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Investigating Reproducibility Issues of the 1331 Excitation Pulse During wbNAA Sequence Implementation

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Synopsis
We attempted to implement a whole-brain NAA (wbNAA) spectroscopy sequence in a vendor-agnostic environment. During the 16 repeated acquisitions, we observed large fluctuations of the water signal exceeding 50%. It was demonstrated that these instabilities originate from the binomial 1¯3 3¯1 excitation pulse. Ongoing work aims to identify the underlying cause of this behavior.
Introduction
Whole-brain magnetic resonance spectroscopy (wbMRS) enables non-invasive quantification of N-acetyl-L-aspartate (NAA), a key neuronal metabolite, across the entire brain. It is particularly useful for investigating diffuse or non-focal neurological conditions. To detect low-concentration metabolites like NAA, the wbNAA sequence combines inversion recovery, water suppression, and binomial 1¯3 3¯1 excitation pulses.
During implementation in Kiel, we observed unexpected water signal fluctuations exceeding 50% between repeated acquisitions, potentially compromising reproducibility. Preliminary findings pointed to the 1¯3 3¯1 excitation pulse as particularly sensitive to magnetic field inhomogeneities.
To explore this, we performed isolated measurements of the 1¯3 3¯1 pulse. Understanding the source of this variability is essential for achieving robust whole-brain NAA quantification.
Methods
All measurements were performed on a whole-body 3T MRI system (Cima.X, Siemens Healthineers) equipped with a 64-channel head/neck coil. The wbNAA sequence included an adiabatic inversion pulse, WET water suppression, and a binomial 1¯3 3¯1 excitation pulse, implemented in a vendor-agnostic framework (pulseq [1]) as described by Soher et al. [2] To isolate the effect of the 1¯3 3¯1 pulse, the same pulse was applied 16 times without other sequence elements and with a repetition time of TR = 10s. A spherical 1.4 L phantom containing brain metabolites (such as NAA, choline, and creatine) was scanned using the wbNAA sequence and then the single, isolated 1¯3 3¯1 pulse. Data processing and visualization were performed in MATLAB R2022b.
Results
The water signal measured over 16 repetitions of the wbNAA sequence showed fluctuations of 61.6% relative to the mean.
To test whether this variability was inherent to the implementation, a conventional FID sequence with a standard 90° excitation pulse was used. Here, signal deviations remained below 1% (0.62%).
When the 1¯3 3¯1 excitation pulse was applied 16 times in isolation, similar variability (50.5%) was observed.
Discussion
The wbNAA sequence showed substantial signal fluctuations (>60%) across repeated measurements, while the conventional FID sequence yielded stable signals (<1%), confirming that the variability is not caused by the pulseq framework or hardware.
When the 1¯3 3¯1 excitation pulse was applied in isolation, similar fluctuations were observed, identifying it as the main source of instability.
As this pulse is crucial for suppressing water signals, its poor reproducibility compromises the reliability of the entire wbNAA sequence. Further investigation is needed to understand and mitigate this effect for robust whole-brain NAA quantification.
Conclusion
We demonstrated that the binomial 1¯3 3¯1 excitation pulse induces pronounced signal variability in repeated measurements, rendering the wbNAA sequence unstable under the tested conditions. Future work will focus

on systematic investigations to identify the underlying mechanisms and to develop modifications that enable reproducible whole-brain NAA spectroscopy.

References

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[2] Soher BJ, Wu WE, Tal A, et al. Automated whole-brain N-acetylaspartate proton MRS quantification. NMR in Biomedicine. 2014;27(11):1275-1284.

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