and hepcidin. Frataxin levels in LVW were extremely low at less than 15 ng/g wet weight (normal: 214.1 ± 81.2). On cross-sections, cardiomyocytes were significantly larger than normal with case means ranging from 635-1856 μm^2 for LVW and 483-1150 μm^2 for VS (normal LVW, 140-460; normal VS, 237-613). Fe accumulations varied from minute granules to coarse aggregates in fibers undergoing phagocytosis. Measured by XRF, regional Fe concentration in LVW and VS were significantly increased while Zn remained normal. Total heart Fe and Zn did not differ from normal levels. Cytosolic and mitochondrial ferritins exhibited extensive co-localization, representing translational and transcriptional responses to Fe, respectively. All cases met the criteria of myocarditis. Inflammatory cells contained CD68 and ferritin, and most expressed the Fe-regulatory hormone hepcidin. In conclusion, inflammation plays a major role in the pathogenesis of FA cardiomyopathy, and hepcidin-induced retention of Fe in macrophages contributes to cardiac damage in FRDA.

8. Maturation of the Fetal Olfactory Bulb

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doi:10.1017/cjn.2015.256

The olfactory bulb exhibits architecture unique amongst laminar cortices, lacking molecular and subplate zones and having superficial synaptic glomeruli. Its ontogenesis also is unique because neuroblasts do not migrate radially but stream in from the rostral telencephalon; an ependymal-lined olfactory ventricle is transitory. The olfactory is the only sensory system to not project to the thalamus but incorporates a thalamic equivalent. It is a repository of progenitor cells in the mature brain. The aim was to define olfactory bulb development in the human foetus: synaptogenesis and cellular maturation.

Immunoreactivity in paraffin sections of synaptophysin, NeuN, calretinin, vimentin and nestin was examined at autopsy in olfactory bulb in 20 foetuses, 9-40wks gestation. Synaptophysin reactivity was seen around the somata of mitral and tufted neurons at 9wks, synaptic glomeruli at 13wks. The granule cell layer in the core exhibited NeuN-reactive nuclei in cells of the outer half at 20wks; 60% of granular neurons reacted by term. Synaptophysin reactivity in the granular layer initiates at 15wk. GABAergic calretinin-reactive neurons and neurites and synaptic glomeruli appeared at 13wks. Nestin- and vimentin-reactive bipolar progenitor cells were shown at all gestational ages, mainly in the granular layer, the ratio to other cells remaining constant. Synapses form in the small accessory olfactory bulb of the nervus terminalis earlier than in the main bulb. Development of synaptic vesicles in the human fetal olfactory bulb is precise both spatially and temporally, but not yet fully mature at term.

In brain malformations and congenital metabolic and genetic diseases, the olfactory bulb may be affected and provide additional neuropathological data. Therapeutic autologous transplantation of olfactory progenitor cells focus renewed interest in the olfactory bulb.

9. Congenital Lymphocytic Choriomeningitis Virus: A Neuropathological Study

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doi:10.1017/cjn.2015.257

Lymphocytic choriomeningitis virus (LCMV) carried and secreted by mice, infects great numbers of people. LCMV infection acquired during childhood or adulthood is usually moderately symptomatic with a full recovery. When the infection occurs prenatally, it results in a wide spectrum of severe brain lesions described mainly on imaging. Neuropathological data have never been reported.

We present 2 fetuses with a prenatal diagnosis of microcephaly with ventriculomegaly, abnormal gyration, and ponto-cerebellar hypoplasia in one case. Parents elected to terminate the pregnancy. A complete autopsy demonstrated no dysmorphic features, no visceral or skeletal malformation. Histological examination of viscera did not show any significant lesion.

Neuropathological examination confirmed microcephaly and ventriculomegaly with a thick yellowish band surrounding the ventricles. Identical histological lesions were observed in both cases associating a polymicrogyria and a diffuse necrosis of parenchyma with massive calcifications all around the ventricles. The most characteristic feature was the unusual aspect of necrosis, distinct from that observed in other infections, characterized by a finely granular appearance looking like sand. Small lymphocytic infiltrates were observed in the leptomeninges and in the choroid but not in the retina. The congenital LCMV infection was confirmed by serologic testing.

This study confirms the strong neurotropism of LCMV and demonstrates that prenatal infection has some particular features such as absent systemic signs, and distinct appearance of the necrosis that allow to distinguish it from other congenital infections and other non infectious conditions.

