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### DIETARY IRON DEFICIENCY EARLY IN RAT LIFE AND MEDIUM TERM CHANGES IN THE FE, CU AND ZN BRAIN CONTENT.

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Behavioural problems in childhood are related to diencephalic structures dysfunction, which are dependent on dietary Fe, Cu and Zn.

**Aim:** To describe Fe, Cu and Zn differences between cortical (CS) and diencephalic structures (DS) between an iron deficient diet group (ID) and a Control.

**Subjects and methods:** Two litters of Wistar rats, had her dams submitted to an ID during lactation, or to an standard diet (Control). The ID group, at P21 weaning, remained in the diet until P30. Then they were put down, had their middle fosse brains were separated throughout the white matter in CS and in the DS. These products were homogenised and analysed by atomic absorption. Results for Fe, Cu and Zn in CS and DS were analysed between diet groups (Mann-Whitney test). CS and DS values for Fe, Cu and Zn, were compare in each diet group (Wilcoxon test).

**Results:** The ID-CS-Fe (Median=31.8 mg/g; Lower Bound=28.05-Upper Bound=33.58) was significantly lower (U=0.000; p=0.0001) than Control-CS-Fe=60.35(58.04–63.75). The ID-DS-Fe=37.8(34.48–40.24) was significantly lower (U=0.000; p=0.0001) than Control-DS-Fe=63.25(58.39–65.34). The ID-CS-Cu=11.5(10.28–13.06) did not show significant differences than the Control-CS-Cu=11.7(10.96–12.35). The ID-DS-Cu=12.6(12.07–13.68) was significantly higher than the Control-DS-Cu=10.9(10.63–11.18) group. The ID-CS-Zn=60.2(54–66.8) was significantly lower (U=18.5; p=0.015) than the Control-CS-Zn=67.3(64.9–72.25). The ID-DS-Zn=51.2(48.64–55.13) did not show significant differences than the Control-DS-Zn=49.33(46.21–52.56) group. In ID groups Fe and Cu were significantly more abundant in CS than in DS (Fe: Z=-2.666; p=0.008)(Cu: Z=-2.549; p=0.011) while Zn did not. In the Control group Fe and Cu did not show statistical differences between CS and DS but Zn did it (Z=-2.8; p=0.005).

**Conclusions:** 1) Iron deficiency early in rat life induces irregular distribution pattern of iron in middle fosse rat brain. 2) The same dietary deficiency is able to induce Copper and Zinc content variations in different areas of the brain.

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### LONG-CHAIN POLYUNSATURATED FATTY ACIDS IN BEHAVIOURAL DISORDERS AND NEUROLOGICAL PATIENTS.

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The omega-3 and omega-6 long-chain polyunsaturated fatty acids (LCPUFA) are crucial to brain development and can be altered, as etiologic explanatory cofactor, both in neurological and psychiatric conditions.

**Aim:** To describe the omega-3 and omega-6 LCPUFA serum pattern in both neurological and psychiatric patients.

**Patients and Methods:** One hundred and seventeen patients were recruited from June 2003 to December 2004. They were categorized into the following groups: Mild Mental Retardation (MR=16); Static Encephalopathy (SE=13); Progressive Encephalopathy (PE=8); Epilepsy (Ep=24); Pervasive disorder (PD=18); Attention Deficit and Hyperactive Disorder (ADHD=20); and a mixed group with recurrent headache, febrile convulsions and soft neurological signs as a Control Group (CG=11). A serum sample was analysed by gas chromatography and mass spectroscopy. Then the total omega-3 and omega-6 LC-PUFA wt/wt percentage was calculated. The Mann-Whitney U test was used to compare every group to CG.

**Results:** 1) Omega-3: The MR group (Median=1.6; CI: 1–4.7) was significantly lower (U=39; p=0.015) than CG (Median=2.3; CI: 1.2–6.9). The SE group (Median=1.7; CI: 1.5–2.3) was significantly lower than CG (U=32; p=0.022). The PE group showed a near significance lower wt/wt % (Median=1.9; CI: 1.4–2.5) (U=23; p=0.091). The Ep, PD and ADHD groups did not show significant differences from CG.

