Evolution of the neurochemical profile in the frontal and occipital cortex of the developing mouse determined by *in vivo* ^{1}H NMR spectroscopy at 14.1 T

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Background: Postnatal development of cerebral structure and function involves regional alteration of the neurochemical profile [1], which can reflect the degree of differentiation and be affected by psychopathological conditions and disorders of the central nervous system [2]. A recent study on the development of the mouse brain [3] reported alterations in NAA, Tau, total creatine and total glutamate plus glutamine (Glx) concentrations some brain regions. The present study investigated non-invasively the development of the full neurochemical profile in the frontal and occipital cortex of mice, using *in vivo* ^{1}H NMR spectroscopy.

Methods: Localised *in vivo* ^{1}H NMR spectroscopy was performed on a 14.1 T, 26 cm VNMRS spectrometer (Varian, Magnex) using a home-built 14 mm diameter quadrature surface coil (used both for RF excitation and signal reception). Field homogeneity was adjusted by FASTMAP [4], and ^{1}H NMR spectra were acquired from VOIs of 2.5 to 3.5 µL placed in frontal or occipital regions of the cortex of C57BL/6 mice (10, 20 and 90 days old, under 1 to 2% isoflurane anaesthesia), using SPECIAL [5,6] with TE of 2.8 ms and TR of 4 s. Typically, spectra were acquired with 480 scans. Metabolite concentrations were estimated with LCModel [7], using corrections for water content [1], and data was compared with the two-way ANOVA followed by Bonferroni's post-test.

Results: Typical *in vivo* ^{1}H NMR spectra acquired in the frontal cortex of mice at postnatal days P10, P20 and P90 are shown in figure 1. Similar spectra were obtained for the occipital cortex, where we observed identical modifications of the neurochemical profile, composed of 20 metabolites (figure 2). As previously reported for the rat cortex [1], there was a clear increase in creatine (Cr), glutamine (Gln), glutamate (Glu), *myo*-inositol (Ins) and *N*-acetylaspartate (NAA), and decrease of taurine (Tau) and phosphoethanolamine (PE) during postnatal development of both frontal and occipital cortical regions in mice (figure 2). Furthermore, we observed a reduction of ascorbate concentration during development in both cortical regions studied. Being able to quantify the concentration of both Glu and Gln, we now show that Glu continuously increases during development, while Gln levels achieved the adult concentration at P20. On the other hand, Ins levels did not change from P10 to P20 but increased from P20 to P90. Tau content was maintained from P10 to P20 and was decreased in the cortical regions of the adult mouse.

Conclusion: The present study reported the normal variations of the neurochemical profile in the frontal and occipital cortex of the mouse, which can be taken as basis for the future investigation of neurochemical defects upon development and differentiation of the cerebral cortex, particularly benefiting of a plethora of transgenic mouse models of pathologies.

References: [1] Tkác *et al.*, Magn Reson Med 50:24 (2003). [2] Hüppi, Clin Perinatol 29:827 (2002). [3] Weiss *et al.* (2008) Magn Reson Mater Phy, in press. [4] Gruetter, Magn Reson Med 29:804 (1993). [5] Mlynárik *et al.*, Mag Reson Med 56:965 (2006). [6] Mlynárik *et al.*, J Mag Reson 194:163 (2008). [7] Provencher, Mag Reson Med 30:672 (1993).