10. Cerebral hyaline astrocytic inclusions in treatment-resistant epilepsy and global developmental delay

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doi:10.1017/cjn.2015.258

Cerebral hyaline astrocytic inclusions (HAI) have been observed in a subset of patients with epilepsy, structural brain anomalies, and developmental delay. We present a case of a 2.5-year-old male with epilepsy and global developmental delay. Chromosomal microarray detected a copy loss at 22q13 that resulted in a partial deletion of SHANK3 gene. The EEGs revealed seizure activity arising from left frontal central region. Invasive video electrocorticography captured clusters of epileptic spasms, all originating from left antero-lateral frontal lobe rostral to the motor cortex. We utilized routine histology to identify the inclusions and mapped their distribution in the resected portion of

the cortex against electrocorticographic data. Histologic analysis revealed the presence of HAI in the posterio-medial portion of the resected cortex, which corresponded to the site of seizure generalization. HAI were present at the resection margin. Immunohistochemistry was largely non-contributory. HAI is a rare but emerging entity that is associated with epilepsy. To our knowledge, the distribution of inclusions in HAI has never been mapped to electrophysiologic data. In our case, seizure generalization correlated with the inclusions distribution. This suggests that the inclusions may: 1) play a role in epileptogenesis; or, 2) be a biomarker of disease distribution. Finally, the presence of the HAI at the resection margin may foreshadow future seizure activity in this patient.

11. White Matter Changes In Cardiac Arrest Encephalopathy

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doi:10.1017/cjn.2015.259

Background: White matter changes are common finding during brain autopsies especially in elderly. Although there are many studies applying radiological-pathological correlation on these lesions, their pathogenesis is still unclear. However, a number of possible causes have been suggested including: hypoxic-ischemia, altered blood brain barrier permeability, vascular pathology and chronic hypoperfusion. As usually there is a multiplicity of causes in any individual case, it is very difficult to pinpoint the major causal factor contributing to observed pathological changes. In this study, we document the white matter pathology in global acute hypoxic/ischemic injury due to cardiac arrest as the major causal factor.

Method: We retrieve 16 cases of cardiac arrest encephalopathy in our archive with post arrest survival range from 6 hours to 14 days. Several special, and immunohistochemical stains were used to study the axonal and myelin pathology.

Result: The pathogenicity of the cardiac arrest was confirmed in all cases by demonstrating the expected gray matter pathology, albeit in varying degree of severity. The white matter changes range from unremarkable in the first 2 days, evidence of cerebral edema (visualized from 3rd day on), and early axonal degeneration, to diffuse myelin pallor secondary to marked axonal loss on day 14.

Conclusion: The white matter changes in post cardiac arrest are mainly due to early cerebral edema and axonal degeneration and the effect on myelin is secondary.

12. Role of Chitinase 3-like-1 in CNS inflammation

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doi:10.1017/cjn.2015.260

The Innate Immune Response (IIR) is an evolutionarily derived process to protect cells and tissues from a broad spectrum of insults. Unfortunately abrogating the insult comes at a cost with compromise of cell or tissue integrity. For the CNS to function it needs to rigorously control its microenvironment and thus is highly susceptible to negative sequelae of the IIR. In the course of studying neuroinflammation in a wide variety of human CNS diseases, we discovered an intriguing molecule, CHI3L1, that appears to be crucial in mitigating untoward CNS effects of IIR. During neuroinflammation the distribution of CHI3L1 is completely unlike that in other tissues. In systemic tissues CHI3L1 is expressed highly in macrophages during the IIR, however in the CNS macrophage expression appears to be severely down-regulated and instead astrocytes express high levels. Experimental studies in animal models of CNS disease have suggested that CHI3L1 is part of a unique anti-inflammatory pathway in the CNS. The mechanism of CHI3L1 down-regulation in CNS macrophages and the role of astrocytic up-regulation remains to be elucidated, however this novel pathway offers a new target to regulate CNS inflammation.

13. Idiopathic Normal Pressure Hydrocephalus: Pathological changes in cortical biopsies in relation to function and response to treatment

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doi:10.1017/cjn.2015.261

Cortical peri-operative biopsies obtained from 11 idiopathic normal pressure hydrocephalus (iNPH) consenting patients (aged 67-88 years, median 74) were immuno-stained for Beta-amyloid (AMYB), Amyloid Precursor Protein (APP), total Tau, phosphorylated tau (AT8), Alpha Synuclein (AS), TDP- 43, P62 & GFAP. 5/11 patients had AMYB deposits, 2 diffuse plaques only, 3 diffuse and cored plaques; 1 also with amyloid angiopathy (CAA). Plaque neurites were labeled for APP and AT8 in all 3 patients with cored plaques; in one were these and neurofibrillary tangles labeled for total tau. The surface area covered by AMYB ranged from 12.8% to 0.08%. The presence of AMYB correlated with age (t, $p = .02$). Neither AS nor TDP-43 pathologies were identified. The density of cortical GFAP+ astrocytes showed a trend towards inverse correlation with age ($r = -0.58$, $p = .06$) but not with AMYB or AT8 pathologies. There were no significant correlations between pre-shunt Evans Ratio and MoCA scores and presence or amount of pathology. Improvement in ventriculomegaly (5/11) did not differ between patients with and without AMYB pathologies. Improvements in MoCA (6/8) were more common in patients without AMYB deposits (X^2,$p = .028$; t, $p = .04$), but also in younger patients (t, $p = .019$). The patient with CAA improved, but the one with total tau pathology did not improve cognitively, although her gait did. In this preliminary study only AD-related pathology was found in iNPH. Cognitive improvement was associated with younger age and absence of amyloid deposits; however, a larger number of patients will be required to dissect these variables.