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Prospective frequency and motion correction for edited $^1$H magnetic resonance spectroscopy

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**Abstract**

The major inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and the dominant antioxidant glutathione (GSH) both play a crucial role in brain functioning and are involved in several neurodegenerative and psychiatric diseases. Magnetic resonance spectroscopy (MRS) is a unique way to measure these neurometabolites non-invasively, but the measurement is highly sensitive to head movements, and especially in specific patient groups, motion stabilization in MRS could be valuable. Conventional MRS is acquired at relatively short echo times (TE), however, for unambiguous detection of GABA and GSH, spectral editing techniques are typically used. These depend on longer TE and use frequency selective spectral editing pulses to separate the low-intensity peaks of GABA and GSH from overlapping resonances, but results in further increased motion sensitivity. Low-intensity metabolite peaks are usually edited one-by-one, however, simultaneous editing of multiple metabolites can be achieved using a Hadamard scheme, resulting in a substantial reduction in scan time. To investigate and correct for motion sensitivity in both conventional short-TE MRS (PRESS) and edited MRS (HERMES), we implemented a navigator-based prospective motion correction strategy including reacquisition of corrupted data. PRESS and HERMES spectra were acquired without motion, with motion with correction (repeated twice), and with motion without correction. Results indicate that when sufficient retrospective outlier removal is used, no significant differences in concentration and spectral quality were observed between motion conditions, without prospective correction. HERMES spectral editing data showed to be more sensitive to motion, as significant differences in metabolite estimates and variability of spectral quality measures were observed for tCr, GABA+ and GSH when only retrospective outlier removal was applied. When using both prospective and retrospective correction, spectral quality was improved to almost the level of the no-motion acquisition. No differences in metabolite ratios for GABA and GSH could be observed when using motion correction. In conclusion, edited MRS showed to be more prone to motion artifacts, and prospective motion correction can restore most of the spectral quality in both conventional and edited MRS.

**1. Introduction**

The major inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and the dominant antioxidant glutathione (GSH) are both suggested to be involved in psychiatric disorders, such as schizophrenia (Das et al., 2019; De Jonge et al., 2017) and depression (Godfrey et al., 2018; Maurya et al., 2016), and neurological disorders, such as Parkinson’s disease (Kaur et al., 2019; Smeyne and Smeyne, 2013) and multiple sclerosis (Carvalho et al., 2014). GABA and GSH can be measured in the human brain in vivo using proton magnetic resonance spectroscopy ($^1$H-MRS), however, long scan times and motion sensitivity compromise their assessment, particularly in more challenging populations such as children and patients with movement disorders. A tool to robustly and accurately assess GABA and GSH in such populations would be beneficial.

Detection of GABA and GSH is particularly sensitive to motion, as all resonances of both GABA and GSH are overlapped by more intense resonances from more abundant metabolites in the $^1$H-MR spectrum acquired at clinical field strengths (e.g. 1.5–3T). Mescher-Garwood (MEGA) (Mescher et al., 1998) spectral editing can be applied to isolate...
the 3.01 ppm resonance of GABA and the 2.95 ppm resonance of GSH but is usually performed for one metabolite at a time, making spectral editing of multiple metabolites time-consuming.

In the GABA molecule, there is a J-coupling between the $^3$CH$_2$ protons resonating at 1.89 ppm, and the $^4$CH$_2$ protons resonating at 3.01 ppm. In GABA-editing, a spectral editing pulse is applied to the 1.89 ppm signal in the edit-on acquisitions while in edit-off acquisitions the J-coupling is not refocused. Subtraction of edit-on and edit-off spectra results in the edited $^1$H-MR spectrum with the resolved GABA resonance at 3.01 ppm. In the GSH molecule, there is a strong coupling effect between the $^7$CH proton resonating at 4.56 ppm and the $^7$CH$_2$ protons resonating at 2.95 ppm. In GSH-editing, a spectral editing pulse is applied to the 4.56 ppm signal in the edit-on acquisition, eventually resulting in the edited $^1$H-MR spectrum with the resolved GSH resonance at 2.95 ppm.

With Hadamard-encoded spectral editing (Saleh et al., 2016) multiple metabolites can be edited within one sequence resulting in a two-fold reduction of scan time in case of simultaneous GABA and GSH editing. The method makes use of the fact that although GABA and GSH both have resonances around 3 ppm, they have coupled resonances at different frequencies. Instead of a two-step scheme, a four-step Hadamard scheme is used with a dual-band spectral editing pulse at 1.89 and 4.56 ppm in the fourth step. The relatively small GABA and GSH signals typically require long scan times, making the method sensitive to motion and magnetic field drifts (Bogner et al., 2014). In particular narrowband spectral editing is highly susceptible to frequency shifts (Edlen et al., 2016). Moreover, the four-step Hadamard scheme is more sensitive to instabilities than the two-step scheme used in MEGA. Motion and frequency drift can be corrected for using either external monitoring equipment (e.g. optical cameras and NMR field probes) (Zaitsev et al., 2010; Wilm et al., 2014) or internal MRI-navigator sequences (Bogner et al., 2014; Hess et al., 2011). MRI-navigators have the advantage that no additional equipment needs to be installed and or calibrated, making them suitable for use in daily practice, and they have the advantage that it is relatively straightforward to perform an additional 0-order field (frequency) correction. This makes the use of navigators attractive for the combination of spectral editing and single-voxel localization, as this both requires the use of a prospective motion and frequency correction scheme to correct for motion effects (Andronesi et al., 2020; Saleh et al., 2020).

