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ACCELERATED POSTNATAL HEAD GROWTH FOLLOWS PRETERM BIRTH

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Objectives: Poor growth after preterm birth is associated with impaired neurodevelopmental outcome. Limited evidence indicates that breast fed infants have improved neurodevelopmental outcomes but slower growth. We aimed to evaluate weight gain and head growth between birth and term in relation to breast milk intake, allowing for illness severity.

Methods: We studied inborn infants delivered at or below 32 weeks gestation who remained in our neonatal unit up to 37 weeks postmenstrual age. We expressed weight and head circumference (HC) as standard deviation score (SDS), growth between birth and discharge as SDS gain (SDSG), and illness severity and breast milk exposure as the number of days of level 1 (full) intensive care (%L1IC) and the number of days breast milk was received (%BM) as a percentage of days from birth to discharge.

Results: Poor postnatal weight gain was accompanied by accelerated head growth There was a highly significant fall in weight SDS between birth and discharge (mean (SD) weight SDS, birth -0.31 (0.96), discharge -1.32 (1.02), $p<0.001$) and a highly significant increase in HC SDS (mean (SD) HC SDS, birth -0.52 (0.95), discharge -0.03 (1.25), $p=0.003$). %L1IC had a highly significant negative impact upon weight SDSG ($p=0.006$) and %BM had a significant positive impact upon HC SDSG ($p=0.043$).

Conclusion: Accelerated postnatal head growth suggests catch-up after antenatal restraint. As this appears facilitated by breast milk, there is an urgent need to evaluate the optimal use of breast milk in preterm neonates. Illness severity is a significant determinant of poor postnatal weight gain.

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MATERNAL AND NEONATAL LIPOPOLYSACCHARIDE RESPONSES ARE ALTERED IN NEONATAL ENCEPHALOPATHY

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Systemic hypoxia-ischaemia at birth may alter the neonatal neutrophil phenotype. Neutrophils from adults (n=15), normal newborns (n=20), newborns requiring resuscitation at birth and their respective paired maternal samples (n=17) were incubated alone or with Lipopolysaccharide (LPS). Surface receptor CD11b and the percentage apoptosis (persistence of inflammatory response) were assessed using flow cytometry. Maternal neutrophil apoptosis is delayed compared with adults and neonates. Neutrophil apoptosis was delayed in neonates requiring resuscitation at birth and was exaggerated further in infants who developed mild neurological signs. Newborns with severe neurological signs had increased apoptosis and decreased CD11b. None of the infants who required resuscitation at birth were LPS responsive irrespective of neurological outcome. Similarly, maternal neutrophils had a delay in apoptosis in all groups but were LPS hyporesponsive in the groups whose infants had moderate/severe neurological signs. Maternal neutrophil function may be a useful adjunct to neonatal diagnosis. Neonates are LPS hyporesponsive after resuscitation. However, downregulation of neonatal responses in hypoxia may also prevent excessive immune activation and tissue damage in this vulnerable group.

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ACTIVE GHRELINE LEVELS IN CHILDHOOD OBESITY

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Introduction: No data are available about the plasma levels of active ghrelin (AGH) in obesity. The present study investigates the AGH levels in obese and control children during oral glucose tolerance test.

Patients and methods: Eleven obese (age [mean ± SEM]: 14.3 ± 0.9 yr, body mass index (BMI): 30.2 ± 1.6 kg/m2) and nine age-matched control (age: 15.8 ± 0.5 yr, BMI: 21.2 ± 0.7 kg/m2) children were investigated. AGH, insulin, glucose, growth hormone (GH) were determined by commercially available RIA kits before and 30, 60 and 120 min after glucose load (75g). Plasma leptin concentrations were measured at 0 min by RIA kit. Comparative analyses between and within groups were calculated by Mann-Whitney U test and ANOVA followed by Dunett post hoc test. Data are expressed as mean ± SEM.

Results: Fasting plasma insulin (32.4 ± 5.6 vs. 16.2 ± 3.0 microU/ml) and leptin (15.2 ± 1.3 vs. 7.2 ± 1.7 microg/l) levels were significantly higher, while AGH (66.3 ± 6.7 vs 97.2 ± 14.4 pg/ml) and GH (0.5 ± 0.2 vs. 3.1 ± 0.8 microg/l) concentrations were significantly lower in obese children, than in controls. The AGH levels decreased significantly at 30 and 60 min in the control group (30 min: 53.3 ± 9.9; 60 min: 57.4± 7.0 pg/ml), but not in the obese group (30 min: 64.7 ± 9.6 pg/ml; 60 min: 49.3 ± 4.6 pg/ml). After 60 min AGH increased in both groups, especially in obese children. Thus, in the obese group the AGH levels at 120 min (91.6 ± 9.8 pg/ml) were significantly higher than the baseline levels (66.3 ± 6.7 pg/ml), while they were lower in controls.

Conclusion: The results suggest that the AGH response to glucose is blunted in the first hour and upregulated in the second hour in the obese children.

