

Age-Related Changes in Cadmium Content and Oxidative Modification of Proteins in Different Regions of Human Spinal Cord

I. A. Volchegorskii, I. B. Telesheva, and V. V. Turygin

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 137, No. 5, pp. 504-506, May, 2004
Original article submitted June 10, 2003

A direct correlation was found between the content of oxidative protein modification products in the cervical enlargement of the spinal cord and age in humans. We revealed a considerable increase in Cd^{2+} concentrations in elderly and old people and an increase in Fe^{2+} concentration in old people. In the lumbosacral enlargement Cd^{2+} concentration was maximum and did not vary with age. The content of oxidative protein modification products significantly increased in the lumbosacral enlargement in older adults and old people. Moreover, old people had high content of Cu^{2+} in the lumbosacral enlargement. Our findings suggest that accumulation of Cd^{2+} play a role in the metabolism of Cu^{2+} and Fe^{2+} , which contributes to age-related intensification of oxidative protein modification in the spinal cord.

Key Words: cadmium; copper; iron; oxidative modification of proteins; spinal; cord

Cadmium (Cd^{2+}) compounds are widely distributed in nature and continuously enter the human organism. Cd^{2+} is accumulated in the liver, kidneys and, to a lesser extent, in the central nervous system (CNS, ~0.2%) [4]. At the same time, Cd^{2+} accumulated in the brain is characterized by pronounced neurotoxicity, which is associated with its effect on metabolism of essential trace elements (Fe^{2+} and Cu^{2+}) and intensification of lipid peroxidation in the nervous tissue [6]. The age-related decrease in the resistance of spinal cord (SC) lipids to oxidative stress is probably mediated by the same mechanism [2]. It cannot be excluded that the neurotoxic effect of Cd^{2+} is related to oxidative modification of proteins (OMP), which underlies metal-produced damage to biological membranes under conditions of oxidative stress [3]. Here we compared age-related changes in the contents of Cd^{2+} , Fe^{2+} , and Cu^{2+} and intensity of OMP in different regions of human SC.

MATERIALS AND METHODS

Preparations of SC were obtained during autopsy of 40 human cadavers (26 men and 14 women, 22-95 years). The people died from traumas or diseases not associated with injury of CNS. Autopsy specimens were taken not later than 12 h after death. There were 4 age groups: younger adults (women, 21-35 years; men, 22-35 years); older adults (women, 36-55 years; men, 36-60 years); elderly (women, 56-74 years; men, 61-74 years); and old people (above 75 years).

The concentration of Cd^{2+} , Fe^{2+} , and Cu^{2+} and content of OMP products were measured in the cervical and lumbosacral enlargement (LSE) and thoracic SC. The content of metals was estimated by the method of atomic absorption spectrometry on a Kvant-Z.ETA atomic absorption spectrometer. The content of OMP products was expressed in mmol protein-bound 2,4-dinitrophenylhydrazones per 1 g tissue [3].

The results were analyzed by Student's *t* test and nonparametric Mann—Whitney test Wald—Wolfowitz test, and Kolmogorov—Smirnov test. Correlation

Chelyabinsk State Medical Academy. **Address for correspondence:** volcheg@yandex.ru. Volchegorskii I. A.

analysis was performed to evaluate the dependence of test parameters on the age of people.

RESULTS

Cd²⁺ concentration was maximum in LSE of SC (Table 1). In all age groups (except for elderly) the relative concentration of Cd²⁺ in LSE was higher than in the cervical enlargement. The content of Cu²⁺ was maximum in the thoracic SC and significantly surpassed that in the cervical enlargement (except for old people) and LSE. No age-related differences were found in Fe²⁺ concentration in different regions of SC.

Cd²⁺ concentration in the cervical enlargement increased with age. The content of this metal peaked in elderly and old people (126-134% of that in younger adults, Table 1). Correlation analysis revealed a direct correlation between Cd²⁺ concentration in the cervical enlargement and age of people ($r=0.532$, $p<0.05$). No correlations were found in other regions of SC. Accumulation of Cd²⁺ was accompanied by an increase in Fe²⁺ concentration in the cervical enlargement of SC. Fe²⁺ concentration in the cervical enlargement in old people surpassed that in elderly (Table 1). Our results are consistent with the data on accumulation of Cd²⁺ and Fe²⁺ in the brain of rats during experimental poisoning with Cd²⁺ [6]. The increase in Fe²⁺ concentration in tissues plays a protective role during Cd²⁺ poi-

soning [1]. The increase in Fe²⁺ concentration in the cervical enlargement of SC probably serves as a compensatory response to age-related accumulation of Cd²⁺. The Fe²⁺-induced activation of free radical processes is an undesirable consequence of compensatory reconstruction. This assumption is confirmed by published data on highest vulnerability of the cervical enlargement of SC to oxidative stress [2]. Our results (Table 1) and published data [1,6] suggest that simultaneous changes in the concentration of Cd²⁺ and Fe²⁺ contribute to intensification of OMP in the cervical enlargement of aging people. A direct correlation between the content of OMP products and age of people was revealed only in the cervical enlargement of SC ($r=0.419$, $p<0.05$). No correlations were found between the content of OMP products in different regions of SC and time after death. These data illustrate high significance of the observed relationship and reliability of the experimental approach. OMP is followed by metabolic elimination of modified proteins [3]. This process probably determines the absence of age-related differences in the content of OMP products in the cervical enlargement of SC. It should be emphasized that the content of OMP products tended to increase in old people (Table 1).

