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Age-Related Changes in Lipid Peroxidation in Various Structures of the Central Nervous System

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Abstract—Age-related changes in contents of lipid peroxidation (LPO) products and sensitivity to oxidative stress were studied in ten structures of the human brain and three parts of the spinal cord. LPO was found to increase with age in all parts of the central nervous system. This regularity was especially pronounced in the brainstem structures (the hypothalamus, mesencephalon, and myelencephalon) and in the cervical and sacrolumbar enlargements of the spinal cord.

The central nervous system (CNS) utilizes oxygen more intensely than other organs and is characterized by a relatively low activity of antioxidant defense (AOD) enzymes [1, 2].

Human aging is accompanied by a decrease in AOD along with an increase in the monoamine oxidase B (MAO-B) activity in the brain [3–5]. The age-related increase in MAO-B activity is thought to aggravate the initial deficiency of cerebral AOD [3–5]. Another picture is observed in the spinal cord, where AOD decreases dramatically notwithstanding the absence of age-related changes in MAO-B activity [6]. Regardless of the causes of AOD suppression with age, AOD insufficiency decreases the resistance to oxidative stress (OS) and allows induction of lipid peroxidation (LPO), one of the key mechanisms of ischemic death and apoptosis of neurons [2]. The known heterochronism of involution in different parts of the CNS [5] can be related with local features of OS sensitivity and contents of LPO products.

In the present work, age-related changes in these parameters were studied in different parts of the human brain and spinal cord.

METHODS

Preparations of the CNS were obtained as autopsy material from 63 men and 15 women who died suddenly at the age of 22–92 years. The material was obtained from the Chelyabinsk Regional Bureau of Forensic Medical Examination. Cases of a lethal outcome of coronary or cerebral thrombosis were excluded. Samples of nervous tissue with signs of ischemic or hemorrhagic insult were excluded. The deaths were most often caused by accidents (road accidents, falls from a height, etc.). The material to be studied was taken no later than 12 h after the death. This time was chosen on the basis of data on stable activities of the AOD enzymes during this period [5]. Four age groups were set: first adult (women of 21–35 and men of 22–35 years), second adult (women of 36–55 and men of 36–60 years), elderly (women of 56–74 and men of 61–74 years), and senile (75 or more years of age).

LPO was studied in several structures of the brain and spinal cord. In the brain, we examined two regions of the hemispheric cortex (fields 6 and 17), basal ganglia (the pale globe, caudate nucleus, and putamen), diencephalic structures (the thalamus and hypothalamus), the cerebellum, the mesencephalon, and the myelencephalon. In the spinal cord, we studied the cervical enlargement, the thoracal part, and the sacrolumbar enlargement.

Contents of LPO products were determined using extraction and spectrophotometry, separately in the heptane and isopropanol phases of the lipid extract [7]. This approach allowed us to differentially determine acyl peroxides in phospholipids extracted with isopropanol and nonesterified intermediates of fatty acid peroxidation in the heptane phase. The results were expressed in oxidation index units as E_{232}/E_{220} (the relative content of diene conjugates (DC)) and E_{278}/E_{220} (the levels of ketodienes (KD) and triene conjugates (TC), respectively). The content of LPO final products, Schiff bases (SB), was determined in both phases of the lipid extract as the E_{400}/E_{220} ratio [8]. Concurrently, 2-thiobarbituric acid–reactive species (TBARS) were determined colorimetrically [9, 10].

The resistance of lipids to free radical oxidation was assessed by the rate of TBARS accumulation in 2–2.5% homogenates of the brain tissue incubated *in vitro* in the air for 1 h at 37°C [9, 10]. The integral parameter of *in vitro* LPO intensity (oxidizability) was expressed as the percent increase in TBARS content with respect to the basal level. This parameter informatively characterized the nervous tissue resistance to OS [5, 6].

