# Dynamics of Activity of Monoamine Oxidase B and Antioxidant Defense Enzymes in Human Brain during Postnatal Ontogeny

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During postnatal development, activity of monoamine oxidase B in human brain structures increases, while activity of Cu,Zn-dependent SOD decreases with compensatory increase in catalase activity and ceruloplasmin content. Under these conditions, the resistance of the pontobulbar structures and thalamus to oxidative stress decreases at the age of 1-12 years and returned to the prenatal level during adolescence. The increase in catalase activity is most pronounced in structures of the forebrain (cortex and neostriatum), cerebellum, and hypothalamus; it is accompanied by ontogenetic increase in oxidative stress resistance, which is maximum at the age of 12-21 years. The maintenance of resistance to oxidative stress (depends on monoamine oxidase B) can be considered as an important condition of structural and functional maturation of cerebral structures during the postnatal ontogeny.

**Key Words:** *monoamine oxidase B; antioxidant defense enzyme; brain; human postnatal development*

Monoamine oxidase (MAO) is an important enzyme of the neurotransmitter metabolism playing an important role in the resulation of emotions and behavior [7,11]. $H_2O_2$ is a substrate-independent product of MAO reaction. It can induce free-radical damage to biomembranes and inhibit Cu,Zn-dependent SOD [6]. The major part of MAO activity in human brain is presented by MAO-B. The cerebral content of this enzyme in humans increases during aging [5]. The age-related increase in cerebral MAO-B during the late ontogeny is accompanied by pronounced decrease in Cu,Zn-SOD activity and resistance to oxidative stress (OS) and accumulation of LPO products in various parts of the brain [4,5]. Therefore, ontogenetic increase in MAO-B activity can be considered as a key mechanism of age-related involution of cerebral structures. Early age dynamics of MAO activity and its role in the regulation of brain resistance to OS at the early stages of ontogeny are poorly studied [11].

The aim of the present study was to analyze the age dynamics of MAO-B and ROS-eliminating enzymes and the resistance of various parts of the brain to OS during postnatal ontogeny.

## MATERIALS AND METHODS

Brain samples were obtained during autopsy of 111 cadavers (age from 1 day to 21 years) dead from traumas or brain-unrelated diseases. The material was proposed by Chelyabinsk Regional Forensic Bureau and Regional Children Pathologoanatomic Bureau. Mechanical asphyxia was the most prevalent cause of death ($n$=42), drowning ranked se-

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cond ($n$=18), and in 51 cases the death was caused by pneumonia, trauma, and poisoning. Samples of fetal brain were obtained during autopsy of 15 fetuses (25-30 weeks gestation) after medical abortions. In all cases the brain samples were obtained not later than 12 h after death. Samples of the nervous tissue with signs of ischemic, hemorrhagic, and traumatic injury were excluded from the study.

According to accepted periodization of children age [1], the obtained brain samples were divided into 8 groups: fetuses of the 2nd half of pregnancy, newborns (1-10 days), infants (from 11 days to 1 year), early childhood (1-3 years), 1st childhood period (3-7 years), 2nd childhood period (8-12 years for boys and 8-11 years for girls), juveniles (13-16 years for boys and 12-15 years for girls), and adolescents (17-21 years for men and 16-20 years for women). Each group comprised 10 brain samples (5 samples of each gender). Activity of MAO-B and antioxidant enzymes and the resistance to OS was evaluated in fields 6 and 17 of the cerebral cortex, dentate gyrus and hippocampus, neurostriatum (nucleus caudatus), diencephalic structures (thalamus and hypothalamus), cerebellum, pons, midbrain, and medulla oblongata. Activity of MAO-B in homogenates was measured spectrophotometrically using benzylamine hydrochloride as the substrate [2]. Activity of Cu,Zn-SOD was recorded colorimetrically [10]. Catalase activity was measured by the rate of decrease of $H_2O_2$ level in the incubation medium [9]. The content of enzyme-active ceruloplasmin (EACP) was determined using a modified method [8]; the incubation time was increased to 180 min. The resistance of the nervous tissue to OS was evaluated by accumulation of 2-TBA-reactive substances in 2.0-2.5% homogenates of brain structures incubated for 60 min on open air at 37°C [2,4]. The integral index of LPO intensity *in vitro* (oxidizability) was expressed in percents of TBA-reactive substances accumulation compared to the initial level.

Intergroup differences were analyzed using Mann—Whitney $U$ test. Interrelations between parameters were evaluated by calculating Spearmen correlation coefficients ($r_s$). Verification of statistical hypotheses was performed at $p$=0.05.

## RESULTS

Activity of MAO-B was maximum in diencephalic, mesencephalic, and pontobulbar parts of the brain (Table 1-3). In the ancient cortex (hippocampus), enzyme activity was 1.04-2.00-fold lower than in brainstem structures. Fields 6 and 17 of the cortex, dentate gyrus, cerebellum, and neostriatum were characterized by minimum values of MAO-B activity. MAO-B activity in the brain gradually increased during postnatal development (Table 1-3).

