · atomic absorption spectroscopy · reference intervals · pediatric chemistry*

Many pathological conditions are characterized by gross abnormalities in trace- and bulk-element concentrations (*1*, *2*). Determination of the status of some metals in serum, especially those subject to diurnal variation such as zinc, is at best uncertain (*3*, *4*). For example, the zinc concentration depends highly on the serum albumin concentration (*5*). Furthermore, the amount of toxic metals assayed in whole blood is largely a function of hepatic metallothionein production (*6*).

Several reports have associated the presence of hitherto "subtoxic" concentrations of various non-nutrient metals with behavioral and learning disabilities in children (*7–11*). Thus, to determine accurately the presence of low concentrations of toxic metals and abnormalities in the balance of trace elements, other tissues are being analyzed in search of reliable indicators of metal status. Analysis of the metal content of hair provides a longer record of trace-element metabolism, because the hair grows, on the average, about 1–2 cm a month (*11*). Diurnal fluctuations are irrelevant to the elemental concentrations in this matrix (*12–14*). Hair has been demonstrated to be a major vehicle for the excretion of toxic metals, which may be concentrated to 10-fold the amount found in blood or urine (*13*). In the present study we examined the metal content of hair of dyslexic children and of their peers with no apparent learning disabilities. We assayed as many of the trace and bulk elements as the sample size permitted and also some toxic metals, especially those associated with neuropathies: lead, mercury, and aluminum.

Subjects and Methods

Subjects. The dyslexic subjects included in this study were of ages 11–15 years, of IQ 90–138 (Wechsler Intelligence Scale for Children), and were attending special educational centers: The Language Development Centre, Eastbourne, Sussex, U.K., and Grenville College, Bideford, Devon, U.K. The control subjects were of the same age and IQ range, attending Comprehensive Schools in Crowborough, Sussex, U.K., and Havering, Essex, U.K.

Sampling. The hair was obtained from the central region of the nape of the neck. The samples were cut and secured at the distal end. The first 2 cm from the scalp end of each sample was severed and analyzed in the manner described.

Materials. "Absorption spectroscopy grade" standard solutions of each of the metals analyzed in this study, nickel nitrate (to assist in selenium determination), PrimaR® nitric acid, perchloric acid, and hydrogen peroxide were purchased from Fisons, Loughborough, Leics., U.K.

Assays. Individual hair samples of known weight (about 50 mg), in duplicate, were soaked in 3 g/L surfactant solution (Triton X-100) for 30 min in acid-washed test tubes. The detergent was discarded and the hair washed a further three times with fresh detergent solution. Duplicate samples of hair intended for calcium or magnesium analysis were not treated with detergent but instead subjected to 2 h of Soxhlet extraction in an equivolume mixture of absolute ethanol and diethyl ether. The solvent was allowed to cool, discarded, and these and the detergent-washed hair samples were then rinsed three times with triply-distilled de-ionized water before being dried in an oven at 50 °C.

The dry hair samples were weighed and placed in microKjeldahl flasks to which was added 12 mL of spectroscopic grade nitric acid. Each flask was left for about 30 min for the reaction to occur, 2 mL of perchloric acid was added to each, and the mixture was heated and evaporated to about 3 mL. After cooling, the solution in each flask was diluted to 10 mL with triply-distilled water. We determined the metals in the solution by atomic absorption spectrometry, using the method of standard additions, except in the case of selenium, where the hair was digested and analyzed as previously (*15*) described. Reagent blanks were run with each batch of samples.

Equipment. An Instrumentation Laboratory (Warrington, Cheshire, U.K.) Model 157 atomic absorption spectrometer, equipped with a Model 555 electrothermal furnace, was used for elemental analyses, with a Linseis (Selb, F.R.G.) Model LS4 twin-channel chart recorder. The hollow-cathode lamps and all other accessories were supplied by Instrumentation Laboratory.

Statistical analyses. We compared elemental concentrations in the hair of dyslexic and normal individuals by Wilcoxon's unpaired rank sum nonparametric analysis; differences were considered significant when p was <0.05.

Results

Table 1 lists the concentrations of some trace, bulk, and toxic metals in the hair of normal and dyslexic children. The mean zinc concentration of the hair of the dyslexic subjects exceeded the normal reported range but was not statistically significantly higher than the control value.

Although copper and magnesium concentrations in the hair of the dyslexic subjects were within the normal reported range, they were significantly higher than those of the control subjects. The toxic elements aluminum and cadmium were excreted in significantly higher quantities in the hair of dys-

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Table 1. Concentrations of Some Elements in the Hair of Dyslexic and Control Children

Element	Dyslexic		Control	
	Concn, μg/g hair			
Calcium	220	(120–803)	380	(211–1008)
Magnesium	56	(26–125)	32	(6–87)[a]
Zinc	313	(126–1,111)	220	(86–522)
Copper	57	(21–107)	31	(8–78)[a]
Selenium	1.1	(0.3–3.2)	0.6	(0.4–0.9)
Aluminum	2.3	(0.4–5.9)	1.3	(0.3–3.5)[a]
Cadmium	2.59	(0–15.0)	0.10	(0–2.7)[a]
Lead	16	(4.1–45.0)	29	(3.3–69.1)
Mercury	2.1	(0–8.9)	1.1	(0–5.5)

Results quoted are the means with the range of results in parentheses. Statistical comparison between the observations (73 dyslexic and 44 controls) were made by Wilcoxon's nonparametric test.