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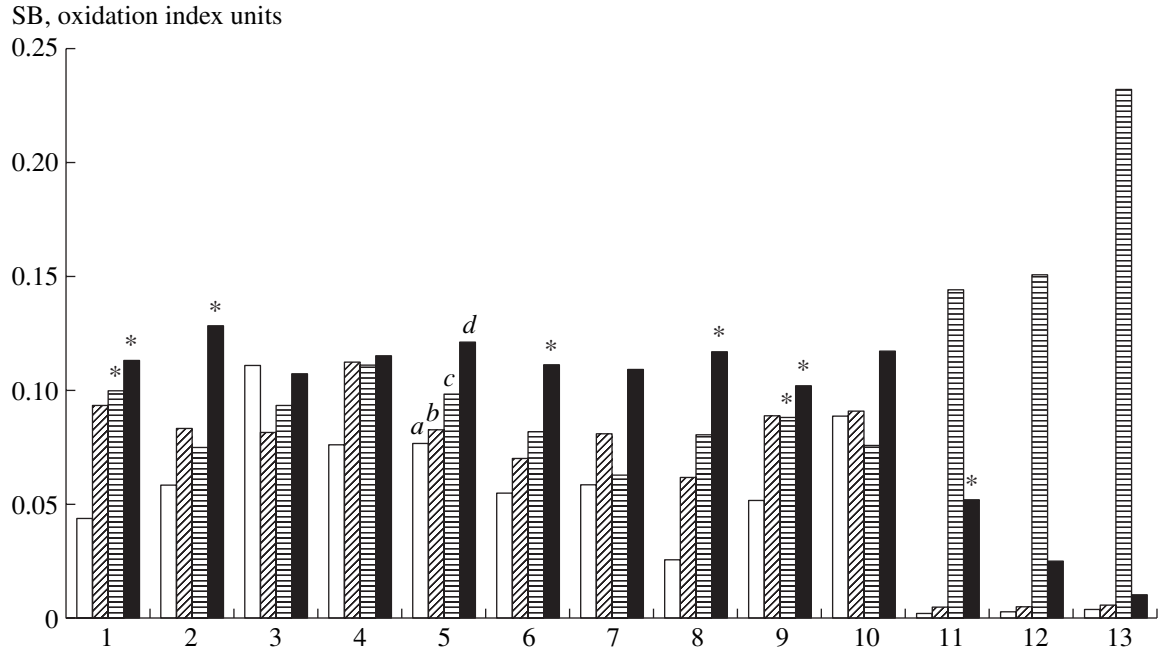

Fig. 1. Age-related changes in contents of the final LPO products (SB in the heptane phase) in the human brain and spinal cord. Here and in Fig. 2, the parameters were assayed in the (*a*) first adult, (*b*) second adult, (*c*) elderly, and (*d*) senile groups, each including five people. Abscissa: (1) cortical field 6, (2) cortical field 17, (3) pale globe, (4) caudate nucleus, (5) putamen, (6) hypothalamus, (7) thalamus, (8) mesencephalon, (9) cerebellum, and (10) myelencephalon; (11) cervical enlargement, (12) thoracal part, and (13) sacrolumbar enlargement of the spinal cord. (*) The difference was significant ($P < 0.05$) in comparison with the first adult group.

The results were processed with the applied program package Statistica 5 for Windows. The significance of differences was evaluated by Student's *t*-test for independent samples and by nonparametric tests (Mann–Whitney, Wald–Wolfowitz, and Kolmogorov–Smirnov). Statistical relationships were studied using Spearman's nonparametric correlation coefficient (r_s).

RESULTS AND DISCUSSION

Contents of LPO products and OS sensitivity in the brain structures studied were 1.5–44.4 times higher than in the spinal cord ($P < 0.05$). This regularity was especially clear at the ages of 21–35 years and was recorded mainly for heptane-extracted LPO products, TBARS, and lipid oxidizability (Tables 1–3; Figs. 1, 2). Local differences in contents of isopropanol-soluble LPO products were less pronounced, and in some cases the difference in the level of isopropanol-soluble LPO products between the brain and spinal cord structures was nonsignificant. Thus, $DC_{(i)}$ was much the same in the hypothalamus, the cervical and sacrolumbar enlargements, and the thoracal part of the spinal cord.

