Dynamics of LPO Products and Oxidative Modification of Proteins in Human Brain during Postnatal Development

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Opposite changes in the content of LPO products and products of oxidative modification of proteins were detected in human brain structures in the course of postnatal development. A clear-cut ontogenetic reduction of LPO products was observed in field 17 of the cortex, archicortex structures, and in the hypothalamus. Age-specific increase in the levels of products of oxidative modification of proteins was recorded in all compartments of the brain; it peaked by the age of 12-21 years and was most pronounced (4-6-fold) in the visual cortex, hippocampus, diencephalic and pontobulbar compartments of the brain.

Key Words: *lipid peroxidation; oxidative modification of proteins; brain; human postnatal development*

Aging is associated with reduction of CNS resistance to oxidative stress and increase in the content of LPO products in cerebral and spinal structures [3]. This regularity is assumed to result from age-specific increase in activity of monoamine oxidase B, concomitant reduction of Cu,Zn-dependent SOD activity, and insufficient compensatory increase in activities of catalase and ceruloplasmin in the brain and thoracic compartment of the spinal cord [2,4]. H_2O_2, a substrate-independent product of monoamine oxidase reaction, is characterized by Cu,Zn-SOD-inhibitory effect and LPO-inducing activity.

Early age-specific changes in cerebral activity of monoamine oxidase B and antioxidant defense enzymes qualitatively do not differ from the corresponding shifts during aging [5]. On the other hand, postnatal development, in contrast to late ontogeny, is associated with not a drop, but an increase in the resistance of the rostral compartments of the brain to LPO induction *in vitro* [5]. Early dynamics of cerebral levels of lipoperoxides and products of oxidative protein modification (OPM) remains unstudied.

We analyzed age-specific changes in the content of LPO and OPM products in different compartments of the brain during different stages of human postnatal ontogeny.

MATERIALS AND METHODS

Brain preparations were obtained during autopsy from 96 human cadavers of subjects dead at the age of 1 day to 21 years from diseases or injuries not directly involving the brain. The material for analysis was obtained from Chelyabinsk Regional Bureau of Forensic Medical Expert Evaluation and from Regional Bureau of Pediatric Pathology. The most frequent causes of death were traumas (30 cases), mechanical asphyxia (17 cases), and in 49 cases death was a result of pneumonia, drowning, and poisoning. Fetal brain preparations were obtained at autopsy of 10 fetuses dead as a result of medical abortions at gestation weeks 28-35. Brain samples were obtained for analysis no later than

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12 h after death in all cases. The preparations with signs of ischemic, hemorrhagic, and traumatic injuries were excluded from the study.

In accordance with universal periodization of childhood [1], brain samples were divided into 8 groups: fetuses of the 2nd half of pregnancy, newborns (1-10 days), nursing babies (11 days to 1 year), infancy and early childhood (1-3 years), childhood period 1 (3-7 years), childhood period 2 (8-12 years for boys, 8-11 years for girls), adolescence (13-16 years for boys, 12-15 years for girls), and youth (17-21 years for men, 16-20 years for women). Each group included 10 brain preparations (5 samples for each gender).

The levels of LPO and OPM products were measured in the cortex (fields 6 and 17), dentate gyrus and hippocampus, neostriatum (caudate nucleus), diencephalic structures (thalamus, hypothalamus), cerebellum, pons, midbrain, and medulla oblongata.

The content of LPO products was measured spectrophotometrically; lipoperoxides in heptane and isopropanol phases of the lipid extract were measured separately. The results were expressed in oxidation index units: E_{232}/E_{220} (percentage of conjugated dienes) and E_{278}/E_{220} (levels of ketodienes and conjugated trienes). The levels of the final LPO products (Schiff's bases; SB) in both phases of the lipid extract were evaluated by the E_{400}/E_{220} ratio [7]. The content of OPM products was measured as described previously [6] and expressed in mmol protein-bound 2,4-dinitrophenylhydrasones/g protein.