This regularity was most pronounced in the hypothalamus and pons: in adolescents enzyme activity in these structures increased 2-3 fold compared to prenatal values. Activity of MAO-B in these brain structures started to increase in the early childhood. In the thalamus, the age-related increase in MAO-B activity was observed later (2nd childhood period) and was less pronounced. The corresponding parameter in adolescents only 1.5-fold surpassed the prenatal values. In the caudate nucleus the increase in enzyme activity was characterized by the same order, but attained a level of statistical significance only by the juvenile age. In the above brain structures, MAO-B activity directly correlated with the absolute calendar age ($r_s$=0.301-0.560; $p$=0.0120-0.0001).

The same regularity was observed in the cerebellum, where significant increase in MAO-B activity was observed in the early childhood period, decreased in the 1st childhood period, and increased again in the 2nd childhood perion (Table 3). However, MAO-B activity in the cerebellum in general correlated with the calendar age ($r_s$=0.258; $p$=0.033). In the cortex, dentate gyrus, mesencephalon, and medulla oblongata, MAO-B activity transiently increased and then considerably decreased, so that this parameter did not correlate with the calendar age. The same was observed in the hippocampus, where MAO-B activity increased in the 2nd childhood period by 140% compared to fetal values, while in juveniles this parameter increased by 70%, and in adolescents it again increased by 110%.

In contrast to MAO-B, activity of Cu,Zn-SOD decreased with age (Table 1-3). This regularity was most pronounced in the hypothalamus, where Cu,Zn-SOD activity in the 1st childhood period decreased 4.4-fold compared to fetal values and, despite minor increase, in the adolescent age remained 2-fold below the prenatal values. Similar dynamics was observed in the caudate nucleus and, especially, in field 17 of the cortex, where Cu,Zn-SOD activity decreased more then 2-fold compared to the corresponding values in fetuses and infants. In the hypothalamus, neostriatum, and field 17 of the cortex, Cu,Zn-SOD activity negatively correlated with calendar age ($r_s$=-0.248 - -0.357; $p$=0.049-0.004). A less pronounced decrease in Cu,Zn-SOD activity was observed in the hippocampus and dentate gyrus (Table 1), where this parameter also depended on calendar age ($r_s$=-0.499 and $r_s$=-0.503, respec-

**TABLE 1.** Activity of MAO-B and Antioxidant Defense Enzymes in Forebrain Structures during Postnatal Ontogeny (*M*±*m*)