A similar rostrocaudal distribution was observed at the brain level in the first adult group (Table 1). The highest content of LPO products was recorded in the neocortical fields and the cerebellum. This feature of the cerebral distribution was observed mostly for TBARS and primary LPO products (DC) in the isopropanol phase of the lipid extract, suggesting that lipoperoxides originated mainly from phospholipids [11], which show the highest levels in the brain cortex and cerebellum. In the first adult group, the phylogenetic age of a brain structure [12] correlated negatively with the contents of the secondary (KD and TC) and final (SB) isopropanol-soluble LPO products (r_s ranged from –0.65 to –0.69; $P < 0.05$). A similar correlation was found for the cerebral distribution of heptane-soluble secondary LPO products in the elderly group (r_s = –0.66; $P < 0.05$). The contents of heptane-soluble lipoperoxides in the brain structures differed to a lesser extent than the contents of TBARS and isopropanol-extractable LPO intermediates (Tables 1, 2). It should be emphasized that heptane-extractable free fatty acid peroxidation products [13] can be released from isopropanol-soluble phospholipids as a result of excision of acyl peroxides by phospholipase A_2 [14]. LPO increases the activity of this enzyme, and, in its turn, the phospholipase reaction intensifies LPO [14]. Hence, the level of heptane-extractable lipoperoxides depends not only on free radical oxidation of polyene acyls but also on the intensity of LPO-induced phospholipolysis.

Our findings suggest that lipids of ancient and old structures of the brain have a relatively high resistance to free radicals. However, the absence of significant correlations between the *in vitro* oxidizability of lipids and the phylogenetic age of the brain structures (r_s was from 0.04 to –0.23; $P > 0.5$) contradicts this hypothesis. Relatively high levels of LPO in the neocortex and cerebellum were most likely caused by a higher intensity

Table 1. Age-related changes in contents of primary (DC) and secondary (KD and TC) LPO products in the human brain

