Quantitative 2D in-vivo spectroscopy using the ERETIC method

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Introduction

In-vivo ^{1}H spectroscopy is a valuable tool for clinical diagnostics of various diseases and provides deeper insight into basic metabolic and physiological processes in the brain. It has been recently demonstrated that the combination of 2D spectroscopy sequences like JPRESS [5] and prior knowledge based fitting (ProFit) [6] can improve the reliable and independent detection and quantification of small and strongly overlapping signals such as GABA, Glutamate (Glu), Glutamine (Gln) and GSH substantially as compared to conventional short-echo 1D MRS protocols at 3T. This is of special interest as neurotransmitter and antioxidants play a significant role in the pathophysiology of psychiatric and neurological disorders, which are still insufficiently understood. However, so far only metabolite ratios e.g. to creatine could be reported, while a fundamental requirement to use spectroscopy in a clinical setting and for most physiological studies is the ability to reliably detect concentration changes of individual metabolite signals from the measured spectrum. This is usually done by using internal or external reference signals of known concentrations. Both of these approaches exhibit certain disadvantages and have never been combined with 2D JPRESS so far. Finding a suitably stable internal reference which stays constant in any disease is also impossible. Using external reference signals requires additional measurements and therefore prolonging total scan time, which is especially problematic for 2D resolved spectroscopy sequences that suffer from long scan-times anyway. A more sophisticated technique which can circumvent some of the disadvantages of both methods is ERETIC (Electric REference To access In vivo Concentration). A reliable reference is produced by injecting an artificial signal of known amplitude, phase and duration [1, 2, 3, 4] into the measured spectrum. In this work a 2D JPRESS sequence was combined for the first time to our knowledge with the ERETIC reference in-vivo to bring the benefits of a stable reference signal to quantitative in-vivo 2D spectroscopy.

Materials & Methods

All measurements were performed on a 3T Philips whole body system using a standard 3T transmit receive birdcage coil. The transmission coil for the ERETIC signal was mounted on top of the birdcage coil as close as possible to the receiver coil to avoid any signal variations due to patient loading. The broad-band tune channel of the scanner was used for the reference signal's transmission. This setup allowed free control of ERETIC signal frequency. To avoid the influence of any sources of parasitic coupling the ERETIC signal was sent over an optical transmission line. The 2D spectra were measured in a healthy volunteer using a maximum echo sampled JPRESS sequence with a t1 increment of 2ms. In a maximum echo sampling scheme this prevents residual water signal tails from overlapping the metabolite signals after the tilting operation. 100 steps were used to encode a bandwidth of 500Hz in the F1 frequency dimension. The TR was set to 2000ms and the minimum echo time was TE=31ms. Excellent water suppression was achieved using a VAPOR [7] presaturation sequence. The offset frequency of the ERETIC signal was set to -600Hz which corresponds to the position of 0ppm in the F2 dimension of the spectrum. In a very short calibration measurement the amplitude of the ERETIC signal was set to NAA level and the phase was regulated to match the rest of the metabolites. To prevent any overlaps of the ERETIC signal tails with the spectral region of interest the position of the ERETIC signal in the first spectral dimension was controlled by implementing a frequency dependent linear phase shift of the reference signal across all the F1 encoding steps.

Results & Discussion

The ERETIC reference signal can be readily incorporated into in-vivo 2D spectroscopic experiments, which finally provides the necessary reference standard that remains stable independent of the investigated disorder. Fig.1 demonstrates that the ERETIC signal is observed at exactly 0ppm in both frequency dimensions and hence overlap with any signals of interest is avoided. However, its position inside the spectrum as well as its intensity can be freely chosen. Incorporating ERETIC into a basis set and fitting the JPRESS spectrum with ProFit finally provides the possibility to observe concentration changes of individual metabolites. This is of special importance for neurotransmitters and their precursors such as GABA or Glu and antioxidants such as GSH, which can not be detected by conventional 1D SV MRS and related concentration changes play a major role in the pathophysiology of psychiatric diseases. However, in order to determine metabolite concentrations in mM additional corrections are necessary, which is difficult since relaxation times of weak and partly strongly coupled metabolite signals that are overlapped by stronger resonance lines can hardly be performed with the necessary reliability.

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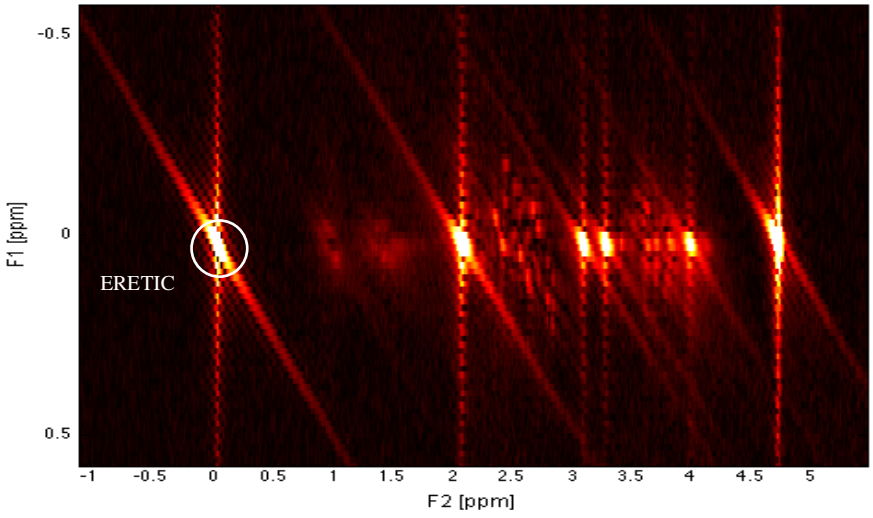

Fig. 1: JPRESS spectrum of a healthy volunteer with the ERETIC reference signal at 0ppm