| Age | MAO-B, nmol/mg/min, $\times10^{-3}$ | SOD, U/mg tissue/min, $\times10^{-2}$ | Catalase, nmol/sec/g tissue | EACP, mg/10 g tissue |
|---|---|---|---|---|
| Cortex (field 6) | | | | |
| fetuses of the 2nd half of pregnancy | 2.50±0.28 | 2.05±0.62 | 1.07±0.11 | 2.30±0.36 |
| newborns | 4.30±0.75[1] | 2.23±0.37 | 1.20±0.23 | 4.33±0.24[1] |
| infants | 2.50±0.39[2] | 2.45±0.26 | 1.04±0.18 | 3.38±0.17[2] |
| early childhood | 2.70±0.31 | 1.55±0.27[2,3] | 1.10±0.17 | 3.49±0.25[2] |
| 1st childhood period | 2.50±0.27[2] | 2.14±1.20 | 1.92±0.19[1,3,4] | 3.38±0.23[1,2] |
| 2nd childhood period | 2.90±0.48 | 2.08±0.40 | 2.18±0.20[1,2,3,4] | 3.61±0.18[1,2] |
| juvenile age | 2.70±0.33 | 2.60±0.85[2] | 1.77±0.18[1,3,4] | 3.67±0.20[1,2] |
| adolescent age | 3.00±0.51 | 1.67±0.34 | 1.57±0.21[6] | 4.18±1.17 |
| Cortex (field 17) | | | | |
| fetuses of the 2nd half of pregnancy | 2.60±0.22 | 2.34±0.39 | 1.25±0.31 | 2.57±0.57 |
| newborns | 2.00±0.28 | 2.04±0.26 | 1.35±0.19 | 3.71±0.20 |
| infants | 2.30±0.21 | 2.42±0.33 | 1.09±0.12 | 3.14±0.19[2] |
| early childhood | 4.00±0.55[2,3] | 2.09±0.48 | 1.28±0.16 | 3.31±0.14[2] |
| 1st childhood period | 4.0±0.4[1,2,3] | 1.75±0.35 | 1.88±0.27 | 3.25±0.13[2] |
| 2nd childhood period | 3.20±0.45 | 1.56±0.39 | 2.33±0.19[1,2,3,4] | 3.50±0.22[2] |
| juvenile age | 2.80±0.33 | 2.08±0.36 | 2.06±0.18[1,2,3,4] | 3.57±0.16[2] |
| adolescent age | 2.2±0.2[4,5,6] | 1.07±0.33[1,4] | 1.74±0.18[4,6] | 3.08±0.28[2] |
| Caudate nucleus | | | | |
| fetuses of the 2nd half of pregnancy | 2.80±0.37 | 2.16±0.22 | 1.58±0.12 | 2.87±0.51 |
| newborns | 3.4±0.5 | 2.21±0.22 | 1.31±0.21 | 4.10±0.23[1] |
| infants | 3.70±0.36 | 1.99±0.33 | 1.30±0.18 | 3.55±0.15[1] |
| early childhood | 3.60±0.49 | 2.19±0.33 | 1.03±0.17[1] | 3.68±0.28[1] |
| 1st childhood period | 3.90±0.49 | 2.16±0.44 | 1.77±0.18[4] | 2.50±0.31[2,3] |
| 2nd childhood period | 3.30±0.55 | 1.91±0.14 | 2.36±0.24[1,2,3,4] | 3.44±0.29 |
| juvenile age | 4.20±0.56[1] | 1.0±0.3[2,3,4,6] | 2.00±0.18[2,3,4] | 3.63±0.21[5] |
| adolescent age | 4.20±0.45[1] | 1.33±0.22[2,5] | 1.45±0.15[4,6] | 3.60±0.47 |
| Hippocampus | | | | |
| fetuses of the 2nd half of pregnancy | 2.60±0.29 | 3.51±0.47 | 1.00±0.31 | 2.38±0.26 |
| newborns | 4.30±0.39[1] | 2.68±0.45 | 1.32±0.23 | 3.17±0.33 |
| infants | 3.50±0.36 | 3.48±0.37 | 1.66±0.10 | 3.44±0.20[1] |
| early childhood | 5.30±0.85[1] | 3.51±0.34 | 0.68±0.15[3] | 3.32±0.38[1] |
| 1st childhood period | 4.20±0.56[1] | 1.97±0.61 | 1.53±0.26[4] | 3.31±0.04[1] |
| 2nd childhood period | 6.3±0.9[1,3] | 2.07±0.35[1,3,4] | 1.86±0.21[1,4] | 3.36±0.04[1] |
| juvenile age | 4.40±0.56[1] | 1.97±0.20[1,3,4] | 2.30±0.34[1,2,4] | 3.51±0.24[1] |
| adolescent age | 5.50±1.22[1] | 1.93±0.22[1,3,4] | 2.33±0.23[1,2,4] | 3.24±0.19[1] |
| Dentate gyrus | | | | |
| fetuses of the 2nd half of pregnancy | 3.90±0.39 | 3.41±0.51 | 0.94±0.11 | 2.01±0.25 |
| newborns | 4.40±0.51 | 2.91±0.33 | 1.22±0.23 | 3.07±0.29[1] |
| infants | 3.70±0.35 | 3.76±0.33 | 1.41±0.14[1] | 3.36±0.35[1] |
| early childhood | 2.80±0.26 | 2.86±0.36 | 1.00±0.16[3] | 3.46±0.16[1] |
| 1st childhood period | 3.90±0.39[4] | 2.06±0.46[3] | 1.76±0.25[1,4] | 3.61±0.14[1] |
| 2nd childhood period | 4.3±0.5[1,3,4] | 1.77±0.49[3] | 2.06±0.11[1,2,3,4] | 3.81±0.17[1,2] |
| juvenile age | 3.70±0.35 | 2.06±0.27[1,3] | 2.26±0.27[1,2,3,4] | 3.28±0.13[1] |
| adolescent age | 2.8±0.2[5,6] | 2.0±0.2[1,2,3] | 2.86±0.2[1,2,3,4,5,6] | 3.20±0.21[1] |

**Note.** Here and in Tables 2, 3: $p<0.05$ compared to [1]fetuses, [2]newborns, [3]infants, [4]early childhood, [5]1st childhood period, [6]2nd childhood period, [7]juvenile age.

**TABLE 2.** Activity of MAO-B and Antioxidant Defense Enzymes in Diencephalic and Mesencephalic Structures during Postnatal Ontogeny (*M*±*m*)

