34 DHA PRETREATMENT CONFERS NEUROPROTECTION IN A RAT MODEL OF PERINATAL HYPOXIA-ISCHEMIA

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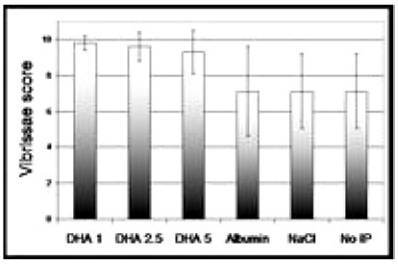
OBJECTIVE: Docosahexaenoic acid (DHA) is a readily-available dietary polyunsaturated fatty acid with anti-inflammatory and neuroprotective properties. We hypothesized that DHA pretreatment would improve functional outcome and reduce brain volume loss in a well-established rat model of perinatal hypoxia-ischemia (HI).

STUDY DESIGN: Seven-day-old Wistar rat pups from 10 litters (N=120) were divided into 3 treatment groups and 3 control groups. Treatment groups received intraperitoneal (IP) injections of DHA 1, 2.5 or 5 mg/kg as DHA-albumin complex. Control groups received 25% albumin, normal saline or no IP injection. Injections were given 2.5 hours prior to right carotid ligation, which was followed by 1.5 hours recovery at 37°C, then 90 minutes in 8% O2, simulating cerebral HI. At 14 days, rats underwent bilateral sensorimotor testing using vibrissae-stimulated forepaw placing response, an accepted measure of functional behavioral development. Bilateral hemisphere and regional areas of cortex, striatum, and hippocampus were measured in regularly spaced sections; volumes were summed and right hemisphere volume loss was calculated [100*(L-R)/L)].

RESULTS: DHA significantly attenuated brain volume loss compared to controls ($p<.0001$ ANOVA, factoring treatment and region). The most consistent effect was found in the hippocampus with 1 mg/kg dose (38% protection vs albumin controls). DHA pretreatment improved vibrissae forepaw placing response to near normal levels. (9.5±0.9 treatment vs. 7.1±2.2 controls; normal function=10 $p<.0001$, t-test). See Figure.

CONCLUSION: DHA pretreatment improves functional outcome and reduces brain volume loss after HI in neonatal rats. Human trials are needed to test whether dietary DHA confers neuroprotection in pregnancies delivering at risk neonates.



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35 MATERNAL ADMINISTRATION OF BETAMETHASONE INHIBITS PULMONARY PROLIFERATION BUT STIMULATES MATURATION AFTER FETAL TRACHEAL OCCLUSION IN THE NITROFEN RAT MODEL - A PLACEBO CONTROLLED STUDY

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OBJECTIVE: Tracheal occlusion (TO) accelerates fetal lung growth but this may be at the expense of maturation indicators. Maternal betamethasone (BM) administration enhances lung maturation. We investigated the effects of both antenatal interventions combined, in terms of proliferation and maturation on a transcriptional level in the saccular phase, using the nitrofen rat model for congenital diaphragmatic hernia (CDH).

STUDY DESIGN: Nitrofen was gavage fed to 23 Wistar rats to induce fetal CDH (ED9.5; term=22d). Fetuses underwent TO (n=27) or no fetal surgery (C;n=31) at ED19 (pseudoglandular phase). BM (0.2 mg/kg, SC) or saline (S) was administered to the mother on ED20 (canalicular phase). Fetuses were harvested at ED21.5 (saccular phase) to assess lung-to-body-weight ratio (LBWR) and gene expression levels (n=24) of Ki67 (proliferation), surfactant B (SPB; maturation) and elastin (elasticity), normalized to GAPDH by quantitative RT-PCR, in CDH fetuses. Means and least square means (LSM) were compared by ANOVA and unpaired t-tests at $p<0.05$.

RESULTS: The increase in LBWR by TO (LSM:$p<0.001$) was not less in BM exposed fetuses. Ki67 was increased by TO (LSM:$p=0.004$) but decreased by BM (LSM:$p<0.0001$), whilst SPB was decreased by TO (LSM:$p=0.01$) but increased by BM (LSM:$p=0.007$). Elastin was increased by BM (LSM:$p=0.006$) but not by TO (LSM:$p=0.098$). Following TO+BM, proliferation was inhibited as compared to TO+S ($p=0.0001$), with recovery of SPB ($p=0.84$) and increased elastin content ($p=0.003$) as compared to saline controls.

CONCLUSION: Maternal BM causes recovery of SPB and elastin, which is decreased after TO, at the expense of a decrease in proliferation.

LBWR and gene expression after maternal administration of BM or S and fetal TO

	C+S	C+BM	TO+S	TO+BM	C+S vs TO+S	C+S vs TO+BM	TO+S vs TO+BM
LBWR (%)	1.95 ±0.06	1.94 ±0.06	4.35 ±0.21	4.67 ±0.24	*	*	ns
Ki-67	1.22 ±0.12	0.28 ±0.02	1.56 ±0.09	0.43 ±0.04	*	*	*
SP-B	1.56 ±0.18	2.19 ±0.25	0.97 ±0.07	1.62 ±0.29	ns	ns	*
Elastin	1.35 ±0.12	2.14 ±0.28	1.67 ±0.20	3.04 ±0.60	ns	*	*

Data expressed as mean±SEM; *: $p < 0.05$, ns: not significant

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