^{13}C-edited ^{1}H NMR Spectroscopy with Selective Resonance Suppression Using Asymmetric Adiabatic RF Pulses

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Introduction

The detection of ^{13}C label incorporation in conjunction with ^{13}C label administration is a powerful tool to explore cerebral metabolism. In contrast to direct detection by ^{13}C NMR, indirect detection can offer higher sensitivity albeit at lower spectral resolution. For instance, the observation of ^{13}C label incorporation into the C6 of NAA at 2.01ppm is easily obscured by the intensive labeling of Glu C3 and Gln C3 (Glx C3), likewise, Gln C4 overlaps with Glu C4, which were shown in the reported indirect detection schemes, such as POCE and multiple quantum techniques [1-5]. The ACED-STEAM sequence [2] stands out in that it allows editing on I_zS_z coherences during the TM period of STEAM, allowing for long ^{13}C editing pulses. The aim of the present study was to combine the ACED-STEAM sequence with narrow transition band adiabatic RF pulses allowing frequency-selective suppression to reveal specific ^{13}C labeled ^{1}H resonances.

Methods

All experiments were carried out on an actively-shielded 9.4T/31cm system (Varian/Magnex) with 12 cm i.d. high-performance gradients (400 mT/m in 120μs) using a homebuilt 10mm (^{13}C)/14mm (^{1}H quad) surface coil. Shimming was performed with FASTMAP [6].

An asymmetric adiabatic RF pulse [7] requiring a peak $B_1/2\pi$ of ~ 1kHz (20ms duration) was used for inversion of ^{13}C during TM with the following modifications: The adiabatic RF pulse was frequency-shifted to provide the center of the transition band (M_z=0, transition bandwidth is approximately 100Hz) on-resonance ('asymmetric pulse') and inversion over ~3.25kHz downfield from the carrier frequency. From this a second shape was created, which provided a mirror profile for inversion ('anti-asymmetric pulse'), i.e. inversion over ~3.25kHz upfield from the carrier frequency. On odd scans the 'asymmetric pulse' was applied to invert downfield and on even scans the 'anti-asymmetric pulse' to invert upfield, yielding a ^{13}C-edited ^{1}H spectrum with opposite sign for ^{13}C coupled ^{1}H resonances depending on the resonance position of the ^{13}C nuclei. This scheme allowed for suppression of ^{1}H resonances coupled to ^{13}C nuclei resonating at the center of the transition band of ^{13}C editing pulse.

Following extensive validation of the sequence in phantoms, in vivo performance was evaluated in five rats in conjunction with ^{13}C enriched-glucose infusions using the following four scans: the aforementioned adiabatic inversion pulses were applied at the ^{13}C resonance for Glu C4 (A: asymmetric pulse, B: anti-asymmetric pulse) and at Glu C3 (C: asymmetric pulse, D: anti-asymmetric pulse), respectively, all four of which were stored separately in memory.

Results and Discussion

The test of the editing sequence on a phantom containing an aqueous solution of 99%-enriched [1,2-$^{13}C_2$] sodium acetate showed excellent suppression of the ^{1}H resonance when the 'asymmetric pulse' was on resonance of the center frequency of sodium acetate C2 (Fig.1). The transition bandwidth of 550Hz was larger than that of the RF pulse per se (~100Hz), which was explained by the quartet (J_{CH} ~130Hz) of doublet (J_{CC}~50Hz) resonance structure of the $^{13}C_2$ resonance of sodium acetate covering a spectral range of 440Hz.

Applying the editing pulses on Glu C4 (subtracting exp A from B) minimized the ^{1}H coupled to Glu C4 resonance and completely resolved the ^{1}H coupled to Gln C4 (Fig.2 top). In the same spectrum it was obvious that the NAA C6 ^{1}H resonance is overlapped by the more intensive signal from Glx C3. Thus, applying the ^{13}C editing pulses to the frequency of Glu C3 (subtracting exp C from D), the ^{1}H coupled to Glx C3 resonance is suppressed, thereby completely uncovered the ^{1}H coupled to NAA C6 (Fig.2 bottom). Note the inverted intensity for the resonances downfield from Glu C3 (such as Glu and Gln C4) compared to those upfield (NAA C6, Lac and Ala C3). The suppression of Glx C3 thus allowed the direct observation of the ^{13}C labelling of the NAA methyl resonance during the first five hours of glucose administration (Fig.3). Because the precision of deconvolution methods critically depends on the degree of spectral overlap, the current approach is expected to significantly improve the measurement of ^{13}C label in NAA C6 as well as of Gln C4 in a variety of circumstances, where spectral resolution is limited. The proposed approach can be extended to other resonances where the ^{13}C chemical shift is resolved but the ^{1}H overlap.

Conclusion

We conclude that the current approach provides a simple scheme for the selective suppression of a ^{13}C-edited ^{1}H resonance based on its ^{13}C chemical shift allowing for the detection of resonances which are difficult to resolve in ^{1}H observe ^{13}C detection, such as Gln C4 and NAA C6.

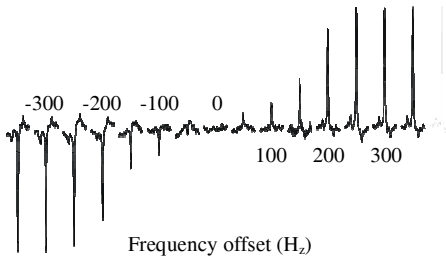

Figure 1. {^{13}C}^{1}H Stack spectra (99% [1, 2-$^{13}C_2$] enriched Sodium acetate) acquired with ACED-STEAM sequence using the asymmetric adiabatic inversion pulse as a function of offset frequency. Frequency step was 50Hz and zero value of the offset frequency is the center frequency of sodium acetate C2.

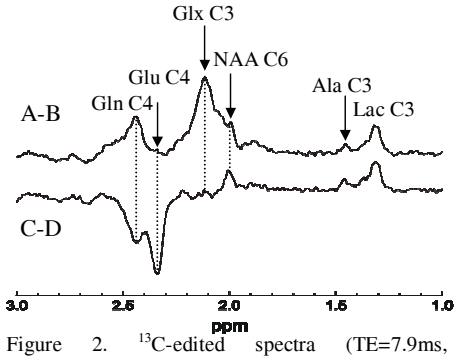

Figure 2. ^{13}C-edited spectra (TE=7.9ms, TR=4s,768 scans)from a 224μl volume in rat brain in vivo during 99% [U-$^{13}C_6$] Glc infusion for validation of the modified ACED-STEAM. The spectra are the combination of the four schemes mentioned in the method. Top: A-B, Bottom: C-D.

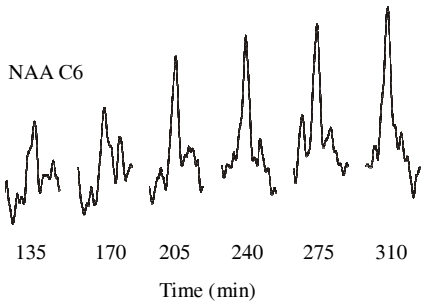

Figure 3. Time-resolved detection of ^{13}C labelling of NAA C6 resonance at 2.01ppm (128scans each, TR=4s), measured from 135 min to 345 min from the start of the ^{13}C glucose infusion (From the same experiment as Figure 2).

References

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Acknowledgements

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