| Age | MAO-B, nmol/mg/min, $\times10^{-3}$ | SOD, U/mg tissue/min, $\times10^{-2}$ | Catalase, nmol/sec/g tissue | EACP, mg/10 g tissue |
|---|---|---|---|---|
| Midbrain | | | | |
| fetuses of the 2nd half of pregnancy | 3.80±0.64 | 3.50±1.09 | 1.95±0.29 | 2.42±0.39 |
| newborns | 3.50±0.71 | 2.20±0.21 | 1.08±0.17[1] | 4.50±0.25[1] |
| infants | 4.40±0.79 | 1.98±0.36 | 0.94±0.16[1] | 3.51±0.16[1,2] |
| early childhood | 4.40±0.61 | 3.24±0.37[2] | 0.97±0.17[1] | 3.28±0.15[2] |
| 1st childhood period | 4.70±0.66 | 2.78±0.35 | 1.67±0.27 | 3.15±0.38[2] |
| 2nd childhood period | 3.00±0.35[5] | 2.21±0.21[4] | 1.68±0.29[3,4] | 3.86±0.15[1,2,4] |
| juvenile age | 4.20±0.69 | 2.11±0.31 | 1.38±0.15 | 4.18±0.23[1,3,4] |
| adolescent age | 4.20±0.39 | 2.13±0.35 | 1.09±0.008[1] | 4.08±0.75[1,2] |
| Thalamus | | | | |
| fetuses of the 2nd half of pregnancy | 3.7±0.6 | 2.05±0.40 | 1.53±0.26 | 3.95±0.75 |
| newborns | 3.00±0.47 | 1.99±0.29 | 1.26±0.20 | 4.18±0.32 |
| infants | 4.00±0.37 | 2.28±0.40 | 1.16±0.16 | 3.54±0.13 |
| early childhood | 4.00±0.25 | 1.94±0.25 | 0.76±0.15[1] | 3.85±0.18 |
| 1st childhood period | 4.00±0.52 | 1.87±0.33 | 2.10±0.25[2,3,4] | 3.63±0.22 |
| 2nd childhood period | 5.1±0.8[2] | 2.29±0.51 | 2.23±0.17[2,3,4] | 5.44±0.56[3,4,5] |
| juvenile age | 5.20±0.57 | 1.93±0.24 | 1.59±0.16[4,6] | 4.04±0.21[6] |
| adolescent age | 5.40±0.61[1,2] | 2.07±0.28 | 1.29±0.17[4,5,6] | 3.29±0.18[6,7] |
| Hypothalamus | | | | |
| fetuses of the 2nd half of pregnancy | 3.00±0.62 | 3.29±0.46 | 1.73±0.43 | 2.33±0.38 |
| newborns | 4.40±0.87 | 3.01±0.88 | 1.30±0.18 | 4.04±0.19[1] |
| infants | 4.50±0.81 | 2.63±0.29 | 1.20±0.15 | 3.63±0.31[1] |
| early childhood | 5.50±0.49[1] | 2.58±0.23 | 1.00±0.13 | 3.25±0.08[1,2] |
| 1st childhood period | 4.8±0.5[1] | 0.8±0.1[1,2,3,4] | 1.50±0.27 | 3.52±0.22[1] |
| 2nd childhood period | 8.3±1.6[1] | 2.05±0.47[5] | 1.89±0.14[3,4] | 3.90±0.24[1] |
| juvenile age | 8.00±0.9[1,2,3,4] | 1.62±0.36[5] | 1.82±0.21[3,4] | 3.59±0.14[1,2] |
| adolescent age | 6.60±0.94[1] | 1.6±0.2[1,3,4,5] | 1.46±0.17 | 3.44±0.27 |

tively; $p$=0.0005 in both cases) and in adolescents decreased 1.6-1.8-fold compared to the fetal value.

Cu,Zn-SOD activity in field 6 of the cortex in early childhood decreased compared to the corresponding parameter in newborns, but then increased to the juvenile age (Table 1). Cu,Zn-SOD activity in the mesencephalon increased in early childhood and then decreased in the 2nd childhood period and in juveniles. In the thalamus, pons and cerebellum, no significant ontogenetic shifts in Cu, Zn-SOD activity were found.

Evident reciprocal nature of the ontogenetic dynamics of Cu,Zn-SOD and MAO-B activities correspond to the pattern of age-related changes in activities of these enzymes in the brain and spinal cord of aging individuals [3,5]. This is probably determined by activation of MAO-B-dependent production of $H_2O_2$ acting as a Cu,Zn-SOD inhibitor [6]. In view of age-related decrease in Cu,Zn-SOD activity in the brain, of particular interest are ontogenetic shifts in cerebral content of EACP, which is considered to be a SOD-like factor of antioxidant defense in the brain [5]. In the majority of brain structures, the content of EACP in newborns increased 1.4-1.9-fold compared to fetal values; then this parameter gradually decreased remaining above the fetal values until juvenile age and attaining the prenatal values in adolescents (Table 1-3). This is also true for the dynamics of EACP content in field 6 of the cortex, caudate nucleus, hypothalamus, and pontobulbar structures. The content of EACP in the mesencephalon of adolescents decreased compared to the corresponding parameter in newborns, but remained considerably increased compared to fetal values. Similar ontogenetic dynamics was observed in the hippocampus, where EACP

**TABLE 3.** Activity of MAO-B and Antioxidant Defense Enzymes in Rhomboid Brain Structures during Postnatal Ontogeny (*M*±*m*)

