Brain

COMPARATIVE NEUROPATHOLOGY OF LISSENCEPHALY WITH ARX MUTATION: CONSIDERATION OF NEOCORTICAL INTERNEURON DISTRIBUTION

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Background X-linked lissencephaly with abnormal genitalia (XLAG) is established as one disease entity. XLAG, showing severe neonatal seizure and developmental delay, is a rare disorder caused by mutations in the aristaless-related homeobox (ARX) gene, located in Xp22.13. Arx-null mice for human XLAG model showed loss of tangential migration of GABAergic interneurons.

Objectives We investigated subpopulation of GABAergic interneurons in the brain of an infant with XLAG, who had a nonsense mutation of the ARX gene, compared with those of age-matched normal control, Miller-Dieker syndrome (MDS) as a type I lissencephaly, and polymicrogyria of Fukuyama type congenital muscular dystrophy (FCMD) as a type II lissencephaly.

Methods We used paraffin-embedded brain tissues of two XLAG, three MDS and four FCMD, with an informed consent of their parents. We performed immunocytochemistry for interneuron and migration markers.

Results Glutamic acid decarboxylase (GAD) and calretinin (CR) containing (+) cells were significantly very few in the neocortex and located in the white matter and neocortical subventricular zone. In the neocortical subventricular region, the GAD+ and CR+ cells had Mash3 protein, like a radial migration marker, and nestin protein. On the contrary, MDS showed relatively low concentration of GAD+ cells. FCMD revealed random distribution of these marked cells.

Conclusions ARX controls not only tangential migration of GABAergic interneurons from the ganglionic eminence, but may serve to induce radial migration from the neocortical subventricular zone. MDS and FCMD also demonstrated abnormal distribution of neocortical interneurons, but those severities are different in each type of lissencephaly.

CEREBRAL PERFUSION FROM INFANT TILL ADOLESCENCE ASSESSED WITH MR PSEUDO CONTINUOUS ASL

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Background and aim Arterial spin labelling (ASL) is a MR technique to assess brain perfusion without necessity of intravascular administered MR contrast [1]. Our aim was to obtain age dependent normal paediatric values of brain perfusion.

Methods We used arterial spin labelling (ASL) in two XLAG, three MDS and four FCMD, with an informed consent of their parents. We performed immunocytochemistry for interneuron and migration markers.

Results Glutamic acid decarboxylase (GAD) and calretinin (CR) containing (+) cells were significantly very few in the neocortex and located in the white matter and neocortical subventricular zone. In the neocortical subventricular region, the GAD+ and CR+ cells had Mash3 protein, like a radial migration marker, and nestin protein. On the contrary, MDS showed relatively low concentration of GAD+ cells. FCMD revealed random distribution of these marked cells.

Conclusions ARX controls not only tangential migration of GABAergic interneurons from the ganglionic eminence, but may serve to induce radial migration from the neocortical subventricular zone. MDS and FCMD also demonstrated abnormal distribution of neocortical interneurons, but those severities are different in each type of lissencephaly.
used. Exclusion criteria were: congenital abnormalities, brain lesions, meningitis, scan artefacts. Measurement sites were cerebellar hemispheres, vermis, basal ganglia, thalamus and all lobes, using a postprocessing tool.

**Results** Perfusion values of thalami and basal ganglia appeared fairly constant at different ages. An increase of perfusion was noted in the cerebellar hemispheres from 3 years of age. The cerebellar vermis showed a relative high perfusion in all ages. A slight progressive increase of perfusion was noted at the level of the frontal lobes and parietal lobes. In general, we found a considerable inter-individual variability, without significant variations between genders.

**Conclusions** ASL shows an age dependence of cerebral perfusion. This normative data can help to identify abnormal cerebral perfusion, which may lead to diagnoses or a better understanding of the neurological presentation of a child.

1 Biagi et al. 2007.

**Brain and Developmental Experimental**

**O-012 INTRAVENTRICULAR HAEMORRHAGE GRADE 1–2 IN EXTREMELY PRETERM INFANTS DOES NOT IMPAIR NEURODEVELOPMENTAL OUTCOME AT 2.5 YEARS: THE EXPRESS COHORT STUDY**

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**Methods** In this prospective population based cohort study the participants consisted of 707 EPI born alive before 27 weeks of gestation; EPI without IVH, EPI with IVH grade 1–2 and 3–4 respectively, and 701 full term controls. They were assessed and compared according to the Bayley scales of infant and toddler development, 3d edition (BSIDII) and at 2.5 years of CA.

**Results** 70% of the live-born infants survived until the follow-up at 2.5 years of CA. The estimated marginal means (EMM) BSIDII scores for EPIs with IVH grade 1–2 were not significantly lower than for EPIs without IVH in cognitive (p = 0.32, EMM = 86.8, CI = 82.5–91.1), language (p = 0.25, EMM = 88.8, CI = 82.0–95.6) or motor (p = 0.2, EMM = 78.8, SE = 3.8, CI = 71.308–86.376) functions.

**Conclusions** Although extremely preterm birth alone is a risk factor for impaired neurodevelopmental outcome, IVH grade 1–2 does not significantly increase that risk.

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**Introduction** Lactoferrin (Lf) is an iron-binding glycoprotein secreted in milk with anti-oxydant, anti-inflammatory and antimicrobial properties. The aim of this work was to assess the neuroprotective effect of Lf in P3 rat pup brain exposed to Lipopolysaccharide (LPS) using high-field (9.4 T) 1H-MR Spectroscopy.

**Materials and methods** At birth, dams received either a Lf-enriched food (1 g/kg/day) or a diet isocaloric (iso) to the Lf during lactation. Rat pups received Lf through breastfeeding. P3 pups were then divided in 4 groups: sham-iso, LPS-iso, sham-Lf and LPS-Lf (n = 10/group). P3 pups from LPS groups were injected in the subcortical white matter with 0.5 μL saline containing LPS (10 μg) and the sham groups with vehicle. Metabolic profile was measured by 1H-MRS in the Hippocampus (Hp) and Striatum (St), 24 h (P4) and 21 days (P24) after LPS. A Mann-Whitney test was used to compare values between the different groups (significance: p < 0.05).

**Results** At 24 h, no evidence for ventriculomegaly was observed. At P24 LPS-iso and LPS-Lf presented significant ventriculomegaly, but ventricle volumes of the LPS-Lf rats (25 ± 2 mm³) tended to be lower than the one of the LPS-iso group (34 ± 3 mm³) (mean ± SEM) At 24 h, LPS groups (i.e. -Lf and -iso) exhibited altered metabolism compared to sham groups involving modification of [Glc]-energy source, [Glu+Gln]-neurotransmission and [GPC+PCho]-components of cell membranes. In addition, LPS-iso group presented also changes in [Mac]-tissue integrity marker, [GABA]-neurotransmitter, [NAA+NAAG]-neuronal marker and [PCr]/[Cr]-energy metabolism compared to sham groups. Interestingly LPS-iso group presented also differences with the LPS-Lf group: [Mac], [PE]-cell membranes and [Cr + Pcr]-energetic metabolism. At P24 the brain metabolism of LPS-exposed rats continued to be disturbed but in a lesser extent for LPS-Lf rats. Further MRI derived data (volumetry and diffusion MRI) are under investigation.

**Discussion and conclusion** Supplemented in the food during the lactation, Lf appears to have a neuroprotective effect: this result could be of high interest for preterm’s brain neuroprotection.