Cerebral Glutamate Metabolism via [2-13C] glucose in Normal Brain

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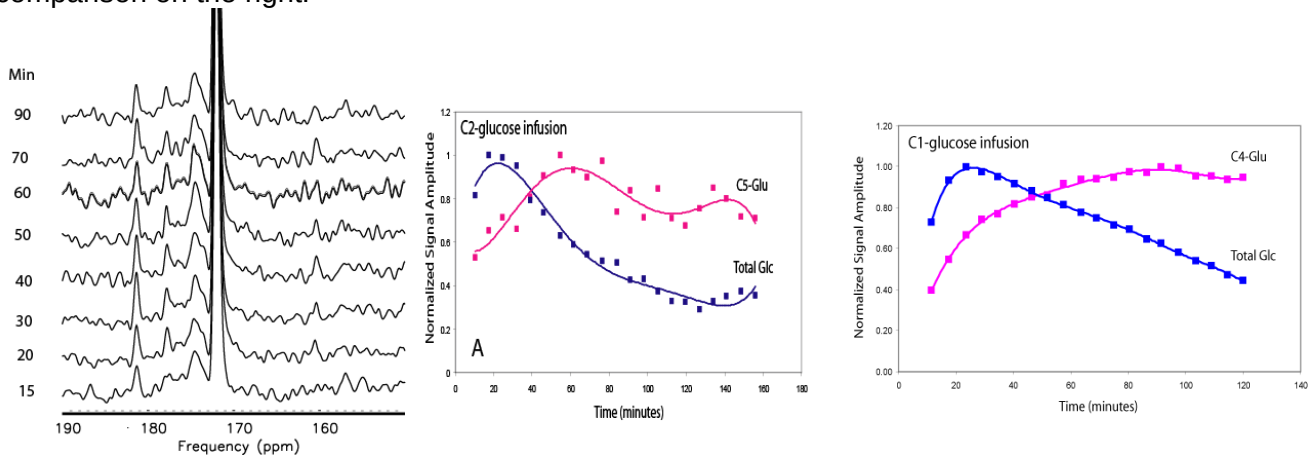
Background: Examination of cerebral glutamate metabolism using non localized data acquisition is often complicated by high intensity of subcutaneous lipid signal overlapping with very low intensity of Glu C4 resonance which could contribute to error in data analysis. The aim of this study was to validate an alternative approach to study cerebral glucose metabolism in normal brain by using 13C magnetic resonance spectroscopy (MRS) using C2 glucose infusion via glutamate C5 resonance.

Methods: The studies were performed in compliance with HIPAA regulation and with the approval of local institutional review board. Five healthy subjects (2 female, age = 30 ± 2years) were recruited from local communities. 13C MRS studies were performed on a clinical GE 1.5T MRI scanner equipped with standalone hardware for proton decoupling while observing carbon signal. Two of the subjects received C2-glucose and the other three received C1-glucose infusion (0.2 g/kg) via arm vein for 15 minutes. Waltz 4 proton decoupling scheme was applied during carbon MRS data acquisition and NOE during re-cycle time with power ratio of 7W/0.7W measured at the probe head. Data acquisition was acquired for 120 min in a 6 min block using a rectangular RF pulse of 250 μs, TR=1.5s and spectral width of 5000 Hz.

Results: Figure 1 (left) shows stack plot of Glu C5 resonance region from 15 to 90 minutes after start of C2-glucose infusion and the time course of the uptake and decay of total cerebral glucose (middle, blue) and the appearance of Glu C5 resonance at 182 ppm (middle, pink) from a healthy subject. A representative plot of time course for total C1 glucose and the appearance of Glu C4 from another healthy subject is shown for comparison on the right.



Conclusion: Glu C5 is the product of the first turn of TCA cycle using [2-13C] glucose as cerebral substrate; it resonates at frequency away from methylene region of subcutaneous lipid (182ppm), thus detection of this resonance is less prone to errors. Although the pathway for the appearance of the product of the first turn of TCA cycle using C1 and C2 glucose as brain substrates may not be the same, here we demonstrated uptake and removal of glucose in healthy subject is very similar for C1 or C2 glucose infusion. Therefore, with proper input functions for metabolic modeling, [2-13C] glucose might be a better alternative substrate to study neuronal glutamate metabolism.

Financial support: K25DA21112 (NS), NARSAD (KH), and Rudi Schulte Research Institutes (BDR).