| Age | MAO-B, nmol/mg/min, $\times10^{-3}$ | SOD, U/mg tissue/min, $\times10^{-2}$ | Catalase, nmol/sec/g tissue | EACP, mg/10 g tissue |
|---|---|---|---|---|
| Cerebellum | | | | |
| fetuses of the 2nd half of pregnancy | 2.80±0.44 | 2.82±0.55 | 1.98±0.29 | 2.97±0.52 |
| newborns | 2.50±0.44 | 2.03±0.25 | 1.28±0.18[1] | 3.71±0.21 |
| infants | 2.70±0.41 | 2.06±0.46 | 1.22±0.19[1] | 3.39±0.21 |
| early childhood | 4.3±0.4[1,2,3] | 2.30±0.31 | 0.99±0.19[1] | 3.38±0.16 |
| 1st childhood period | 2.50±0.28[4] | 2.39±0.51 | 1.97±0.37[4] | 3.57±0.17 |
| 2nd childhood period | 4.4±0.76[1,5] | 2.56±0.28 | 2.09±0.21[2,3,4] | 4.39±0.27[1,3] |
| juvenile age | 3.70±0.47 | 2.15±0.30 | 1.88±0.18[2,3,4] | 3.89±0.15[4] |
| adolescent age | 3.7±0.6 | 1.78±0.38 | 2.04±0.16[2,3,4] | 2.99±0.42[6] |
| Pons Varolii | | | | |
| fetuses of the 2nd half of pregnancy | 2.30±0.26 | 2.73±0.48 | 1.25±0.25 | 2.60±0.40 |
| newborns | 3.60±0.73 | 1.72±0.36 | 1.20±0.18 | 4.10±0.19[1] |
| infants | 3.30±0.54 | 2.21±0.37 | 0.92±0.15 | 3.56±0.13[1,2] |
| early childhood | 4.40±0.25[1] | 2.03±0.32 | 0.71±0.12[2] | 3.36±0.15[2] |
| 1st childhood period | 3.40±0.29[1] | 2.03±0.48 | 1.93±0.25[3,4] | 3.05±0.52 |
| 2nd childhood period | 4.40±0.63[1] | 2.35±0.34 | 1.40±0.19[3,4] | 3.98±0.28[1] |
| juvenile age | 4.30±0.84[1] | 1.67±0.33 | 1.41±0.13 | 3.87±0.11[1,4] |
| adolescent age | 7.0±0.6[1,6] | 1.86±0.32 | 1.33±0.15[4,5] | 3.38±0.25 |
| Medulla oblongata | | | | |
| fetuses of the 2nd half of pregnancy | 4.5±0.6 | 1.30±0.36 | 1.87±0.18 | 3.15±0.44 |
| newborns | 5.50±1.29 | 2.13±0.14 | 1.23±0.23 | 4.60±0.21[1] |
| infants | 7.00±0.78[1] | 2.08±0.30 | 0.89±0.12[1] | 3.78±0.30 |
| early childhood | 3.90±0.39[3] | 2.33±0.31 | 0.63±0.15[1] | 3.38±0.10[2] |
| 1st childhood period | 3.90±0.37[3] | 1.39±0.32 | 1.45±0.30 | 3.12±0.34[2] |
| 2nd childhood period | 4.90±0.76 | 2.72±0.37[5] | 1.68±0.25[3,4] | 3.54±0.21[2] |
| juvenile age | 5.20±0.68 | 2.92±0.83 | 1.38±0.14[3,4] | 3.87±0.16[2,4] |
| adolescent age | 6.20±0.86 | 1.50±0.21[6,7] | 1.11±0.12[1,4] | 3.59±0.31[2] |

content first increased in early childhood, somewhat decreased during the 1st and 2nd childhood periods, but remained above the prenatal values until juvenile age. The cerebellum was characterized by latest increase in EACP content (this parameter transitory increased during the 2nd childhood period and in juveniles). Similar changes in EACP content were observed in the thalamus. The most pronounced age-related increase in the content of EACP was observed in the dentate gyrus, the only brain structure, where this parameter directly correlated with age ($r_s$=0.304; $p$=0.028). Hence, the observed age-related changes in the content of EACP can compensate for the ontogenetic decrease in Cu,Zn-SOD activity, primarily in field 6 of the cortex, dentate gyrus, hippocampus, and hypothalamus characterized by opposite dynamics of these enzymes (Table 1-2).

The age-related decrease in Cu,Zn-SOD activity was accompanied by a pronounced transitory decrease in catalase activity in the majority of brain structures (Table 1-3). This regularity was most pronounced in the mesencephalon and medulla oblongata, where the 2-fold decrease in catalase activity was first recorded in newborns and infants, respectively, and, despite subsequent increase in enzyme activity, persisted until adolescence. In the thalamus and pons, the sharp decrease in catalase activity during the early childhood was compensated by subsequent increase in this parameter by 3-21 years. Similar dynamics of catalase activity was observed in the cerebellum and neostriatum, where this parameter considerably surpassed the prenatal level during the 2nd childhood period and gradually decreased to the fetal level in adolescents. In contrast to brainstem structures, catalase activity