In the current study, both a short-TE PRESS (point-resolved spectroscopy) and an Hadamard encoded spectral edited PRESS $^1$H-MRS sequence were combined with prospective frequency and motion correction. Experiments were performed without motion, with motion with correction and with motion without correction to estimate the impact of motion and motion correction on spectral data quality in a frontal brain region.

2. Methods

2.1. Participants

Twenty healthy human participants (21–35 years, mean±SD = 29±5 years, 9 females) were included in the study. Participants underwent two scan sessions with approximately one week between sessions. The study was approved by the Ethics Committee of the Capital Region of Denmark and performed according to the directives of the Declaration of Helsinki (amendment of Fortaleza, 2013). All participants provided written informed consent prior to the examination.

2.2. MR acquisition

MRS experiments were performed on a 3T MR scanner (Philips, Best, the Netherlands) in combination with a 32-channel receive head coil. A $T_1$-weighted sequence (288 slices, slice thickness = 0.85 mm, TR = 6.0 ms, TE = 2.7 ms, flip angle = 8°, FOV = 245 × 245 × 208, acquisition matrix = 288 × 188, scan duration = 5:43 min) was obtained for anatomical reference. A single-voxel short-TE PRESS sequence (Bottomley, 1987) (TR = 1272 ms, TE = 24 ms, 64 acquisitions, 1024 points, 2000 Hz bandwidth, total acquisition time 1:24 min) and a Hadamard encoded and reconstructed MEGA-edited PRESS sequence (HERMES) (Saleh et al., 2016) for GABA and GSH (TR = 2000 ms, TE = 80 ms, 128 acquisitions, 1024 points, 2000 Hz bandwidth, total acquisition time 4:16 min; Fig. 1) were obtained. For slice selective excitation, an asymmetric sinc-gauss pulse of 7 ms and 1987 Hz was used (at max b1=13.5). For slice selective refocusing, an numerically-optimized amplitude modulated pulse called ‘GST1203′ of 6.9 ms and 1264 Hz bandwidth was used. For spectral editing, single lobe sinc-gaussian pulses of 15 ms duration, similar to Mikkelsen et al. (2017). For the double editing steps in HERMES, dual-band pulses were generated by point-by-point addition of single banded pulses offset at 1.89 and 4.56 ppm (Fig. 1). VAPOR water suppression was used in both PRESS and HERMES experiments. Since the macromolecule signal was not suppressed but is co-edited in GABA-editing and thus contaminates the resolved GABA signal, the term GABA+ will be used. The MRS voxel (25 × 25 × 25 mm$^3$) was placed in the medial anterior cingulate cortex (ACC; Fig. 2).

For prospective motion and frequency correction, the iMOOC framework (Andersen et al., 2019) was used. In every repetition time (TR), a volumetric navigator is recorded that is registered to the first navigator of the series. The extracted motion parameters are then used to update both the location of the next navigator as well as the MRS voxel. As navigator, a 3D echo-planar imaging (EPI) sequence was used that included a slice selective frequency correction (resolution = 7 × 7 × 8 mm$^3$; 29 slices, flip angle = 2°, similar to vNAV (Tisdall et al., 2012)). The vNAV duration was 473 ms with a 300 ms delay for reconstruction and motion updating. 3D EPI navigators were interleaved before water suppression in every acquisition, leaving around 1 s delay between navigator and spectral acquisition. The vNAV had a small effect on the steady state magnetization, due to 29 excitations of 2°, approximately 2% of the steady state magnetization was spoiled at the point before water suppression. Due to T1 relaxation during the water suppression sequence, 99% of the metabolite signal was available at signal excitation.

To summarize the 6 motion parameters into one parameter, the motion score parameter by Tisdall et al. (2012) was used, which is the equivalent displacement on the surface of a sphere with 64 mm radius (approximating a human head). The amount of motion was analyzed for every acquisition and quantified as average motion score per TR. The
Instructed motion consisted of participants sequentially performing four types of movement that occur often in practice (sneezing, coughing, deep breathing, nodding) for five seconds at a time with twenty seconds of rest between movements. Participants were instructed through a screen, using written instructions for the type of movement and a fixation cross for rest.

