Comparative Analysis of Age-Related Changes in Activities of Monoamine Oxidase-B and Antioxidant Defense Enzymes in Various Structures of Human Brain

I. A. Volchegorskii, S. E. Shemyakov, V. V. Turygin, and N. V. Malinovskaya

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Activities of monoamine oxidase B, Cu-Zn-dependent superoxide dismutase (SOD), and catalase, and concentration of enzyme-active ceruloplasmin were measured in brain preparations from 43 humans died at the age of 21-92 years. Activity of monoamine oxidase B in the neocortex, cerebellum, basal ganglia, and stem structures increased with age, while SOD activity decreased and catalase and ceruloplasmin concentrations slightly increased. A contribution of age-related increase of cerebral monoamine oxidase activity into ontogenetic impairment of the antioxidant defense in human brain is discussed.

Key Words: *monoamine oxidase B; superoxide dismutase; catalase; ceruloplasmin; cerebral antioxidant defense; aging*

Monoamine oxidase (MAO; EC 1.4.3.4) catalyzes catabolism of monoamine neurotransmitters in cells and plays an important role in neurochemical regulation of behavior [4]. The predominant form of this enzyme in human brain is MAO-B (80-95% of cerebral MAO) [13]. Cerebral MAO-B activity increases with age because of age-related accumulation of glial cells, the main source of MAO-B [5,14]. The age-related increase in MAO-B activity is regarded as a key mechanism of nervous tissue involution [5]. This is due to MAO-dependent generation of H_2O_2, a potent inductor of free-radical damage to biological membranes [8,15]. Here we analyzed age-related changes in activities of MAO-B and enzymes eliminating active oxygen forms in different structures of human brain.

MATERIALS AND METHODS

Autopsy material was obtained from 43 humans (33 male and 10 female, 21-92 years) died from injuries or diseases not involving the nervous or cardiovascular systems. Specimens were collected no later than 12 h postmortem. Four age groups were distinguished: mature age I (21-35 years for women and 22-35 years for men), mature age II (36-55 years for women and 36-60 years for men), elderly (56-74 years for women and 61-74 years for men), and senile (over 75 years). MAO and antioxidant defense enzyme activities were measured in two regions of the cortex (fields 6 and 17), basal ganglia (caudate nucleus, shell, globus pallidus), diencephalic structures (thalamus, hypothalamus), cerebellum, midbrain, and medulla oblongata. MAO-B activity in homogenates of these brain structures was measured using benzylamine hydrochloride as the substrate [1,2]. The activity of Cu-Zn-dependent superoxide dismutase (SOD) (EC 1.15.1.1) was measured colorimetrically [12]. Catalase activity (EC 1.11.1.6) was evaluated by the rate of H_2O_2 utilization in the incubation medium [7]. The content of enzyme-active ceruloplasmin (EACP) (ferro:O_2-oxidoreductase, EC 1.16.3.1) was evaluated by a modified method [6]; incubation was prolonged to 180 min. The results were processed statistically using Statistica 5.0 for Windows software. The significance of differences was evaluated using Student's *t* test for independent variables.

Department of General and Bioorganic Chemistry, Department of Normal Anatomy, Chelyabinsk State Medical Academy

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TABLE 1. Age-Related Changes in Activities of MAO-B (per mg tissue), SOD, Catalase (per g tissue), and EACP (per 10 g tissue) in Various Structures of Human Brain ($M \pm m$)