[a] Significantly ($p < 0.05$) different from control.

lexics. The hair of the dyslexic children contained an average of 25-fold as much cadmium as that of the normal subjects, the mean value for this element in dyslexics being in excess of the normal reported range (*14*). About 81% of the dyslexic subjects had detectable cadmium (>0.05 μg/g hair), as compared with only 25% of the control subjects.

The concentrations of all the other elements measured—calcium, selenium, lead, and mercury—were within the normal reported ranges and there were no statistically significant differences between the hair of the dyslexic and control subjects.

Discussion

Perhaps the most significant observation in the present experiment is the above-normal cadmium concentration in the hair of dyslexic subjects. A previous report (*10*) in which the concentrations of 14 elements were determined in the hair of children with learning disabilities, also described increased concentrations of several toxic metals, including lead and cadmium. Clearly, the interpretation of these results requires caution and hinges upon the relationship between the concentrations of the elements in hair and the body burden of the element.

A major criticism of hair analysis in the past has been the wide interlaboratory variation in results (*13*, *14*). In recent years, as the potential of this easily accessible material has been recognized, many of the factors responsible for previous analytical errors have been described and may be technically eliminated. Thus, in the present study the hair of the control group and the dyslexics was sampled from the same region of the body, because elemental content may differ in distinct anatomical regions (*13*). The hair analyzed in the present study was sampled from the scalp end, to lessen the effect of changing elemental concentrations along the hair shaft (*13*). As far as was possible, the dyslexic and control groups were individually matched with respect to age, sex, IQ, and hair color of the donors, and identical reagents and techniques were used in the digestion process. Hair from persons who had used dyes or other reagents likely to influence hair elemental content was not included in the study. In addition, every effort was made to eliminate the geographical variations in trace-element exposure inherent in this experiment (*1*), and thus the largest group of both control and dyslexic children were resident in the same county (Sussex) at the time of sampling. The influences of dietary or socioeconomic variations between the two groups were restricted, we believed, by the large population size included in the study.

Several experimental and clinical studies have recommended hair copper analysis as a good indicator of body, especially hepatic, copper content (*4*, *16*), whereas hair zinc reflects nutriture rather than the tissue status of this element (*4*). Increased copper and decreased zinc in brain tissue have been associated with schizophrenia (*17*). However, increased hair copper has been reported in several pathological conditions, including anemia, hepatitis, hyperthyrosis, and nephrocalcinosis, but not, paradoxically, Wilson's disease (*18*). Thus, although an increased concentration of copper in hair is likely to be a valid indication of the body burden, hypercupremia is a relatively unspecific condition, so that interpretation of the significance of this finding is very difficult. Similarly, the significantly increased magnesium content of the hair of dyslexic children could indicate increased excretion, and consequently, either a lower body-metal content or an increased body burden of this bulk element. Decreased serum magnesium and calcium have been reported in behavioral disorders and schizophrenia (*20*). Low brain magnesium and, indeed, calcium have been demonstrated to influence the metabolism of some of the most important neurotransmitters in the brain (*21*).

Interpretation of the increased excretion of toxic elements in the hair is less complex; increased brain aluminum, for example, has been associated with various encephalopathies (*21*). Aluminum is also reportedly increased in Alzheimer's disease (*22*), although this may be less significant, because this element also accumulates in the brain with increasing age (*23*).

The presence of what was hitherto assumed to be "subtoxic" concentrations of lead is generally accepted as a contributory if not causative factor in various learning and behavioral disorders (*8–11*, *25*). Hair lead has been demonstrated, both experimentally and clinically, to be a good indicator of body burden. Indeed, hair concentrates lead to a greater extent than does any other tissue, including bone (*14*, *24*). Cadmium is an extremely toxic element not usually associated with neurotoxicity, its main toxic actions being exerted on the heart, liver, and kidneys (*2*, *6*). A possible way in which cadmium might influence the learning ability of the dyslexic children is as an antimetabolite, because this element interferes with the absorption of zinc, iron, copper, and calcium and decreases ceruloplasmin and ferritin concentrations (*26*). Although the cadmium content of hair reportedly is a reliable indicator of body exposure to this metal, a recent experimental study (*24*) has demonstrated that in young rats hair analysis yielded a falsely high (by two- or threefold) index of exposure. The placenta forms an efficient barrier to cadmium penetration, but it is estimated that a child retains a third of its normal lifetime accumulation during the first three years of life (*26*).

In conclusion, the higher cadmium content excreted in the hair of the dyslexic children could be an important observation with regard to the origin of this condition. Confirmation of this observation must be the first priority, however, and this requires further sampling of other tissues that would provide a reliable record of previous exposure, such as dental material.

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