The significance of differences between the groups was evaluated using Mann—Whitney *U* test. The relationships between the parameters were evaluated using Spearman correlation coefficient (*r*)

RESULTS

The content of LPO products decreased during postnatal development in the majority of studied brain compartments, especially in the endbrain structures, where changes in the content of LPO products during ontogeny were the most pronounced (Table 1). The level of isopropanol-soluble conjugated dienes in field 6 of the cortex decreased significantly in comparison with fetal values as early as during the nursing age and remained decreased during infancy and early childhood and in adolescence and youth. Similar shifts in the sensory cortical regions (field 17) were observed only in adolescence and youth. On the other hand, field 17 was characterized by most pronounced reduction in the content of secondary isopropanol-soluble LPO products (ketodienes and conjugated trienes). The level of this category of lipoperoxides in the visual cortex negatively correlated with the calendar age (r=-0449; p=0.021). The same relationship (r=-0.338; p=0.049) was detected between the age and content of isopropanol-soluble SB in the visual cortex.

Less bright ontogenetic changes were noted for heptane-soluble lipoperoxides in endbrain structures (Table 1). The content of heptane-extracted ketodienes and conjugated trienes in field 17 increased significantly in infancy and early childhood in comparison with the fetal level and again reduced to the prenatal values by adolescence. The age-associated dynamics of heptane-soluble SB in the visual cortex was identical. A significant reduction of heptane-soluble ketodienes and conjugated trienes in the caudate nucleus was observed only in adolescence. No significant correlations between the calendar age and levels of heptane-extracted lipoperoxides were detected in any of the above structures of the endbrain.

The ontogenetic dynamics of the archicortex lipoperoxides deserves special discussion (Table 1). The hippocampus and dentate gyrus were characterized by a pronounced increment in the levels of primary and secondary lipoperoxides in the newborns in comparison with fetuses. Later the lipoperoxide content decreased in the archicortex. A deviation from this regularity was observed for the dynamics of heptane-soluble conjugated dienes in the hippocampus: their level remained elevated in nursing babies and during childhood period 1. The content of isopropanol-extracted SB in the dentate gyrus also remained high from the age of 11 days to 3 years and during childhood period 2. Only heptane-soluble LPO products in the archicortex demonstrated a significant negative correlation with the calendar age: hippocampal and dentate gyrus SB (r=-0.497; p=0.0052 and r=-0.512; p=0.0045, respectively) and dentate gyrus ketodienes and conjugated trienes (r=-0.484; p=0.0067).

The level of lipoperoxides in diencephalic compartments of the brain also decreased during the postnatal development (Table 2). This was particularly demonstrative in the hypothalamus, where a significant reduction of the content of heptane-soluble conjugated dienes and SB was observed in infancy and early childhood and in adolescence. The content of heptane-extracted ketodienes and conjugated trienes in the hypothalamus decreased by youth. Only in nursing babies, the level of isopropanol-soluble conjugated dienes was lower than in fetuses. The content of isopropanol-soluble SB, ketodienes, and conjugated trienes in the hypothalamus transitorily increased in infancy and early childhood and decreased in adolescence to a level

below the fetal. The level of SB continued to decrease and reached the minimum by youth. The hypothalamic levels of secondary LPO products in both extract phases and of heptane-soluble conjugated dienes and isopropanol-soluble SB negatively correlated with calendar age: r from -0.434 to -0.507 (p=0.027-0.008). A similar relationship in the thalamus (r=-0.454; p=0.038) was observed only for isopropanol-soluble SB: their content decreased significantly in comparison with the prenatal values by adolescence (Table 2). Other LPO parameters in this brain compartment did not correlate with age and were characterized by transitory increase at the age of 11 days to 3 years with subsequent reduction in adolescence and youth. The only exclusion was the dynamics of heptane-soluble conjugated dienes: their level in the thalamus increased significantly by adolescence.