Brain structure	Parameter	Group			
		first adult	second adult	elderly	senile
Cortex (field 6)	$DC_{(i)}$	0.290 ± 0.0594	0.373 ± 0.0355	0.543 ± 0.0462^{+}	0.679 ± 0.0531*$^{+}$
	KD and $TC_{(h)}$	0.135 ± 0.0418	0.203 ± 0.0276	0.267 ± 0.0289	0.240 ± 0.0321
	$DC_{(i)}$	0.453 ± 0.0832	0.388 ± 0.0233	0.542 ± 0.0560*	0.619 ± 0.392+
	KD and $TC_{(i)}$	0.134 ± 0.0125	0.234 ± 0.0368	0.134 ± 0.0352	0.162 ± 0.0851
Cortex (field 17)	$DC_{(i)}$	0.337 ± 0.0502	0.383 ± 0.0316	0.562 ± 0.0439*$^{+}$	0.637 ± 0.0426*$^{+}$
	KD and $TC_{(h)}$	0.147 ± 0.0353	0.181 ± 0.0173	0.221 ± 0.0271	0.223 ± 0.0397*
	$DC_{(i)}$	0.425 ± 0.0208	0.433 ± 0.0391	0.473 ± 0.0779	0.586 ± 0.0290*$^{+}$
	KD and $TC_{(i)}$	0.159 ± 0.0239	0.248 ± 0.0595	0.108 ± 0.0315	0.0804 ± 0.017*$^{+}$
Caudate nucleus	$DC_{(i)}$	0.332 ± 0.0379	0.322 ± 0.0586	0.499 ± 0.0437*	0.632 ± 0.0619*$^{+}$
	KD and $TC_{(h)}$	0.159 ± 0.0401	0.161 ± 0.0154	0.351 ± 0.0875	0.195 ± 0.0317
	$DC_{(i)}$	0.382 ± 0.0291	0.407 ± 0.0187	0.492 ± 0.0500	0.615 ± 0.0357*$^{+\#}$
	KD and $TC_{(i)}$	0.152 ± 0.0267	0.241 ± 0.0429	0.106 ± 0.0231^{+}	0.0752 ± 0.010*+
Pale globe	$DC_{(i)}$	0.346 ± 0.0672	0.472 ± 0.0550	0.633 ± 0.0725*	0.718 ± 0.0606*$^{+}$
	KD and $TC_{(h)}$	0.150 ± 0.0542	0.231 ± 0.0281	0.325 ± 0.0883	0.255 ± 0.0284
	$DC_{(i)}$	0.394 ± 0.0246	0.406 ± 0.0106	0.472 ± 0.0606	0.623 ± 0.0368*$^{+}$
	KD and $TC_{(i)}$	0.122 ± 0.0198	0.203 ± 0.0333	0.121 ± 0.0172	0.0796 ± 0.0129+
Putamen	$DC_{(i)}$	0.288 ± 0.0729	0.375 ± 0.0469	0.538 ± 0.0762*	0.631 ± 0.0297*$^{+}$
	KD and $TC_{(h)}$	0.168 ± 0.0535	0.171 ± 0.0347	0.227 ± 0.0259	0.242 ± 0.0367
	$DC_{(i)}$	0.394 ± 0.0164	0.436 ± 0.0079	0.510 ± 0.0389	0.608 ± 0.0262*$^{+}$
	KD and $TC_{(i)}$	0.159 ± 0.0154	0.273 ± 0.0597	0.124 ± 0.0206	0.0918 ± 0.0122*$^{+}$
Hypothalamus	$DC_{(i)}$	0.355 ± 0.0371	0.429 ± 0.0490	0.537 ± 0.0526*	0.679 ± 0.0224*$^{+\#}$
	KD and $TC_{(h)}$	0.142 ± 0.0329	0.163 ± 0.0177	0.210 ± 0.0184	0.260 ± 0.0367
	$DC_{(i)}$	0.372 ± 0.0097	0.347 ± 0.0204	0.538 ± 0.0567	0.713 ± 0.0743*$^{+}$
	KD and $TC_{(i)}$	0.117 ± 0.0112	0.221 ± 0.0557	0.103 ± 0.0128	0.0623 ± 0.0132*$^{+}$
Thalamus	$DC_{(i)}$	0.381 ± 0.0426	0.423 ± 0.0127	0.543 ± 0.0657	0.689 ± 0.0347*$^{+}$
	KD and $TC_{(h)}$	0.175 ± 0.0268	0.169 ± 0.0132	0.186 ± 0.0405	0.283 ± 0.0267*$^{+}$
	$DC_{(i)}$	0.389 ± 0.0083	0.426 ± 0.0238	0.551 ± 0.0588	0.645 ± 0.0326*$^{+}$
	KD and $TC_{(i)}$	0.137 ± 0.0107	0.269 ± 0.0475*	0.121 ± 0.0219^{+}	0.0904 ± 0.0100*$^{+}$
Mesencephalon	$DC_{(i)}$	0.323 ± 0.0241	0.265 ± 0.0602	0.634 ± 0.0895*$^{+}$	0.769 ± 0.0523*$^{+}$
	KD and $TC_{(h)}$	0.093 ± 0.0157	0.151 ± 0.0218	0.190 ± 0.0342*	0.246 ± 0.0334*
	$DC_{(i)}$	0.378 ± 0.0227	0.407 ± 0.0187	0.553 ± 0.0759	0.678 ± 0.0369*$^{+}$
	KD and $TC_{(i)}$	0.123 ± 0.0114	0.235 ± 0.0472	0.119 ± 0.0118	0.0934 ± 0.0184^{+}
Cerebellum	$DC_{(i)}$	0.406 ± 0.0348	0.371 ± 0.0310	0.502 ± 0.0345	0.599 ± 0.0516*$^{+}$
	KD and $TC_{(h)}$	0.146 ± 0.0369	0.159 ± 0.0310	0.226 ± 0.0276	0.220 ± 0.0356*
	$DC_{(i)}$	0.399 ± 0.0179	0.470 ± 0.0452	0.518 ± 0.0464	0.593 ± 0.0245*
	KD and $TC_{(i)}$	0.155 ± 0.0149	0.260 ± 0.0429*	0.281 ± 0.0145	0.0798 ± 0.0086*$^{+}$
Myelencephalon	$DC_{(i)}$	0.499 ± 0.0815	0.488 ± 0.0355	0.556 ± 0.0582	0.685 ± 0.0387^{+}
	KD and $TC_{(h)}$	0.251 ± 0.0694	0.186 ± 0.0328	0.186 ± 0.0235	0.253 ± 0.0451
	$DC_{(i)}$	0.395 ± 0.0123	0.419 ± 0.0172	0.527 ± 0.0552	0.668 ± 0.0287*$^{+}$
	KD and $TC_{(i)}$	0.114 ± 0.0151	0.236 ± 0.0408*	0.113 ± 0.0145^{+}	0.0972 ± 0.0098^{+}

