GABA quantification at 3 T: SPECIAL vs. MEGA-PRESS
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Introduction
Knowledge of the level of the chief inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in various brain regions is of great interest in a number of psychiatric disease conditions [1] including anxiety, mood and addictive disorders, schizophrenia and epilepsy, as well as in occupational health [2] and neurobiological research. Fortunately, GABA belongs to the few non-singlet brain metabolites that have a sporting chance to be quantifiable in a clinical setting using proton MR spectroscopy at 3 T. Conventional spin echo spectroscopy generally failing because of insufficient SNR, MEGA editing [3, 4] has been the method of choice for GABA determination for many years. However, as spin echo based methods enabling ultrashort echo times (TE) arise, a closer look at their capability of GABA quantification is indicated. We therefore set out to compare, at 3 T, MEGA-PRESS and the spin echo full intensity acquired localized MRS technique (SPECIAL), the latter allowing for very short TE by using only one refocusing pulse [5, 6].

Methods and Subjects
MR examinations were performed on 36 healthy subjects (11 female, age 40 ± 8.4 y) on a 3 T Verio scanner (Siemens, Germany) using a transmit-receive head coil (Rapid Biomedical, Germany). T1-weighted images (MDEFT, TE = 3.8 ms, TR = 20.53 ms; TI = 550 ms) of the whole brain at a resolution of 1 x 1 x 1.5 mm³ were acquired for voxel positioning. First- and second-order shims were adjusted using FAST(EST)MAP [7]. Single volume spectra were acquired in a voxel of 25 x 40 x 20 mm³ comprising the anterior cingulate cortex (fig. 1) using (i) the vendor-provided MEGA-PRESS sequence at TE = 68 ms, TR = 3 s, n = 256 (ie 128 scans each with the editing pulse at 1.9 and 1.5 ppm); and (ii) SPECIAL at TE = 6.6 ms, TR = 3 s, n = 256. Metabolite quantification was carried out using LCModel with simulated basis sets. GABA concentration was estimated for MEGA-PRESS by referencing its signal via the NAA signal in the difference spectrum to that of the NAA concentration determined using the water-scaled spectrum with the editing pulse at 1.5 ppm. For SPECIAL the signal of the non-water-suppressed spectrum was used. For both analyses the baseline of the LCModel fit was constrained.

Results and Discussion
Spectra and corresponding fits are shown in fig. 2. Mean (± SD) GABA concentrations (mM) and CRLB (%) were 1.63 (0.59) and 13.4 (9.1) for MEGA-PRESS; 2.01 (0.75) and 13.6 (3.3) for SPECIAL. Whereas for 5 out of the 36 MEGA-PRESS spectra CRLB for GABA was above 20 %, all 36 SPECIAL spectra passed the 20 % CRLB test. Concentrations for the two methods tend to be slightly higher than literature values.

Known issues of GABA quantification by MEGA-PRESS are systematic errors due to the insufficiently known baseline which can thus not be adequately accomodated by LCModel, and due to the unknown and therefore uncorrected T2 relaxation of GABA. No such baseline issues are known about SPECIAL the newcomer sequence in this contest whose ability to quantify GABA still has to be established. The GABA concentrations determined by both methods are correlated with r = 0.46 (p = 0.016). Such an r value for nominally identical quantities is far from ideal but nevertheless a correlation exists and is highly significant. It is commonly accepted that MEGA-PRESS estimates GABA quite well, although with the aforementioned systematic errors. The correlation to the SPECIAL results then indicates that SPECIAL is capable of detecting GABA as well. The highly complex nature of the SPECIAL spectra that incorporate a much larger amount of resonances in combination with the short echo time makes it more vulnerable to baseline effects. On the other hand, SPECIAL is much less sensitive to T2 relaxation effects and has the advantage of providing good fit results for up to 12 additional metabolites (not shown here).

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References
1. Wong, CGT et al, Ann Neurol 2003; 54: S3
2. Dydak U et al, Environm Health Persp 2011; 119: 219
5. Mlynarik, V et al, MRM 2006; 56: 965