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ENHANCEMENT OF NFAT ACTIVATION AND FUNCTION BY ASPIRIN IN T CELLS

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Background: IL-4 is central to the development of TH2 responses and atopic conditions. We have reported cyclo-oxygenase (COX)-independent inhibition of IL-4 transcription by therapeutic concentrations of acetylsalicylic acid (ASA) and salicylic acid (SA) (Blood 2001;97:1742). We hypothesized that salicylates target the Ca2+-dependent IL-4 transactivator, NFAT. Methods: To elucidate this point, we transfected Jurkat T cells (JKT) with luciferase plasmids driven by the proximal IL-4 promoter (pIL4.96), or by artificial promoters consisting of either a multimeric consensus NFAT/AP-1 composite site (pNFAT) or the AP-1-independent IL-4 P1 NFAT consensus (pIL-4.P1). Cells were stimulated with the Ca2+ ionophore A23187 and treated with ASA (1 mM) or the benchmark COX inhibitor, flurbiprofen (FBP, 0.01 mM). Results: Luciferase expression in pIL4.96 transfectants was significantly reduced by ASA (58.8±3.8% of control) but not FBP (96.8±8.8%; n=8). In stark contrast, NFAT-dependent transcription was upregulated by ASA in both pNFAT (614.5±120.6%; n=12) and pIL4.P1 transfectants (937.5±371%; n=8). NFAT function was only weakly enhanced by FBP in these experiments (133.2±14.72% of pIL4.P1; n=3). In parallel experiments the effects of salicylates on NFAT activation in JKT and peripheral blood T cells (PBT) was analyzed by immunofluorescent staining and Western blot using NFAT-1 and NFAT-2 specific antibodies. As previously shown, Ca2+-mediated stimulation induced the rapid (<30 min) and transient nuclear translocation of NFAT family members. Treatment with ASA caused prolonged NFAT nuclear expression presumably due to delayed cytosolic re-export. NFAT nuclear overexpression was apparent at 2 and 3 hours post-stimulation in both JKT and PBT. Conclusions: We conclude that the effects of salicylates on IL-4 expression cannot be ascribed to inhibition of NFAT activity, and point to the involvement of a novel, unique molecular pathway of IL-4 transcriptional activation in T cells. Uncovering this pathway might lead to the development of selective immune regulatory regimens in the control of atopic disease.

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MALONDIALDEHYDE IN PLASMA AND EXHALED BREATH CONDENSATE COLLECTED FROM VENTILATED INFANTS

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Aim: Malondialdehyde (MDA) is a product of lipid peroxidation that is a marker of oxygen free radical damage. The aim of our study was to measure MDA in exhaled breath condensate (EBC) collected from ventilated infants and to use it as a marker of oxidative stress in the lungs of these patients.

Methods: MDA concentration was determined by high-performance liquid chromatography in plasma and EBC collected from 17 ventilated infants with humidification. In 11 infants, blood was taken at the same time as EBC collection. FiO2, alveolar-arterial oxygen difference (AaDO2), mean airway pressure (MAP), oxygenation index (OI) and peak inspiratory pressure (PIP) were recorded at the time of sample collection to estimate potential oxidative stress to the lungs, and correlated with MDA concentration.

Results: The detection limit for breath condensate MDA was 0.0015 micromolar. MDA was measurable in breath condensate in 13 patients, but was below the detection limit in 4 patients. Median MDA concentration was 0.004 (range: 0 - 0.022) micromolar in EBC. Median MDA plasma concentration was 0.375 (range: 0.054 - 5.171) micromolar. Plasma MDA concentration was strongly correlated with both FiO2 (r squared=0.22; $p=0.008$) and AaDO2 (r squared=0.28; $p=0.006$), and weakly correlated with MAP (r squared=0.14; $p=0.04$). There was no relationship between plasma MDA and either OI or PIP. Although we found a significant correlation between the concentration of MDA in plasma and in EBC (r squared=0.32; $p<0.03$), EBC MDA concentration did not significantly correlate with FiO2, MAP, PIP or OI.

Conclusion: Our results suggest that MDA concentration in plasma correlates with oxidative stress of the lungs of ventilated infants. Although MDA can be measured in EBC collected from ventilated infants, even during humidication, and correlates with MDA concentration in plasma, the amounts are very low and normalisation to EBC electrolytes may be necessary.

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INVESTIGATION OF THE HEMODYNAMIC RESPONSE TO FLASH VISUAL STIMULATION IN NEONATES USING NEAR INFRARED SPECTROSCOPY

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Background/Aims: Near-infrared spectroscopy (NIRS) is used to study the hemodynamic response to visual stimulation in sleeping neonates. The specific aims of this study were to determine whether a response in the visual cortex can be detected in term neonates during the first days of life and, if so, to determine the direction and magnitude of changes in deoxyhemoglobin (HHb) during stimulation.

Methods: Ten healthy, term neonates, aged 2 to 14 d, were subjected to binocular visual stimulation using red lights, flashing at a frequency of 0.5 or 1 Hz. Lights were directed towards each eye at a distance of approximately 5 cm. Stimulation periods of 20 s were alternated with rest periods of approximately 20 s. An in-house developed NIRS imaging instrument, the MCP-II, measured localized changes in concentrations of oxyhemoglobin (O2Hb) and HHb. The NIRS sensor contains 4 light sources and 4 photodetectors covering an area of 2.5 by 3.75 cm with 10 different light paths at 100 Hz. The centre of the sensor was positioned 1 cm above the inion.

Results: The concentrations of O2Hb and HHb during the last 10 s of the stimulation period were compared to the concentrations during the 10 s preceding stimulation. In 6 out of 10 subjects, a significant ($p< 0.01$) increase in O2Hb and/or a significant decrease in HHb was observed in one or more locations. During stimulation, O2Hb increased by a mean of 1.3 micromol/l, HHb decreased by a mean 0.5 micromol/l, and total Hb increased by a mean of 0.9 micromol/l.

Conclusions: Our results show that a hemodynamic response to visual stimulation, similar to that observed in adults, can be measured in sleeping neonates. The increase in O2Hb and simultaneous decrease in HHb during stimulation suggest an increase in cerebral blood flow that overcompensates for the increased oxygen consumption in the activated cortical area.