Postnatal changes in LPO parameters in the mesencephalic and pontobulbar compartments of the brain in general corresponded to shifts in the endbrain structures and its diencephalic compartments. The level of heptane-soluble conjugated dienes in the midbrain decreased significantly during infancy and early childhood and during adolescence in comparison with the prenatal values (Table 2). The mesencephalic levels of isopropanol-soluble SB were characterized by a three-phasic postnatal dynamics with a significant reduction in nursing babies in comparison with the fetal values, subsequent increase in infancy and early childhood, and repeated reduction at the age of 12-21 years (Table 2). The levels of heptane-soluble SB, ketodienes, and conjugated trienes in the midbrain increased significantly in infancy and early childhood and reduced to the prenatal level by the age of 12-16 years. Similar age-associated dynamics of isopropanol-soluble conjugated dienes, ketodienes, and conjugated trienes was detected in the medulla oblongata and pons (Table 3). Similar age-specific changes in heptane-extracted ketodienes and conjugated trienes were detected in the medulla oblongata.

The midbrain was the only brain compartment where the content of some LPO products directly correlated with age. For example, the content of isopropanol-soluble conjugated dienes (r=0.543; p=0.004): in adolescence decreased in comparison with infancy and early childhood and increased in youth in comparison with nursing age, infancy, early childhood, and adolescence (Table 2). Similar age-associated changes in heptane-soluble conjugated dienes were seen in the medulla oblongata (Table 3). Contrary to this, a significant increase of this category of LPO products was observed in the pons and cerebellum at the age of 11 days to 3 years and 12-21 years (Table 3). A significant decrease in the level of isopropanol-soluble ketodienes and conjugated trienes was observed in the cerebellum at the age of 11 days to 3 year and of SB in adolescence. The levels of heptane-soluble SB in the cerebellum and medulla oblongata decreased significantly in adolescents. The medulla oblongata was the only structure of the hindbrain, for which a negative correlation between the content of LPO products and age was detected. This relationship was demonstrated for isopropanol-soluble SB (r=-0.441; p=0.024), the level of which reduced 2-fold in youth in comparison with the prenatal level (Table 3).

The results of correlation analysis indicate that the content of LPO products decreased most significantly in the course of postnatal development in the sensory cortical field 17, ancient cortical structures, and hypothalamus. This regularity is in good agreement with previously revealed postnatal increase in the resistance of these brain compartment to oxidative stress *in vitro*, which is largely associated with the ontogenetic increase in catalase and ceruloplasmin activities [5]. A transitory increase in lipoperoxide levels and their subsequent reduction in the majority of stem structures of the brain in different terms of the period between 11 days and 3 years (Tables 2, 3) is also in line with a previously detected transitory drop of catalase activity in these brain compartments and concomitant reduction of their oxidative stress resistance [6].

It cannot be excluded, that LPO limitation in the course of postnatal ontogeny can be associated with not only increase in activities of catalase and ceruloplasmin, but also with predominant redistribution of active oxygen forms to the OPM processes. This probability is illustrated by obviously opposite postnatal changes in the levels of LPO and OPM products in the brain structures (Tables 1-3). The level of OPM products tended to increase starting from the newborn age in the majority of cases (Tables 1-3). This parameter somewhat decreased during the nursing period and infancy and early childhood, after which is again increased, reaching a statistically significant maximum in the majority of brain compartments in adolescents. The archicortex formations (Table 1) and the medulla oblongata (Table 3) were exclusions: in these structures the initial statistically significant increment in OPM levels was observed during the nursing age. The hippocampus was the only compartment of the brain, in which the OPM content reached the maximum level in youth. All the hindbrain structures and the diencephalic compartments of the brain and the midbrain were characterized by a direct relationship between OPM characteristics and the calendar age

TABLE 1. Age-Specific Changes in the Content of Primary LPO and OPM Products in Endbrain Structures during Human Postnatal Ontogeny (*M*±*m*)