Brain structures	Age			
	mature I	mature II	elderly	senile
Cortex (field 6)				
MAO, nmol/min	0.0380±0.0057	0.038±0.006	0.1080±0.0476	0.0770±0.0128*+
SOD, U/min	0.0320±0.0029	0.0150±0.0017*	0.0120±0.0018*	0.0074±0.0011*+
Catalase, nmol/sec	2.86±0.21	2.99±0.15	3.82±0.15*+	4.38±0.18*+o
CP, mg	3.43±0.21	4.29±0.17*	4.96±0.27*	5.82±0.19*+o
Cortex (field 17)				
MAO, nmol/min	0.0410±0.0069	0.0560±0.0098	0.091±0.025	0.1060±0.0143*+
SOD, U/min	0.0310±0.0018	0.0160±0.0013*	0.0150±0.0044*	0.0094±0.0005*+
Catalase, nmol/sec	2.75±0.17	3.440±0.057*	4.12±0.15*+	4.44±0.19*+
CP, mg	3.12±0.27	4.25±0.17*	4.92±0.34*	6.05±0.32*+o
Caudate nucleus (head)				
MAO, nmol/min	0.0710±0.0106	0.0980±0.0212	0.1390±0.0234*	0.2160±0.0339*+
SOD, U/min	0.0270±0.0037	0.0140±0.0036*	0.0083±0.0013*	0.0074±0.0012*
Catalase, nmol/sec	2.86±0.21	3.61±0.35	4.17±0.09*	4.43±0.19*
CP, mg	3.27±0.25	4.01±0.32	4.49±0.31*	5.51±0.23*+o
Globus pallidus				
MAO, nmol/min	0.0840±0.0074	0.1190±0.0259	0.2070±0.0315*	0.2630±0.0575*+
SOD, U/min	0.0320±0.0017	0.0170±0.0029*	0.0095±0.0018*	0.0062±0.0012*+
Catalase, nmol/sec	2.56±0.19	3.30±0.25*	3.330±0.076*+	4.56±0.18*+o
CP, mg	3.54±0.26	4.11±0.14	4.63±0.22*	5.55±0.20*+o
Shell				
MAO, nmol/min	0.0790±0.0098	0.0870±0.0121	0.1850±0.0418*+	0.2040±0.0484*+
SOD, U/min	0.0360±0.0021	0.0150±0.0022*	0.0140±0.0032*	0.0072±0.0008*+
Catalase, nmol/sec	3.05±0.13	3.70±0.38	4.11±0.29*	4.55±0.23*
CP, mg	3.33±0.19	4.30±0.41	4.80±0.35*	5.84±0.27*+o
Hypothalamus				
MAO, nmol/min	0.2740±0.0696	0.3120±0.0619	0.428±0.050	0.6970±0.1561*+o
SOD, U/min	0.0360±0.0021	0.0150±0.0022*	0.0140±0.0032*	0.0072±0.0008*+
Catalase, nmol/sec	2.74±0.25	3.07±0.30	3.85±0.12*+	4.18±0.25*+
CP, mg	2.96±0.16	4.37±0.22*	4.29±0.38*	5.99±0.38*+o
Thalamus				
MAO, nmol/min	0.1660±0.0404	0.1260±0.0135	0.3310±0.0764+	0.669±0.156*+
SOD, U/min	0.0340±0.0009	0.0140±0.0038*	0.0130±0.0034*	0.0091±0.0011*
Catalase, nmol/se	3.00±0.18	3.35±0.43	4.03±0.15*	4.42±0.28*
CP, mg	2.88±0.25	3.83±0.20*	4.50±0.26*	5.78±0.33*+o
Midbrain				
MAO, nmol/min	0.0870±0.0055	0.1160±0.0242	0.2330±0.0646	0.423±0.145*
SOD, U/min	0.0340±0.0018	0.0200±0.0025*	0.0110±0.0014*+	0.0084±0.0009*+
Catalase, nmol/sec	2.74±0.17	3.29±0.37	3.73±0.19*	4.42±0.26*+
CP, mg	3.87±0.39	4.09±0.29	4.84±0.26	6.12±0.29*+o
Cerebellum				
MAO, nmol/min	0.0360±0.0091	0.0290±0.0061	0.0550±0.0169	0.0540±0.0081+
SOD, U/min	0.0230±0.0038	0.0140±0.0027*	0.0083±0.0011*	0.0069±0.0012*+
Catalase, nmol/sec	2.56±0.32	3.57±0.26*	3.99±0.16*	4.31±0.32*
CP, mg	2.87±0.09	3.81±0.16*	4.38±0.19*	5.72±0.28*+o
Medulla oblongata				
MAO, nmol/min	0.2970±0.0252	0.2810±0.0393	0.4100±0.0915	0.5280±0.0826*+
SOD, U/min	0.0320±0.0037	0.0180±0.0016*	0.0140±0.0034*	0.0089±0.0011*+
Catalase, nmol/sec	2.45±0.11	2.83±0.33	3.29±0.22*	4.20±0.21*+o
CP, mg	2.98±0.19	4.29±0.16*	4.19±0.14*	5.52±0.26*+o

Note. $p<0.05$: *compared to mature age I, +compared to mature age II, ocompared to elderly age.

RESULTS

Activity of MAO-B in the studied structures of human brain was different (Table 1). Minimum activity was found in the cerebellum and cortex, 2-fold higher activity in the basal ganglia (caudate nucleus, globus pallidus, and shell) and midbrain; medulla oblongata, hypothalamus, and thalamus were characterized by the highest MAO-B activity 2-3-fold surpassing that in the striatal and mesencephalic structures. This distribution of MAO activity in different brain structures does not depend on age and probably reflects the predominance of monoaminergic structures in the basal ganglia and brain stem in comparison with the cerebellum and cortex, a phylogenetically young structure [11].

Activities of the studied antioxidant enzymes in cerebral structures were similar and virtually did not depend on phylogenetic age of brain structures (Table 1).

During ontogeny, MAO-B activity increased in all studied brain structures. Maximum enzyme activities were detected in senile individuals: MAO activity in various cerebral structures 2-4-fold surpassed that in mature age I. The maximum (4-fold) increase of enzyme activity was observed in the thalamus and minimum (1.5-fold) in the cerebellum. The increase of MAO activity during ontogeny was paralleled by a decrease of SOD activity in all brain structures (Table 1). Activity of this enzyme decreased virtually 2-fold in mature age II group compared to mature age I, and in senile subjects it dropped 3-5-fold. This age-specific suppression of SOD activity in the brain can be due to intensive production of H_2O_2, a substrate-independent product of MAO reaction [2,4] inactivating SOD [3]. Catalase activity in the studied brain structures and the content of EACP possessing SOD-like effects [10] gradually increased during aging and reached a maximum in subjects over 75 (Table 1). These shifts should be regarded as a compensatory process aimed at elimination of H_2O_2 excess at the expense of increased catalase activity and compensation for deficient SOD activity via accumulation of EACP synthesized in glial cells [9]. This compensation cannot be satisfactory, because the age-specific shifts in catalase activity and EACP content are less pronounced than changes in MAO and SOD activities. EACP content in the elderly increased only 1.5-2-fold and catalase activity only 1.47-1.78-fold compared to mature age I.

These results indicate that the age-related increase of MAO-B activity in the brain and parallel decrease in the activity of Cu-Zn-dependent SOD provide the basis for enhanced production of H_2O_2 and $O_2^{\bullet -}$ in the presence of insufficient compensatory increase in catalase activity and EACP content. The dynamics of ontogenetic changes in the studied enzymes attests to the existence of a MAO-B dependent mechanism attenuating antioxidant defense of the brain in aging humans.

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