Notes: Here and in Table 3: Contents of LPO products are presented as the oxidation indices E_{232}/E_{220} (DC) and E_{278}/E_{220} (KD and TC). The subscripts (h) and (i) indicate, respectively, the heptane and isopropanol phases of the lipid extract. Here and in Tables 2 and 3, the difference was significant in comparison with the (*) first adult, (+) second adult, or (#) elderly group; each group included five people.

Table 2. Age-related changes in TBARS content and lipid oxidizability in the human brain

Brain section	Parameter	Group			
		first adult	second adult	elderly	senile
Cortex (field 6)	TBARS	2.40 ± 0.322	2.04 ± 0.342	1.92 ± 0.275	1.57 ± 0.477
	OX	82.0 ± 41.98	90.7 ± 40.52	69.2 ± 12.97	145.6 ± 34.79
Cortex (field 17)	TBARS	2.32 ± 0.290	2.15 ± 0.0369	1.80 ± 0.379	1.72 ± 0.621
	OX	77.0 ± 32.87	140.0 ± 78.6	110.3 ± 29.76	218.2 ± 127.8
Caudate nucleus	TBARS	1.44 ± 0.160	1.35 ± 0.102	1.02 ± 0.111	1.54 ± 0.425
	OX	58.1 ± 12.43	75.9 ± 12.32	165.4 ± 41.51*	74.2 ± 6.25
Putamen	TBARS	1.58 ± 0.251	1.31 ± 0.350	1.06 ± 0.086	1.30 ± 0.475
	OX	114.9 ± 49.09	79.0 ± 26.69	158.0 ± 44.89	100.8 ± 17.11
Pale globe	TBARS	2.0 ± 0.201	1.65 ± 0.227	1.24 ± 0.083*	2.02 ± 0.742
	OX	115.6 ± 38.77	64.8 ± 19.29	105.9 ± 18.63	81.0 ± 20.23
Hypothalamus	TBARS	1.80 ± 0.154	1.21 ± 0.196	0.92 ± 0.201*	1.04 ± 0.421
	OX	57.9 ± 10.30	91.0 ± 34.15	145.2 ± 25.19*	200.2 ± 53.68*
Thalamus	TBARS	1.50 ± 0.200	1.20 ± 0.197	0.99 ± 0.204	0.87 ± 0.294
	OX	137.2 ± 50.31	75.2 ± 11.87	139.6 ± 30.88	236.1 ± 64.19^{+}
Mesencephalon	TBARS	1.72 ± 0.181	1.49 ± 0.168	1.15 ± 0.0128*	1.28 ± 0.280
	OX	70.9 ± 20.45	59.4 ± 7.72	89.3 ± 26.97	113.3 ± 18.61^{+}
Cerebellum	TBARS	2.27 ± 0.234	2.27 ± 0.192	1.68 ± 0.222	1.89 ± 0.692
	OX	79.0 ± 28.79	60.6 ± 21.23	101.4 ± 34.35	105.9 ± 51.89
Myelencephalon	TBARS	1.99 ± 0.253	1.32 ± 0.238	1.12 ± 0.215*	1.20 ± 0.598
	OX	85.1 ± 28.69	90.7 ± 20.27	134.9 ± 27.78	198.8 ± 42.91*$^{+}$

Notes: Here and in Table 3, TBARS content is indicated as $E_{532} \times 10^{-3}$/mg; oxidizability of lipids (OX) is expressed in percent.

of mitochondrial oxidation in these structures as compared to the more caudal and more hypoxia-resistant parts of the brain [15]. Note that the leakage of electrons from mitochondrial respiratory chains is considered to be an important factor in LPO induction *in vivo* [1].

The contents of heptane-extractable lipoperoxides and primary and final isopropanol-soluble LPO products in the brain structures increased with age and reached a maximum at 56–75 years (Table 1; Figs. 1, 2). The levels of isopropanol-soluble KD and TC and SB in the senile group were 1.4–6.6 times higher than in the first adult group. The level of heptane-soluble LPO products increased less markedly with age and was only 1.3–4.5 times higher in the senile than in the first adult group.