Object of analysis	Lipid extract phase						OPM products (per g protein)
		heptane			isopropanol		
	CD	KD and CT	SB	CD	KD and CT	SB	
Cortex (field 6)							
fetuses	0.8240±0.0309	0.361±0.026	0.0500±0.0019	0.6860±0.0213	0.413±0.153	0.0920±0.0254	125.86±6.05
newborns	0.8700±0.0245	0.580±0.051	0.408±0.061	0.5810±0.0955	0.2290±0.0285	0.023±0.016	214.67±91.08
nursing babies	0.7100±0.1169	0.3240±0.1258	0.1080±0.0915	0.4860±0.0537[1]	0.204±0.057	0.0400±0.0379	61.05±14.28
infancy and early childhood	0.5890±0.0342	0.353±0.132	0.1490±0.0557	0.5460±0.0563[1]	0.2540±0.0626	0.184±0.074	49.59±4.31
childhood, period 1	0.492±0.012	0.363±0.020	0.208±0.018	0.4440±0.0125	0.1935±0.0235	0.0330±0.0075	124.88±15.32[3,4]
childhood, period 2	0.656±0.230	0.4940±0.2525	0.270±0.220	0.616±0.031	0.146±0.024	0.025±0.015	165.03±54.26[4]
adolescence	0.6540±0.0393	0.3220±0.0139	0.1570±0.0147[1]	0.5320±0.0292[1]	0.1560±0.0272	0.0450±0.0072[4]	345.60±7.89[3-6]
youth	0.6500±0.0606	0.4020±0.0565	0.2030±0.0583	0.5650±0.0425[1]	0.1910±0.0196	0.0400±0.0102[4]	225.38±62.99
Cortex (field 17)							
fetuses	0.6630±0.0272	0.2080±0.0308	0.0480±0.0066	0.604±0.011	0.3810±0.1221	0.0890±0.0157	58.37±5.70
newborns	0.6910±0.1865	0.453±0.211	0.255±0.140	0.643±0.001	0.2950±0.0185	0.075±0.016	106.67±25.44
nursing babies	0.5170±0.0997	0.289±0.110	0.1390±0.0739	0.4700±0.0468	0.2190±0.0343	0.054±0.039	75.82±30.00
infancy and early childhood	0.6490±0.0236	0.3770±0.0684[1]	0.1770±0.0327[1]	0.6270±0.0309	0.3690±0.0796[1]	0.1420±0.0191	75.56±9.65
childhood, period 1	0.635±0.021	0.237±0.033	0.126±0.020	0.5310±0.0085	0.155±0.027	0.0250±0.0025	144.96±38.40[1]
childhood, period 2	0.689±0.159	0.4870±0.1395	0.301±0.145	0.531±0.079	0.120±0.033	0.0260±0.0075	337.93±169.85[1]
adolescence	0.5880±0.0349	0.2220±0.0226[4]	0.0630±0.0035[4]	0.520±0.019[1,4]	0.1790±0.0353[4]	0.0380±0.0018	362.05±25.70[1-4]
youth	0.7320±0.0628	0.5140±0.0669	0.2340±0.0657	0.5600±0.0593[4]	0.1800±0.0328[4]	0.035±0.011[4]	192.10±91.57
Caudate nucleus							
fetuses	0.6320±0.0239	0.2840±0.0232	0.0590±0.0143	0.5300±0.1856	0.2430±0.0221	0.117±0.010	77.85±13.73
newborns	0.8180±0.1745	0.589±0.090	0.2840±0.1015	0.431±0.060	0.1030±0.0875	0.013±0.010	156.30±53.82
nursing babies	0.7510±0.0575	0.3330±0.0907	0.1530±0.0671	0.500±0.068	0.1910±0.0515	0.0580±0.0399	59.63±15.87
infancy and early childhood	0.4720±0.1446	0.2260±0.0619	0.0510±0.0105	0.628±0.030	0.2530±0.0482	0.0680±0.0245	35.55±4.53[1,2]
childhood, period 1	0.6400±0.0415	0.2870±0.0065	0.200±0.011	0.584±0.050	0.216±0.014	0.0190±0.0115	118.13±18.62[4]
childhood, period 2	0.6060±0.2335	0.4010±0.2825	0.261±0.210	0.598±0.037	0.1840±0.0575	0.0270±0.0185	144.92±44.19[4]
adolescence	0.590±0.037	0.1650±0.0241[1]	0.0460±0.0041	0.5440±0.0323	0.1810±0.0246	0.0670±0.0121[1]	166.45±11.47[1,4,5]
youth	0.6950±0.0763	0.457±0.085	0.2770±0.0858	0.5760±0.0254[2]	0.1930±0.0161	0.0380±0.0109	231.97±93.72
Hippocampus							
fetuses	0.5470±0.0819	0.3110±0.0557	0.2890±0.0295	0.2840±0.0175	0.0440±0.0057	0.0070±0.0002	39.41±3.47
newborns	0.8790±0.0101[1]	0.5660±0.0584[1]	0.4360±0.0181[1]	0.5730±0.0514[1]	0.2040±0.0325[1]	0.0120±0.0027	167.71±39.28

