Abstract Preview - Step 3/4

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Topic: 7. Brain imaging: MRI/FMRI

Title: GLUTAMINE SYNTHESIS RATE IN THE HYPERAMMONAEMIC RAT BRAIN USING SIMULTANEOUS LOCALIZED IN VIVO ^{1}H AND ^{15}N MRS

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Text:

Objectives:
Glutamine synthetase is a critical step in the glutamate-glutamine cycle, the major mechanism of glutamate neurotransmission and is implicated in the mechanism of ammonia toxicity. ^{15}N MRS is an alternative approach to ^{13}C MRS in studying glutamate-glutamine metabolism. ^{15}N MRS studies allow to measure an apparent glutamine synthesis rate (Vsyn) which reflects a combination of the glutamate-glutamine cycle activity (Vnt) and net glutamine accumulation. The net glutamine synthesis (Vsyn-Vnt) can be directly measured from ^{1}H NMR. Therefore, the aim of this study was to perform in vivo localized ^{1}H MRS interleaved with ^{15}N MRS to directly measure the net glutamine synthesis rate and the apparent glutamine synthesis rate under ^{15}N labeled ammonia infusion in the rat brain, respectively.
Methods:
^{1}H and ^{15}N MRS data were acquired interleaved on a 9.4T system (Varian/Magnex Scientific) using 5 rats. $^{15}NH_4Cl$ solution was infused continuously into the femoral vein for up to 10h (4.5mmol/h/kg) (1). The plasma ammonia concentration was increased to 0.95±0.08mmol/l (Analox GM7 analyzer). ^{1}H spectra were acquired and quantified as described previously (2). ^{15}N unlocalized and localized spectra were acquired using the SIRENE sequence (3); and quantified using AMARES and an external reference method (4). The metabolic model used to analyze the total Gln and 5-^{15}N labeled Gln time courses is shown on Fig 1a.
Results:
Glutamine concentration increased from 2.5±0.3mmol/kg to 15±3.3mmol/kg whereas the total glutamate concentrations remained unchanged (Fig. 1b). The linear fit of the time-evolution of the total Gln from the ^{1}H spectra gave the net synthesis flux (Vsyn-Vnt), which was 0.021±0.006µmol/min/g (Fig. 1d). The 5-^{15}N Gln peak (-271ppm) was visible in the first and all subsequent scans, whereas the 2-^{15}N Gln/Glu peak (-342ppm) appeared after ~1.5h (Fig. 1c). From the in vivo 5-^{15}N Gln time course, Vsyn=0.29±0.1µmol/min/g and a plasma NH_3 fractional enrichment of 71±6% were calculated. Vnt was 0.26±0.1µmol/min/g, obtained assuming a negligible Gln efflux (5). Vsyn and Vnt were within the range of ^{13}C NMR measurements (6).

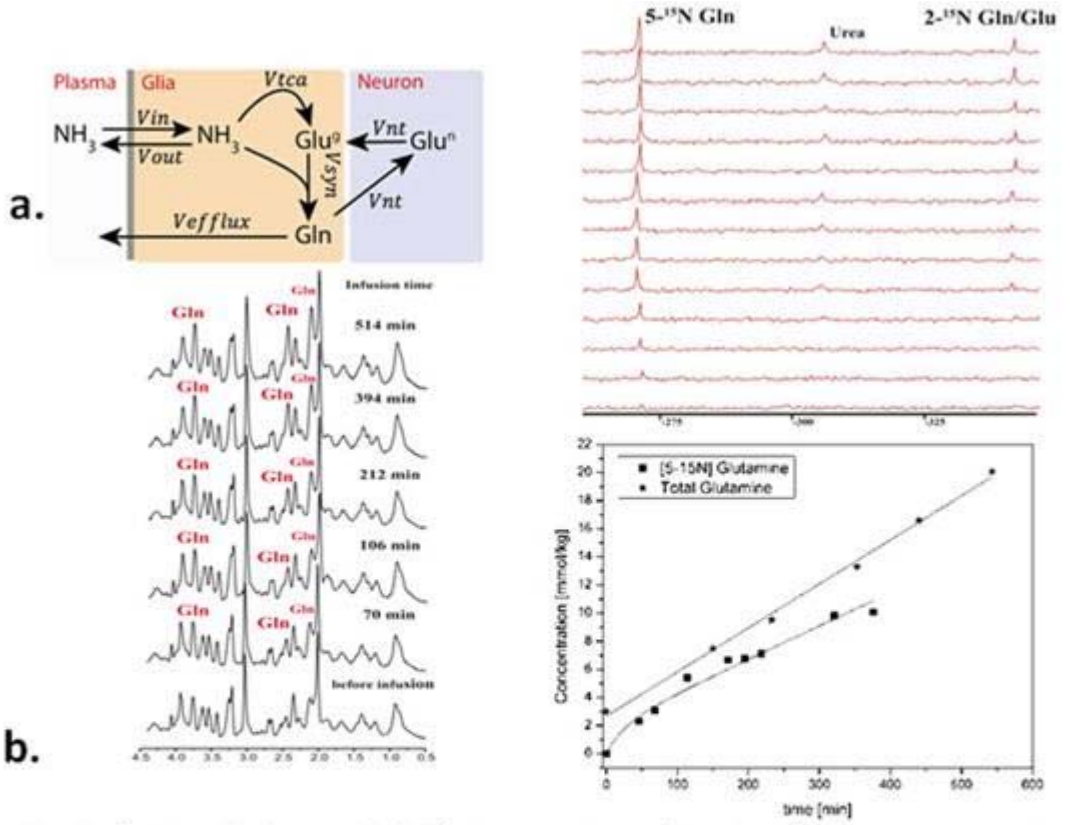

Fig 1: a) Metabolic model; b) One series of *in vivo* ^{1}H spectra acquire 9.4T in the rat brain; c) A series of in vivo unlocalized ^{15}N spectra acqu at 9.4T in the rat brain at different time points (from bottom to top: 23, 69, 115, 173, 193, 218, 321, 376, 398, 420, 463, 529min). The ^{15}N chem shifts were referenced to nitromethane; d) The time courses corresponding fits of total Gln and 5-^{15}N Gln from one rat.

[Fig. 1]

Conclusion:
The combination of ^{1}H and ^{15}N NMR allowed for the first time a direct and localized measurement of Vnt and apparent glutamine synthesis rate. Vnt is approximately one order of magnitude faster than the net glutamine accumulation.

References:
[1] Kanamori K et al., NMRBiomed 1993;6:21. [2] Mlynarik V et al., JMagnReson 2008;194:163. [3] Choil Y et al., MagnResonMed 2000 ;44 :387 [4] Gruetter R, et al., MagnResonMed 1991;20:327 [5] Kanamori K et al., BiochemJ 1993 ;293 :461. [6] Sibson NR et al, ProcNatlAcadSci 1997;94:2699.

Preferred Presentation Type: **Oral Presentation**

Conference: XXIVth International Symposium on Cerebral Blood Flow, Metabolism and Function and the IXth International Confe
Quantification of Brain Function with PET · Abstract: A-164-0007-00456 · **Status: Submitted**

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