The OS sensitivity of lipids in human nervous tissue considerably increased with age. This was manifested by a pronounced increase of the *in vitro* oxidizability of lipids, which was maximum in the elder age groups (Table 2). In these groups, the oxidizabilities of lipids of the caudate nucleus and hypothalamus were nearly threefold higher than in the first adult group. The oxidizabilities of lipids in the thalamus, hypothalamus, mesencephalon, and myelencephalon in the senile group were significantly higher than in the adult groups. It should be emphasized that, in the senile group, these brain structures (especially, the hypothalamus, mesencephalon, and myelencephalon) displayed a very high level of lipoperoxides, which in some cases was even higher than in the neocortex and cerebellum.

The observed decrease in lipid resistance to free radical oxidation and the accumulation of LPO products in the brainstem structures seems to be associated with the age-related MAO-B–dependent weakening of AOD [3, 5]. This hypothesis agrees with the highest activity of MAO-B [3, 5] and the lowest OS resistance (Tables 2, 3) of these brain structures in senile people.

The obvious age-related decrease in AOD and the accompanying intensification of LPO in the brainstem structures changed the rostrocaudal distribution of lipoperoxides in the brain in the senile group as compared to the younger groups. This was manifested by a change in the correlation between the phylogenetic age of a brain structure and the content of LPO products. Unlike in the first adult group, a positive correlation (r_s = 0.7–0.82; $P < 0.05$) was observed in the senile group for the heptane-extractable primary and secondary LPO products and for the isopropanol-extractable LPO intermediates.

The age-related changes in the contents of TBARS and isopropanol-soluble secondary LPO products in the

Table 3. Age-related changes in the primary (DC) and secondary (KD and TC) LPO products, TBARS, and lipid oxidizability in the human spinal cord

Spinal cord part	Parameter	Group			
		first adult	second adult	elderly	senile
Cervical enlargement	$DC_{(h)}$	0.114 ± 0.0718	0.176 ± 0.0853	0.342 ± 0.1429	0.421 ± 0.0643*
	KD and $TC_{(h)}$	0.025 ± 0.0164	0.018 ± 0.0112	0.239 ± 0.0998	0.159 ± 0.0782*+
	$DC_{(i)}$	0.389 ± 0.0102	0.559 ± 0.0484*	0.546 ± 0.0383*	0.486 ± 0.0397*
	KD and $TC_{(i)}$	0.136 ± 0.0078	0.225 ± 0.0543	0.182 ± 0.0399	0.149 ± 0.0087
	TBA	1.17 ± 0.311	1.14 ± 0.156	1.10 ± 0.137	1.07 ± 0.052
	OX	33.0 ± 7.73	53.5 ± 11.55	73.5 ± 19.10	100.4 ± 15.01*+
Thoracal part	$DC_{(h)}$	0.108 ± 0.0666	0.118 ± 0.0722	0.188 ± 0.1264	0.384 ± 0.0556*+
	KD and $TC_{(h)}$	0.018 ± 0.0110	0.021 ±0.0128	0.115 ± 0.0815	0.161 ± 0.0802
	$DC_{(i)}$	0.287 ± 0.0726	0.475 ± 0.0467*	0.566 ± 0.0999	0.432 ± 0.0117*
	KD and $TC_{(i)}$	0.198 ± 0.0253	0.232 ± 0.0515	0.232 ± 0.1119	0.139 ± 0.0083
	TBA	0.71 ± 0.17	0.99 ± 0.18	1.04 ± 0.16	0.75 ± 0.07
	OX	39.7 ± 3.18	37.8 ± 11.06	57.2 ± 11.48	119.8 ± 68.47
Sacrolumbar enlargement	$DC_{(h)}$	0.094 ± 0.0575	0.127 ± 0.0823	0.148 ± 0.0905	0.172 ± 0.0505
	KD and $TC_{(h)}$	0.013 ± 0.0082	0.028 ± 0.0186	0.040 ± 0.0247	0.035 ± 0.0308
	$DC_{(i)}$	0.365 ± 0.0197	0.439 ± 0.0147*	0.490 ± 0.0702	0.531 ± 0.0279*+
	KD and $TC_{(i)}$	0.097 ± 0.0219	0.189 ± 0.0451*	0.202 ± 0.1052	0.162 ± 0.0178*
	TBA	1.20 ± 0.18	1.01 ± 0.16	1.22 ± 0.10	0.70 ± 0.08*#
	OX	30.3 ± 7.73	36.1 ± 5.23	60.4 ± 9.57*	51.5 ± 17.58