TABLE 1.

Object of analysis	Lipid extract phase						OPM products (per g protein)
		heptane			isopropanol		
	CD	KD and CT	SB	CD	KD and CT	SB	
nursing babies	0.7670±0.0592[1]	0.4890±0.0809	0.245±0.064	0.4670±0.0608	0.2210±0.0586	0.0840±0.0418	93.33±22.56[1]
infancy and early childhood	0.6370±0.0724	0.3610±0.0717	0.1730±0.0604[2]	0.5720±0.0284[1]	0.2760±0.0506	0.1310±0.0584	28.89±5.71[3]
childhood, period 1	0.525±0.108[1]	0.2820±0.0978[2]	0.054±0.039[1-3]	0.497±0.047[1]	0.1730±0.0479[2]	0.030±0.022	46.97±22.68
childhood, period 2	0.6510±0.1371	0.5140±0.1795	0.2900±0.1382	0.4850±0.0504[1]	0.1500±0.0139	0.0100±0.0014	67.80±23.63
adolescence	0.7130±0.0439[2]	0.507±0.1016	0.263±0.053[2,5]	0.464±0.0613[1]	0.098±0.0387	0.012±0.0050	41.48±10.49
youth	0.655±0.0401[2]	0.339±0.0442[2]	0.142±0.035[1,2]	0.460±0.030[1,2,4]	0.102±0.013[1,2]	0.013±0.0081[3,4]	164.6±22.2[1,4-7]
Dentate gyrus							
fetuses	0.5270±0.0836	0.4080±0.0577	0.2540±0.0392	0.4280±0.0213	0.1110±0.0169	0.0110±0.0029	42.94±4.38
newborns	0.8610±0.0576[1]	0.5120±0.1045	0.2700±0.0687	0.5500±0.0417[1]	0.1710±0.0146	0.0320±0.0108	126.58±43.80
nursing babies	0.805±0.0701	0.4960±0.0667	0.2920±0.0557	0.501±0.048	0.2310±0.0588	0.0820±0.0334[1]	112.16±22.06[1]
infancy and early childhood	0.7320±0.0494	0.4050±0.0586	0.2300±0.0588	0.6140±0.0569[1]	0.2480±0.0513	0.1170±0.0344[1]	32.93±8.94[3]
childhood, period 1	0.5500±0.1474[2]	0.3300±0.1235	0.1710±0.1262	0.4760±0.1241	0.1700±0.0498	0.0560±0.0257	76.18±20.73
childhood, period 2	0.547±0.1780	0.3950±0.1778	0.2730±0.1533	0.475±0.012[2,5]	0.1500±0.0129	0.0430±0.0114[1]	97.18±20.85[1,4]
adolescence	0.6260±0.1286	0.272±0.024[2,3]	0.105±0.039[1-3]	0.4380±0.0828	0.128±0.042[2,3]	0.0450±0.0162	75.97±9.33[1,4]
youth	0.5840±0.0693[2]	0.2720±0.0112[2]	0.089±0.020[1-4]	0.476±0.050	0.142±0.022[2,3]	0.0460±0.0175	116.48±35.78