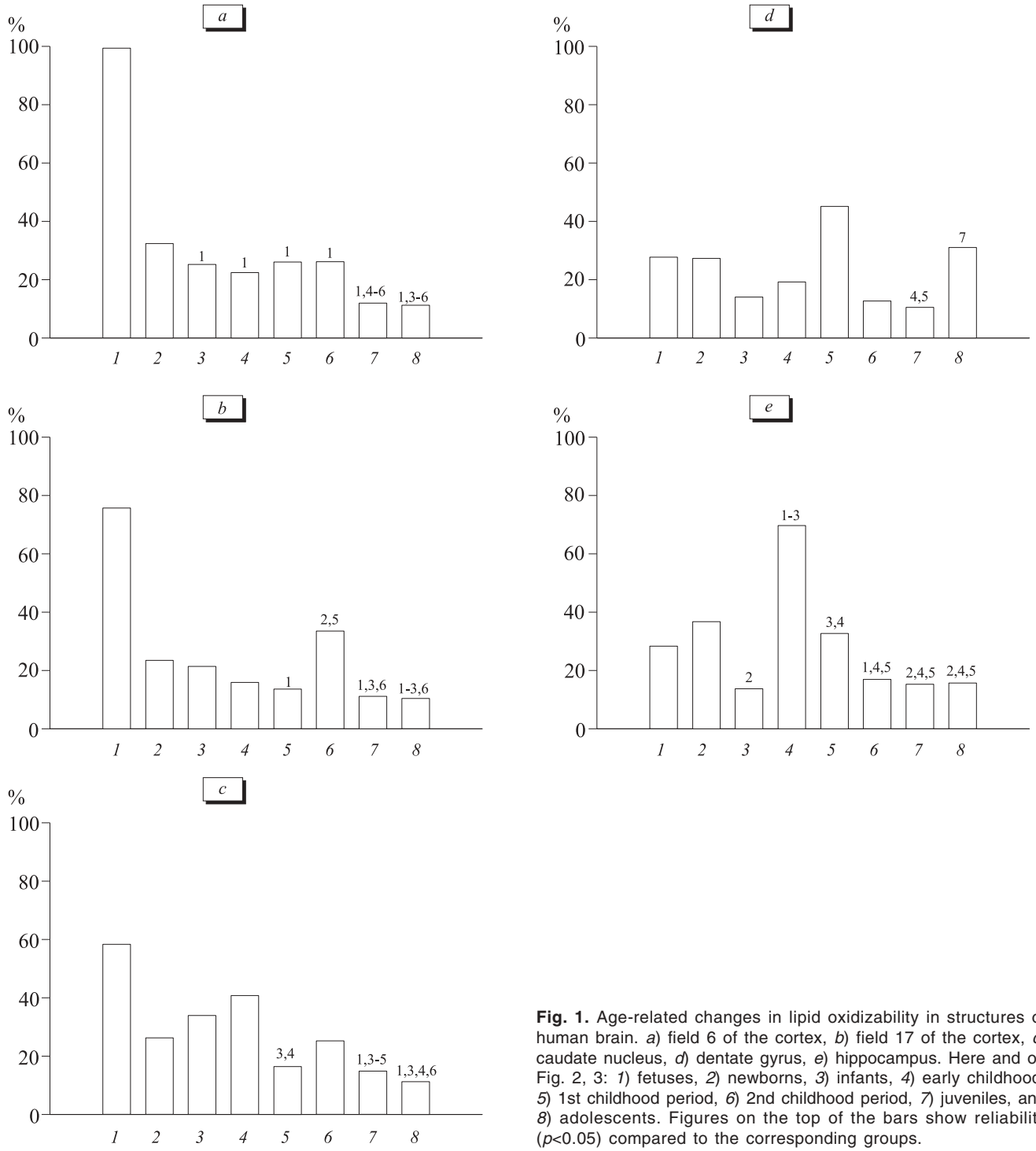


**Fig. 1.** Age-related changes in lipid oxidizability in structures of human brain. *a*) field 6 of the cortex, *b*) field 17 of the cortex, *c*) caudate nucleus, *d*) dentate gyrus, *e*) hippocampus. Here and on Fig. 2, 3: *1*) fetuses, *2*) newborns, *3*) infants, *4*) early childhood, *5*) 1st childhood period, *6*) 2nd childhood period, *7*) juveniles, and *8*) adolescents. Figures on the top of the bars show reliability ($p<0.05$) compared to the corresponding groups.

in the caudate nucleus and cerebellum positively correlated with calendar age ($r_s$=0.207; $p$=0.038 and $r_s$=0.327; $p$=0.0002, respectively).

Fields 6 and 17 of the cortex, dentate gyrus, and hippocampus, in contrast to other brain structures were only characterized by reliable increase in catalase activity compared to prenatal age (Table 1). The increase in enzyme activity in the cortex was transient and was most pronounced in the 2nd childhood period and in juveniles. In the dentate gyrus and hippocampus, the pronounced increase in catalase activity was observed starting from the 1st childhood period; in adolescents this parameter increased more than 2-fold. This regularity was most pronounced in the dentate gyrus, where catalase activity in adolescents 3-fold surpassed the