brain structures deserve special attention. The contents of these LPO products in the brain noticeably decreased with age and became minimum at 55–75 years. These LPO products are carbonyls, which interact with amino groups of nitric bases of phospholipids and ε-amino groups of lysine, with consequent production of the aging pigment lipofuscin. Lipofuscin is a derivative of SB (the final LPO products), which accumulate in the brain with age (Fig. 2). Increased production of the aging pigment is accompanied by utilization of carbonyl lipoperoxides and was likely to have caused the age-related decrease in the contents of these LPO intermediates in the brain.

The regional differences in LPO were less pronounced in the spinal cord than in the brain. In the first adult group, these differences were most clear in the case of isopropanol-soluble KD and TC, whose levels were maximum in the thoracal part of the spinal cord (Table 3). In the second adult group, only isopropanol-extractable SB showed regional differences (Fig. 2): their content was minimum in the cervical enlargement of the spinal cord. In the senile group, the content of isopropanol-soluble DC in the sacrolumbar enlargement of the spinal cord was higher than in the thoracal part and the content of heptane-soluble DC was higher in the cervical than in the sacrolumbar enlargement.

In general, the age-related changes in oxidizability of lipids in the spinal cord corresponded to changes in the resistance of cerebral lipids to the *in vitro* induction of LPO (Table 3). A threefold increase in the OS sensitivity of the cervical enlargement of the spinal cord was recorded in the senile group compared to the first adult group. In the sacrolumbar enlargement, the lipid oxidizability in the elderly groups was twofold higher than in the second adult group.

In parallel with the age-related decrease in the OS resistance, lipoperoxides accumulated in the spinal cord parts under study. This regularity was especially pronounced in the cervical enlargement in the case of isopropanol-soluble primary LPO products (Table 3). The lowest content of these LPO intermediates was recorded in the cervical enlargement in the first adult group. The levels of isopropanol-soluble DC also increased significantly in the thoracal part and sacrolumbar enlargement in the second adult and the senile groups. Similar, although less pronounced, changes were observed for heptane-soluble DC: these products accumulated to a considerable extent in the cervical enlargement and thoracal part of the spinal cord only in the senile group. No significant age-related changes were found in the level of heptane-soluble DC in the sacrolumbar enlargement.

The age-related accumulation of the secondary LPO products in the spinal cord was less pronounced and extended than the age-related accumulation of the primary products. Contents of isopropanol-extractable