Note. Here and in tables 2, 3: CD: conjugated dienes; KD: ketodienes; CT: conjugated trienes. $p<0.05$ *vs.* [1]fetuses; [2]newborns; [3]nursing babies; [4]infancy and early childhood; [5]childhood period 1; [6]childhood period 2; [7]adolescence.

TABLE 2. Age-Specific Changes in the Content of LPO and OPM Products in Diencephalic and Mesencephalic Structures during Human Postnatal Ontogeny (*M*±*m*)

Object of analysis	Lipid extract phase						OPM products
		heptane			isopropanol		
	CD	KD and CT	SB	CD	KD and CT	SB	
Midbrain							
fetuses	0.6240±0.0285	0.1920±0.0223	0.0470±0.0067	0.574±0.034	0.1650±0.0168	0.0820±0.0124	70.39±9.48
newborns	0.714±0.114	0.3800±0.0905	0.1540±0.0575	0.4500±0.0265	0.0900±0.0705	0.080±0.002	116.45±21.95
nursing babies	0.5060±0.1218	0.2320±0.1247	0.1030±0.0764	0.4870±0.0527	0.171±0.038	0.0520±0.0381[1]	67.74±34.44
infancy and early childhood	0.495±0.031[1]	0.4190±0.6554[1]	0.1730±0.0182[1]	0.6240±0.0217	0.327±0.027[1,3]	0.1410±0.0251[3]	41.55±10.79
childhood, period 1	0.652±0.053	0.484±0.054	0.1200±0.0055	0.6820±0.0665	0.161±0.056	0.0110±0.0055	175.60±30.57[1,4]
childhood, period 2	0.6820±0.1315	0.5200±0.1225	0.3440±0.1045	0.549±0.066	0.1980±0.0375	0.0170±0.0055	148.85±30.93[1,4]
adolescence	0.4750±0.0373[1]	0.186±0.020[4]	0.0480±0.0028[4]	0.5200±0.0101[4]	0.152±0.023[4]	0.0290±0.0043[1,4]	256.0±12.1[1-6]
youth	0.6820±0.0633	0.416±0.053[1,7]	0.2020±0.0766	0.747±0.048[2,3,7]	0.2850±0.0537[7]	0.0350±0.0049[1,4]	273.67±94.43
Thalamus							
fetuses	0.5400±0.0336	0.2480±0.0254	0.1250±0.0081	0.5600±0.0217	0.1140±0.0094	0.0570±0.0046	53.80±9.20
newborns	0.6750±0.1575	0.410±0.165	0.279±0.180	0.5180±0.0315	0.219±0.015	0.0880±0.0485	77.98±17.31
nursing babies	0.6870±0.0816	0.5150±0.1017[1]	0.239±0.111	0.5800±0.0527	0.2490±0.0637	0.1000±0.0587	50.05±12.54
infancy and early childhood	0.659±0.071	0.4040±0.0806	0.157±0.034	0.729±0.065[1]	0.3330±0.0567[1]	0.1100±0.0388	50.99±25.02
childhood, period 1	0.7530±0.0393	0.4570±0.0273	0.162±0.013	0.588±0.024	0.2120±0.0164	0.0790±0.0069	50.74±12.41
childhood, period 2	0.825±0.011	0.5520±0.0075	0.3000±0.0065	0.5810±0.1035	0.2320±0.0445	0.0520±0.0335	80.75±20.88
adolescence	0.7230±0.1132	0.446±0.141	0.2050±0.1073	0.4100±0.0522[1]	0.183±0.049	0.0620±0.0459	74.44±15.70
youth	0.5320±0.0822[1]	0.3840±0.0683	0.1030±0.0093[1]	0.6680±0.0327	0.357±0.040[1]	0.1700±0.0241[1]	54.23±2.19
Hypothalamus							
fetuses	0.6330±0.0325	0.3500±0.0345	0.157±0.008	0.5650±0.1105	0.201±0.018	0.0370±0.013	141.22±26.55[1,3]
newborns	0.618±0.097	0.3790±0.1835	0.2380±0.1935	0.5090±0.0545	0.2450±0.0035	0.029±0.027	111.33±20.45[1,3]
nursing babies	0.6060±0.0711[1]	0.4630±0.0322[1]	0.1400±0.0084	0.5300±0.0176[4]	0.1120±0.0177[4]	0.0230±0.0045[1,4]	239.83±7.80[1-6]
infancy and early childhood	0.5330±0.0652	0.3660±0.0463	0.1870±0.0438	0.4910±0.0281[4]	0.177±0.050[2,4-6]	0.0420±0.0111	393.31±159.63
childhood, period 1	0.6100±0.0305	0.419±0.092	0.2250±0.0555	0.5130±0.1285	0.1700±0.0045	0.025±0.003	105.75±26.68
childhood, period 2	0.6350±0.1035	0.396±0.185	0.2660±0.1485	0.523±0.139	0.2025±0.0380	0.0490±0.0355	126.02±67.51
adolescence	0.6380±0.0315[1]	0.4210±0.0284	0.1020±0.0096[1]	0.4710±0.0283	0.125±0.022[1,4]	0.0420±0.0071[1,4]	217.3±10.5[1-5]
youth	0.5950±0.0549	0.305±0.046[1,2]	0.1340±0.0222[2]	0.600±0.049	0.1530±0.0143[4]	0.017±0.004[1,4,7]	172.21±56.72