2) Omega-6: The MR group (Median=34.3; CI: 25.1–36.3) was near significance lower (U=49; p=0.056) than CG (Median=38.84; CI: 33.60–41.54). The SE group (Median=33.2; CI: 22.9–35.8) was significantly lower than CG (U=30; p=0.015). The PE group was also significantly lower (Median=30.2; CI: 19.6–35.7) (U=12; p=0.007). Again Ep, PD and ADHD groups did not show significant differences from CG.

**Conclusions:** 1) The neurological patients except Ep tend to show omega3 and omega6 LCPUFA lower levels than controls. 2) The behavioural problem patients did not show any differences to the CG.

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### DIETARY IRON DEFICIENCY EARLY IN RAT LIFE AND MEDIUM TERM CHANGES IN LEARNING AND MOTOR SKILLS.

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Iron deficiency has been invoked as an etiologic factor of behavioural disorders and learning disabilities in children like ADHD. However no animal model has been develop to check out such a effect.

**Aim:** To submit Wistar rats to an iron deficient diet from the newborn period to the post natal day 30 (P30) and check out attention tasks, passive avoidance, and open field versus a normally fed group.

**Subjects and methods:** Thirty newborn Wistar rats from three litters of teen pups each, had their dams fed with an Iron deficient diet during lactation (ID group). They were weaned in P21, remaining in the ID diet until P30. In P27 were submitted to three -T- maze test training trials. In P30 a fourth -T- maze test trial and an open field test were performed. The percentage of the correct -T- maze solving (TMS), and the number of squares crossed (SC), and active time (AT) were registered by video tape reviewing. A Control group was set-up in the same conditions except for the diet.

**Results:** The ID group and the Control group did not differ in the TMS percentages. In the OF test the ID showed significantly lower active time (Median=5; Range: Min=1-Max=32) than the Control group (Median=9.5; Range: Min=4-Max=33) (U=183.5; p=0.000); the number of SC were significantly lower in the ID group (Median=4; Range: Min=1-Max=34) than the Control group (Median=9.5; Rank: Min=4-Max=33) (U=187.5; p=0.000).

**Conclusions:** 1) Iron deficient diet does not cause differences in learning skills in the -T- maze test. 2) Spontaneous motor activity seems to be lower among those which were submitted to the iron deficient diet in the OF performance.

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### DRUGS, THERAPEUTIC INTERVENTIONS, DISEASES AND RENAL FUNCTION IN PRETERM NEWBORN INFANTS. A MULTICENTER STUDY

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**Introduction:** The early neonatal period is characterized by a rapid maturation of kidney function. Moreover, a variety of therapeutic interventions and the administration drugs may have harmful renal consequences. Goal We tested the hypothesis that drugs or therapeutics in the neonatal period could increase the risk for ARF in preterm newborns.

**Methods:** All preterm infants (261) with a G.A. < 36 weeks admitted in the NICUs of 7 Italian University hospitals (March 2000-March 2003) were involved. Data were collected in detailed questionnaires, and entered into a computerized relational database. B.W., G.A., Apgar scores, blood pressure, respiratory status, lab assays, radiological exams, clinical outcomes and all therapeutical interventions (catheters, intubation, phototherapy, drugs) were recorded. Statistical analysis was performed using the Statistical Package for Social Sciences for Windows (SPSS Inc., Chicago, IL). 246 subjects enrolled in the study are divided into four groups according to G.A.: group A, 22–25; group B, 26–28; group C, 29–32; and group D, 33–36 weeks.

**Results:** All the diseases diagnosed and the therapeutic interventions applied to these preterm infants resulted inversely correlated with the G.A. (p<0.001 for all examined parameters, except as regards NEC: p=0.019). No differences at birth were observed among the 4 groups as regards either BUN or Crs values, while statistical significant differences were evident from the 3rd to the 21st day of life. The diagnosis was made on the basis of high Crs concentrations at 60th hour of life or later (values > 1.3 mg/dl or > 1 mg/dl respectively in subjects with a G.A. < or > 33 weeks) and/or presence of oliguria. In neonates with impaired renal function, an important increase in Crs values was observed in all groups from the 3rd to the 10th day of life, with statistical significant differences among groups on day 7 (p=0.03) and day 10 (p=0.006). Then, values decreased but remained higher, compared to subject with normal renal function, in all neonates at 28th day of life. An inverse correlation is evident between G.A. and the percentage of neonates with impaired renal function (2= 25.707, p<0.001); 56% of neonates in group A resulted with impaired renal function, while in group D only 15% had Crs pathological values.