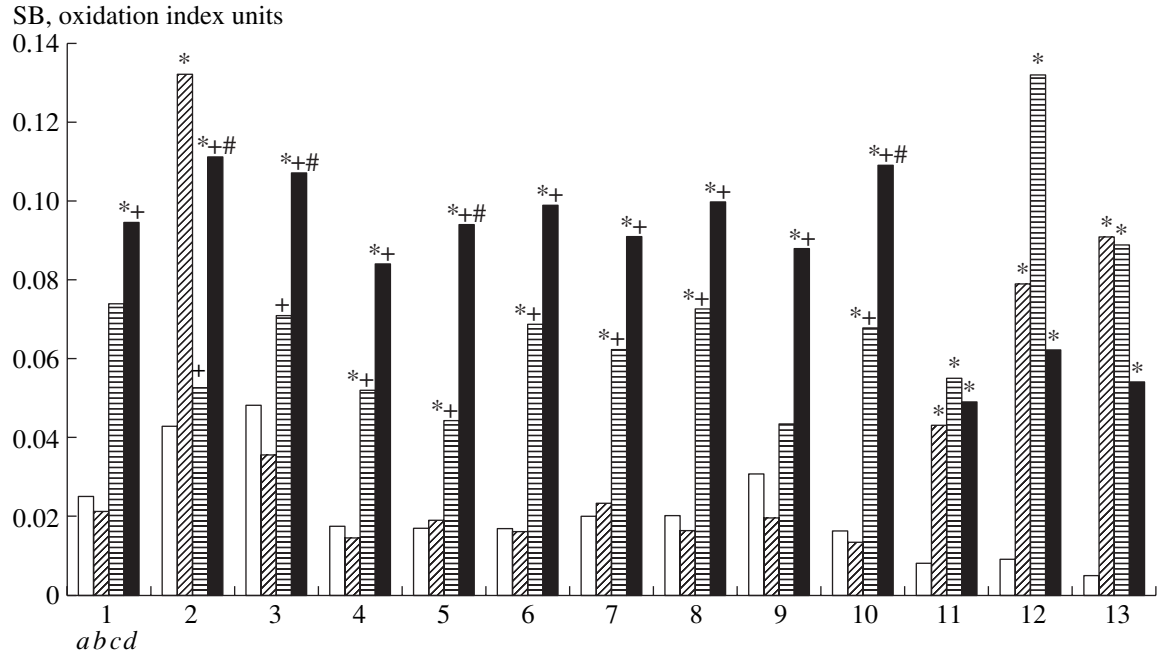

Fig. 2. Age-related changes in contents of the final LPO products (SB in the isopropanol phase) in the human brain and spinal cord. The difference was significant ($P < 0.05$) in comparison with the (*) first adult, (+) second adult, or (#) elderly group.

KD and TC increased significantly only in the sacrolumbar enlargement of the spinal cord in the second adult and senile groups compared with the first adult group (Table 3). Levels of heptane-extractable KD and TC in the cervical enlargement of the spinal cord in the senile group were significantly higher than in the first and second adult groups.

Age-related changes in TBARS were found only in the sacrolumbar enlargement of the spinal cord (Table 3). The TBARS content was significantly lower in the senile group compared to the first adult and elderly groups. These changes seem to be caused by an increased expenditure of carbonyl lipoperoxides for generation of the final LPO products (SB). This hypothesis is supported by a more than tenfold increase in accumulation of isopropanol-extractable SB in the sacrolumbar enlargement of the spinal cord in the senile group. Contents of isopropanol-soluble SB in the cervical enlargement and thoracal part of the spinal cord also increased with age and were 6–6.8 times higher than in the first adult group (Fig. 2). Heptane-extractable SB accumulated most intensely in the cervical enlargement in the senile group: their content was more than 22-fold higher than in the first adult group (Fig. 1).

The distribution of LPO products in the spinal cord of the senile people (Table 3; Figs. 1, 2) was in good agreement with the age-related changes in sensitivity of the spinal cord parts to the *in vitro* induction of LPO. The age-related decrease in OS resistance and the associated accumulation of SB were most pronounced in the cervical and sacrolumbar enlargements of the spinal cord. It is possible that a compensatory age-related increase in the catalase activity in these parts of the spinal cord [6] is a result of OS, which increases expression of the *bcl*–2 protooncogene and intensifies synthesis of a highly active catalase form [16].

To summarize, our study showed an age-related decrease in OS resistance of nervous tissue, which was associated with an increase in LPO in all CNS parts examined. This regularity was especially clear in the brainstem structures and in the cervical and sacrolumbar enlargements of the spinal cord.

CONCLUSIONS

(1) Contents of the secondary and final LPO products decrease from the hemispheric cortex and cerebellum towards the brainstem in people aged from 21–35 to 55–60 years. The sensitivity of cerebral lipids to the *in vitro* induction of LPO does not depend on the rostrocaudal location or phylogenetic age of brain structures.

(2) Human aging is associated with increased sensitivity of cerebral lipids to the *in vitro* induction of LPO, and LPO products are accumulated in the brain. The age-related increase in LPO is most pronounced in the brainstem structures.

(3) The brainstem structures of senile people (75–90 years) have the highest contents of the primary LPO products, whose levels decrease from the brainstem towards the hemispheric cortex.

(4) LPO products accumulate in the spinal cord with age, and an age-related increase in LPO is recorded in the cervical and sacrolumbar enlargements.

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