TABLE 3. Age-Specific Changes in the Content of LPO and OPM Products in the Hindbrain Structures during Human Postnatal Ontogeny (*M*±*m*)

Object of analysis	Lipid extract phase						OPM products
		heptane			isopropanol		
	CD	KD and CT	SB	CD	KD and CT	SB	
Cerebellum							
fetuses	0.4650±0.0381	0.3850±0.0225	0.1550±0.0122	0.676±0.019	0.2530±0.0191	0.1090±0.0097	78.81±9.43
newborns	0.735±0.116	0.376±0.164	0.249±0.074	0.5900±0.1155	0.1890±0.0115	0.031±0.001	141.81±38.24
nursing babies	0.6670±0.0653	0.3170±0.0717	0.1360±0.0557	0.5410±0.0182[1]	0.296±0.049	0.0630±0.0273	65.55±15.43
infancy and early childhood	0.6100±0.0965[1]	0.3660±0.0854	0.2370±0.0886	0.5960±0.0225[1]	0.3170±0.0417	0.133±0.048	51.93±15.41
childhood, period 1	0.6120±0.0475	0.3060±0.0145	0.163±0.038	0.4510±0.0285	0.148±0.012	0.0130±0.0025	183.39±68.08
childhood, period 2	0.5820±0.0485	0.368±0.048	0.172±0.047	0.499±0.071	0.134±0.007	0.035±0.005	216.05±115.08[4]
adolescence	0.5130±0.0597[1]	0.2940±0.0306	0.0990±0.0108[1]	0.457±0.033[1,3,4]	0.2380±0.0358[7]	0.034±0.005[1,4]	168.73±9.42[1,3,4]
youth	0.617±0.047[1,2]	0.3270±0.0345	0.1260±0.0303	0.541±0.067[5,7]	0.1100±0.0169[1,3,4]	0.0750±0.0331	241.47±50.95
Pons							
fetuses	0.4680±0.0416	0.3980±0.0315	0.0920±0.0045	0.5610±0.0243	0.1820±0.0101	0.0480±0.0095	52.49±6.62
newborns	0.76±0.06	0.5650±0.0055	0.265±0.078	0.4190±0.1185	0.1780±0.0025	0.0230±0.0055	92.10±28.25
nursing babies	0.7440±0.0907	0.4350±0.1081	0.2340±0.0971	0.6950±0.0772	0.3050±0.0588	0.1060±0.0307	49.38±0.91
infancy and early childhood	0.659±0.015[1]	0.365±0.035	0.1590±0.0359[1]	0.7430±0.0368[1]	0.4340±0.0038[1]	0.119±0.045	31.96±8.10
childhood, period 1	0.627±0.085	0.386±0.045	0.166±0.012	0.544±0.061	0.1730±0.0125	0.0170±0.0055	168.54±53.09[3,4]
childhood, period 2	0.6860±0.2495	0.517±0.258	0.3690±0.2535	0.562±0.084	0.152±0.024	0.0290±0.0225	143.61±65.64
adolescence	0.529±0.073[1]	0.315±0.024	0.0870±0.0067[4]	0.5340±0.0183[4]	0.1290±0.0131[1,3,4]	0.0350±0.0103	261.80±10.06[1-4]