**Conclusion:** In more than 50% of patients of group A have renal problems. Instead, in neonates of group D the percentage of subjects with renal impairment is considerably lower (15% vs 56%); it is evident the role played by some drugs, therapeutic interventions and diseases.

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### PLACENTAL IGF-I RECEPTOR AND SEPTAL HYPERTROPHIC CARDIOMYOPATHY IN INFANTS OF DIABETIC MOTHERS

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**Background/Aims:** Septal hypertrophic cardiomyopathy (sHCM) is a characteristic anomaly of the infant of diabetic mother (IDM). Insulin-like growth factor-I (IGF-I) has been identified to contribute to the various tissue overgrowth in these infants. We have previously shown that maternal IGF-I levels were significantly elevated among neonates with sHCM. IGF-I does not cross the placenta and its physiologic action is mediated through the receptor, IGF-IR. IGF-IR are present in various tissues including the heart muscle. We have thus investigated whether there is an association between placental IGF-IR in IDMs with and without sHCM.

**Methods:** A cohort of 50 diabetic and 50 normal pregnancies booked in the Hospital UKM, Kuala Lumpur, over a period of two years (Jan. 2001- Dec. 2002) were enrolled into a larger related study. The placentae of six diabetic pregnancies with neonatal sHCM and six randomly selected diabetic pregnancies without neonatal sHCM were compared to the placentae from six normal pregnancies for IGF-IR expression by immunohistochemistry. The staining for IGF-IR in the decidua, cytotrophoblast, syncytiotrophoblast and fetal endothelium for these 18 samples were assessed randomly by the pathologist who was blinded to the respective diagnoses. The intensities of IGF-IR staining were classified as 0 (negative), 1+ (weak), 2+ (medium), 3+ (strong).

**Results:** Placental IGF-IR staining was negative in the fetal endothelium for all three groups. In the normal controls, and diabetic group without neonatal sHCM, IGF-IR were 3+ in decidua, 2+ in cytotrophoblast and 2+ in syncytiotrophoblast. In contrast, IGF-IR were all 2+ in the decidua, cytotrophoblast and syncytiotrophoblast from the diabetic group with neonatal sHCM.

**Conclusions:** Reduced placental IGF-IR expression in the decidua of diabetic pregnancies suggests that IGF-IR is down-regulated in response to elevated maternal IGF or mediators of neonatal sHCM. Modulation of activity at the IGF-IR level may be a target for therapy against the development of fetal/neonatal sHCM in diabetic pregnancies.

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### FRACTURES IN A NEONATAL AND INTENSIVE CARE UNIT: FREQUENCY AND EVOLUTION OVER TIME.

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**Objective:** Aim of the study was to analyse fractures possible causes in premature or at term newborn babies, taking into account hematocrit, nutritional, clinical and instrumental parameters.

**Methods:** A retrospective analysis involving 12,573 newborns (preterm and at term) identified 39 patients with fractures. The following parameters were analysed to assess their correlation to the development of fractures: central venous catheter (CVC) and/or umbilical venous catheter (UVC) placement, prematurity, steroid and diuretic medication, physiotherapy, biochemical parameters (calcemia, phosphatemia and serum alkaline phosphatase), diagnostic procedures (X-ray and ultrasound).

**Results:** Our data suggest that a high birth weight did not represent a further risk factor for fractures. Comparison between time of fracture and gestational age (GA) has shown that fractures occurred later in babies with lower GA. In addition CVC or UVC placements, as well as steroid or diuretic medication, did not favour fractures. Bronchopulmonary dysplasia (BPD) or necrotizing enterocolitis (NEC) were not responsible for an increased fracture incidence. On the contrary a twofold fracture incidence was found in preterm babies undergoing physiotherapy in comparison to at term babies.

**Conclusions:** Calcium metabolism and the interventional and diagnostic procedures we assessed did not correlate with increased onset of fractures; special preterm feeding formulas did not appear to reduce the risk of fractures over the time. Physiotherapy is the only factor determining an increased risk of fractures among those examined.