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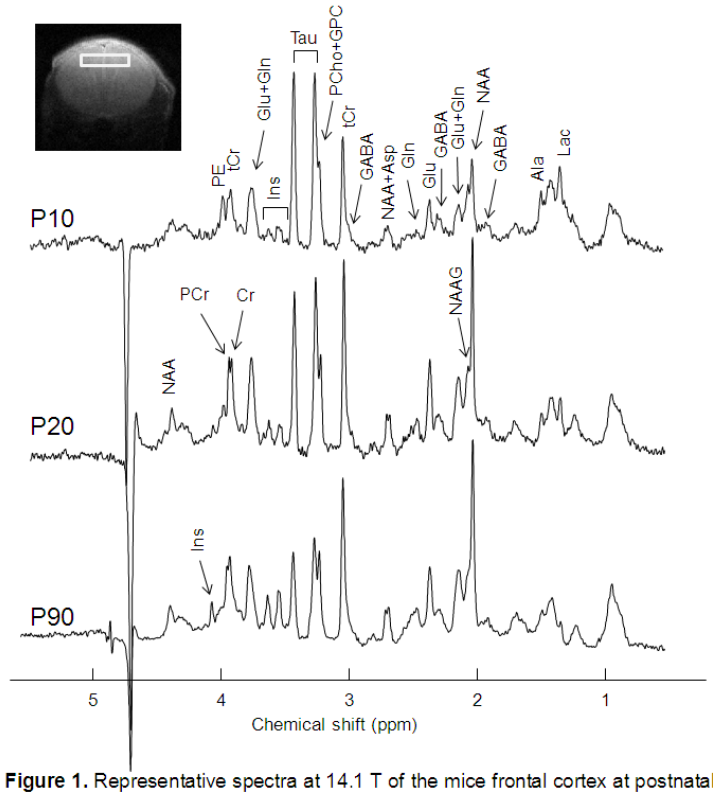

Figure 1. Representative spectra at 14.1 T of the mice frontal cortex at postnatal days P10, P20 and P90. The image shows the position of the VOI in the frontal cortex of the P10 mouse. Abreviations: PE, phosphoethanolamine; tCr, total creatine; Ins, *myo*-inositol; Tau, taurine; Pcho, phosphocholine; Cho, choline; NAA, *N*-acetylaspartate; Gln, glutamine; Glu, glutamate; GABA, γ-aminobutyrate; Ala, alanine; Lac, lactate; NAAG, *N*-acetylaspartylglutamate.

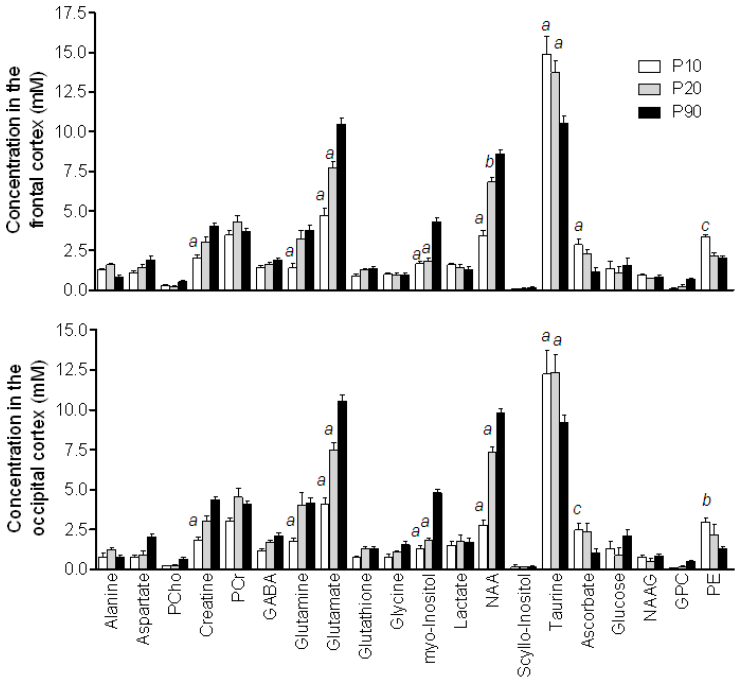

Figure 2. Neurochemical profile at 14.1 T in frontal (top graph) and occipital (bottom graph) cortex of mice at postnatal days P10 (n=6, white bars), P20 (n=4, gray bars) and P90 (n=9, black bars). Data presented as mean±SEM; *a* P<0.001, *b* P<0.01, *c* P<0.05 compared to P90 (adult mice).