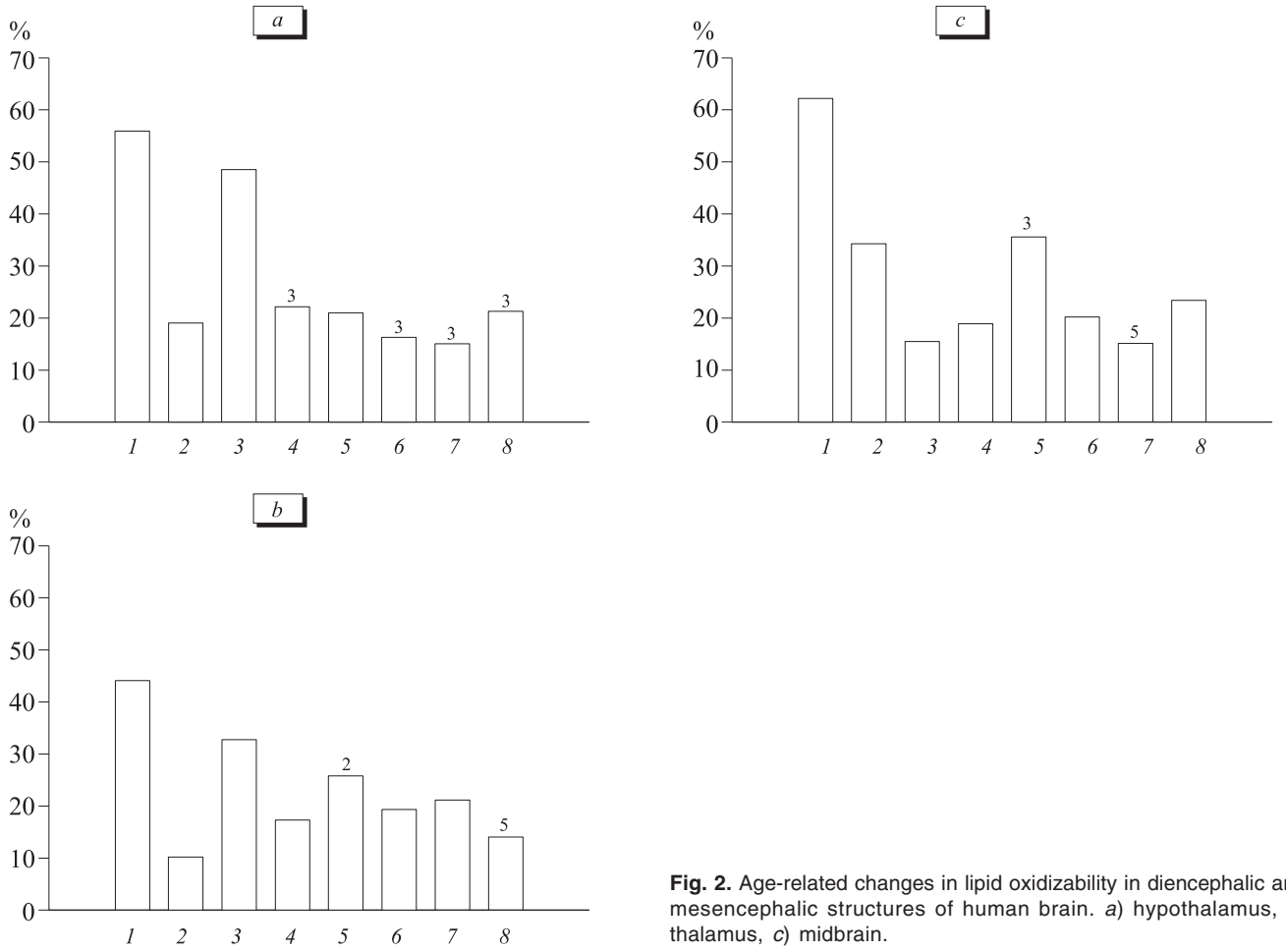


**Fig. 2.** Age-related changes in lipid oxidizability in diencephalic and mesencephalic structures of human brain. *a*) hypothalamus, *b*) thalamus, *c*) midbrain.

prenatal value. In all studied brain structures, catalase activity directly correlated with the calendar age ($r_s$=0.395-0.717; $p$=0.0130-0.0001).

The observed age-related increase in catalase activity can be considered as a compensatory reaction aimed at the maintenance of antioxidant defense of the brain under conditions of ontogenetic MAO-B dependent decrease in Cu,Zn-SOD activity [5]. This compensation is most effective in the cortex, where the age-related increase in catalase activity was in general comparable or surpassed the ontogenetic increase in MAO-B activity and concomitant decrease in Cu,Zn-SOD activity. This assumption is confirmed by age dynamics of the resistance of brain structures to OS (Fig. 1-3). Fields 6 and 17 of the cortex are characterized by pronounced ontogenetic decrease in lipid oxidizability, which peaked in adolescents and negatively correlated with age ($r_s$=-0.472; $p$=0.0005 and $r_s$=-0.455; $p$=0.0009, respectively). Similar regularity was observed in the neostriatum ($r_s$=-0.415; $p$=0.00042), cerebellum ($r_s$=-0.408; $p$=0.0005), and hippocampus ($r_s$=-0.249; $p$=0.044), despite pronounced transitory increase in lipid oxidizability in this structure in early childhood (Table 1, 3). Hypothalamus was the only brainstem structure characterized by a negative correlation between lipid oxidizability and the calendar age ($r_s$=-0.292; $p$=0.016). The resistance of the medulla oblongata to OS considerably increased in infants; lipid oxidizability increased during the early childhood and 1st childhood periods, and decreased again in the 2nd childhood period. Similar dynamics of the resistance to OS was observed in the mesencephalon and pons (Table 2, 3). Changes in lipid resistance to OS in the pontobulbar and mesencephalic structures did not correlate with age, none of the parameters demonstrated significant correlation with the time elapsed after death.