youth	0.703±0.031[1]	0.3870±0.0489	0.1820±0.0402	0.5920±0.0298[4]	0.1730±0.0101[4]	0.0310±0.0021	279.14±136.83
Medulla oblongata							
fetuses	0.590±0.028	0.2100±0.0225	0.2450±0.0462	0.5420±0.0213	0.1590±0.0143	0.0560±0.0062	30.68±3.42
newborns	0.835±0.026	0.6360±0.0985	0.4050±0.0935	0.538±0.069	0.2350±0.0565	0.055±0.017	47.02±8.20
nursing babies	0.6870±0.0815	0.3210±0.1242	0.1450±0.0756	0.5650±0.0271	0.1730±0.0502	0.1150±0.0803	57.12±6.11[1]
infancy and early childhood	0.5340±0.0885	0.3640±0.0264[1]	0.1560±0.0525	0.651±0.017[1,3]	0.428±0.103[1]	0.1200±0.0505	34.57±3.36[3]
childhood, period 1	0.615±0.015	0.248±0.010	0.168±0.012	0.487±0.035	0.101±0.006	0.0210±0.0125	124.60±34.78[1,4]
childhood, period 2	0.789±0.065	0.3640±0.1305	0.2310±0.1195	0.5800±0.0645	0.130±0.025	0.0110±0.0025	366.09±186.0[1,4]
adolescence	0.4490±0.0393[1]	0.188±0.001[4]	0.0620±0.0049[1]	0.509±0.018[1,4]	0.1310±0.0125[4]	0.0530±0.0011	161.90±13.7[1-4]
youth	0.6680±0.0633[7]	0.3620±0.0578	0.185±0.051	0.593±0.044[3]	0.1610±0.0167[4,5]	0.0230±0.0051[1,7]	275.35±93.15

(r=0.429-0.639; p=0.025-0.0003). Among the endbrain structures such a correlation (r=0.438; p=0.022) could be detected only for the cortical field 6.

The results of this study demonstrated opposite changes in LPO and OPM in the brain during human postnatal development. Limitation of LPO should be regarded as a result of ontogenetic strengthening of the mechanisms of antioxidant defense of the brain [5], providing protection of cell membranes from oxidative stress and the structural and functional maturing of human cerebral structures. The maximum accumulation of OPM products in the brain stem structures and archicortex at the age of 12-21 years can be regarded as a possible mechanism of ontogenetic development of the neuroendocrine regulation systems. It is assumed that the process maturation of these systems is linked with free radical modification of the hypothalamic and hippocampal receptors and reduction of their sensitivity to the "negative feedback" endocrine signals.

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