Age-related changes in the intensity OMP were most pronounced in LSE of SC. The concentration of Cd²⁺ in this region was maximum in people of dif-

TABLE 1. Age-Related Changes in the Concentration of Cd²⁺, Fe²⁺, and Cu²⁺ (per 1 g tissue) and Content of OMP Products (per 1 g tissue) in Different Regions of Human SC ($M\pm m$)

SC region	Age			
	younger adults	older adults	elderly	old people
Cervical enlargement				
Cd ²⁺ , mg	0.2428±0.0228	0.2682±0.0214	0.3248±0.0192*	0.3066±0.0135*
Cu ²⁺ , mg	4.8334±0.4692	4.8998±0.7343	6.0252±1.0021	5.4332±0.3134
Fe ²⁺ , mg	39.0776±4.7473	40.2956±5.4311	31.8312±3.7652	42.0708±1.6300***
OMP, mmol	1.5170±0.8220	1.6524±0.4500	1.8841±0.5631	5.9686±2.7011
Thoracic region				
Cd ²⁺ , mg	0.2926±0.0162	0.2832±0.0517	0.3694±0.0343	0.3268±0.0450
Cu ²⁺ , mg	9.1292±1.4864 ⁺	8.1168±1.7140 ⁺	10.5914±1.2854 ⁺	7.9000±1.3226
Fe ²⁺ , mg	39.9368±6.9785	37.1222±7.6439	41.7078±8.2068	36.7202±5.2137
OMP, mmol	2.4887±0.0623	3.4524±1.0894	3.8603±1.7094	5.6362±1.9210
LSE				
Cd ²⁺ , mg	0.3786±0.0375 ⁺	0.4194±0.0476 ⁺	0.4170±0.0449	0.4318±0.0372 ⁺
Cu ²⁺ , mg	4.7166±0.4920 ⁺⁺	3.7166±0.5674 ⁺⁺	5.2666±0.6332 ⁺⁺	5.7832±0.4121 ^{**}
Fe ²⁺ , mg	33.4668±4.9012	38.6578±5.5719	30.4802±4.8892	34.4268±4.5131
OMP, mmol	1.5286±0.4034	6.1769±1.4915 ^{**}	1.7548±1.0952 ^{**}	5.7914±1.4107 ^{*,***}

Note. $p<0.05$: *compared to younger adults; **compared to older adults; ***compared to elderly; ⁺compared to the cervical enlargement; ⁺⁺compared to the thoracic region.

ferent age groups (Table 1). The content of OMP products in LSE 4-fold increased in older adults. This index decreased in elderly and did not differ from that in younger adults. The content of OMP products in old people increased and was similar to that in older adults. Most likely, phasic changes in the content of OMP products in LSE of SC reflect an imbalance between the intensity of OMP and rate of elimination of its products. It cannot be excluded that accumulation of Cu^{2+} in this region of SC in old people (Table 1) suppresses generation of OMP-inducing free radicals [3]. This suggestion is confirmed by a negative correlation between the concentrations of Cu^{2+} and Fe^{2+} in LSE of SC ($r=-0.478$, $p<0.05$). It is important that the content of ceruloplasmin increases more than by 5 times in LSE of SC in old people [2]. Ceruloplasmin is a Cu^{2+} -dependent enzyme for antioxidant protection. Moreover, Cu^{2+} and ceruloplasmin exhibit the same distribution in different regions of SC [2]. The content of these compounds is maximum in thoracic SC. This region is not characterized by age-related variations in the content of OMP products.

Our results indicate that age-related accumulation of Cd^{2+} in the cervical enlargement and high content of this metal in LSE contribute to intensification of OPM in SC of aging people. The corresponding age-related changes in Fe^{2+} concentration in the cervical enlargement suggest that Cd^{2+} is involved in OMP by the Fe^{2+} -mediated mechanism. The distribution of Cu^{2+} and age-related changes in the intensity of OMP in SC illustrate the existence of a Cu^{2+} -mediated mechanism of OMP inhibition.

REFERENCES

1. A. P. Avtsyn, L. S. Strochkova, and A. A. Zhavoronkov, *Arkh. Patol.*, **50**, No. 9, 6-11 (1988).
2. I. A. Volchegorskii, I. B. Telesheva, and V. V. Turygin, *Byull. Eksp. Biol. Med.*, **135**, No. 1, 49-51 (2003).
3. E. E. Dubinina, S. O. Burmistrov, D. A. Khodov, and I. G. Porotov, *Vopr. Med. Khim.*, **41**, No. 1, 24-26 (1995).
4. L. M. Mikhaleva, *Arkh. Patol.*, **50**, No. 9, 81-85 (1988).
5. O. L. Sanina and N. K. Berdinskikh, *Vopr. Med. Khim.*, **32**, No. 5, 7-14 (1986).
6. T. Hussain, M. M. Ali, and S. V. Chandra, *Ind. Health*, **23**, No. 3, 199-205 (1985).