Our findings demonstrated stereotypic increase in MAO-B activity accompanied by a decrease in Cu,Zn-SOD activity and compensatory increase in catalase activity and EACP content in structures of human brain during the postnatal development. Under these conditions, the resistance to OS of the pontobulbar structures and thalamus decreases at the age of 1-12 years and then lipid oxidizability returned to the prenatal level during adolescence. The forebrain structures (cortex and neostriatum), cerebel-

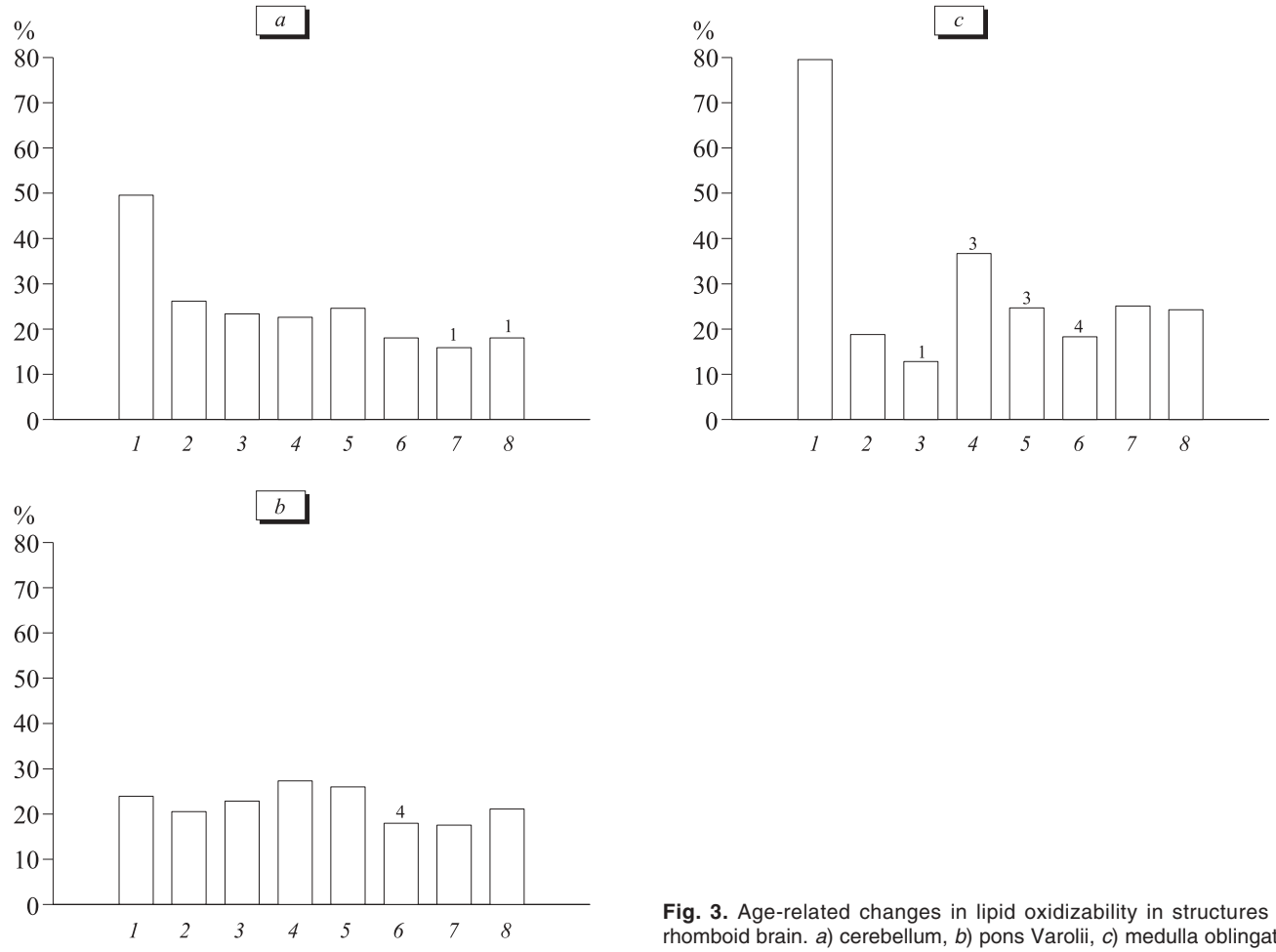


**Fig. 3.** Age-related changes in lipid oxidizability in structures of rhomboid brain. *a*) cerebellum, *b*) pons Varolii, *c*) medulla oblingata.

lum, and hypothalamus were characterized by the most pronounced increase in catalase activity paralleled by ontogenetic increase in OS resistance, which peaked at the age of 12-21 years. Our findings illustrate the efficiency of compensatory mechanisms of antioxidant defense preventing impairment of brain resistance to OS with increasing MAO-B activity in the dynamics of postnatal development. The maintenance of brain resistance to MAO-B-dependent OS can be considered as an important condition of structural and functional maturation of cerebral structures during the postnatal ontogeny.

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