2.4. Spectral fitting and quantification

Residual phase and frequency fluctuations in the single FIDs were removed before summing by maximizing the spectral correlation between single FIDs and the average spectrum, using the 2.8 to 3.4 ppm range, which includes both the creatine and choline resonances (Andreychenko et al., 2012). Afterwards, retrospective outlier removal (Tapper et al., 2019) was performed for all spectra. Single acquisitions in which more than 5% of the data points deviated three SD’s or more from the mean of the data points of all other acquisitions at a given frequency were removed before fitting. For edited HERMES spectra, frequency alignment, phasing and artifact detection was performed for each of the four steps separately before a final step that performed phase and frequency alignment on the four steps before summing to generate the GABA+, GSH and summed-metabolite spectrum. For HERMES, in the case the criteria for removing a single acquisition were met, the corresponding acquisitions in the three other steps were also removed.

Short-TE spectra were fitted in LCModel version 6.3–1 L (Provencher, 1993) with a basis set containing the following 17 metabolites: alanine, aspartate, creatine (Cr), phosphocreatine (PCr), GABA, glucose, glutamine (Gln), glutamate (Glu), glycero-phosphocholine (GPC), phosphorylcholine (PC), GSH, myo-inositol, lactate, N-acetyl aspartate (NAA), N-acetyl aspartyl glutamate (NAAG), scyllinositol and taurine. Levels of Glx (Glu+Gln), total NAA (tNAA; NAA+NAAG), total creatine (tCr; Cr+PCr) and total choline (GPC+PC) amplitudes were used for statistical analyses. An overall linewidth (full width at half maximum (FWHM)) as well as the Cramér–Rao lower bound (CRLB) per metabolite were reported.

Edited spectra were fitted using in-house developed software using linear combination modeling implemented in Matlab (The Mathworks Inc., Natick, MA, USA). Fitted amplitude to a Lorentzian model, linewidth and CRLB’s were reported per metabolite for GABA+, GSH and total creatine (tCr).

Metabolite level estimates from both PRESS and HERMES are reported as relative to tCr.

2.5. Statistics

Differences in spectral quality measures for CRLB and linewidth between the four different motion states were tested with a Bonferroni-corrected repeated-measures ANOVA. For both PRESS and HERMES, the CRLB of the tCr signal was used. For PRESS, the FWHM from LCModel was used and for HERMES, the FWHM of the tCr signal was used. For HERMES, the CRLB’s of the GABA+ and GSH signals were also used. When the assumption of sphericity was not met according to Mauchly’s test, the Greenhouse-Geisser correction was applied. A significance level of 5% was applied. Overall significant differences were further qualified using Bonferroni-corrected post hoc pairwise comparisons. Statistical analyses were performed in SPSS 25 (IBM Corp., Armonk, NY, USA). Coefficients of variation (CV), defined as SD/mean, were calculated for spectral quality measures and metabolite ratios for each measurement.

3. Results

Sample sizes for all scans are summarized in Table 1. Data from one participant were incomplete due to not showing up for the second session and thus excluded from the analyses. One PRESS spectrum without motion could not be acquired because of scanner issues, values for this
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Fig. 3. Recorded motion traces from one volunteer for both PRESS (top) and HERMES (bottom) without instructed motion (left), with motion with correction (middle), and with motion without correction (right). Translations and rotations (first and second row) are combined into a single motion score (third row), on which a 1 mm threshold (red dotted line) is used to trigger data reacquisition. Reacquired averages are indicated with an ‘x’. Furthermore, the frequency offset (fourth row) measured and corrected for, to stabilize the magnetic field offset during scanning. HERMES: Hadamard encoding and reconstruction of MEGA-edited spectroscopy, PRESS: point-resolved spectroscopy.

datapoint were average-imputed. All participants complied with the instructed motion.

3.1. Motion scores

The average motion scores in scans without motion were 0.2 (±0.1) and 0.3 (±0.1) mm/TR for PRESS and HERMES, respectively. For scans with motion with correction, average motion scores were 1.3 (±0.6) and 1.5 (±0.6) mm/TR for session 1 and 1.5 (±0.5) and 1.7 (±0.7) mm/TR for session 2; and for scans with motion without correction, average motion scores were 1.1 (±0.5) and 1.4 (±0.7) mm/TR. Example motion traces from one volunteer are displayed in Fig. 3 for both PRESS and HERMES without motion, with motion with correction, and with motion without correction.

3.2. Prospective and retrospective outlier removal

Removal of outliers was performed in two ways. First, for scans with correction, reacquisition of data was performed when motion exceeded a threshold of 1 mm. This extended scan time with on average 35% (range 11–54%) and 42% (range 24–71%) for PRESS, and 35% (range 15–53%) and 39% (range 16–54%) for HERMES in session 1 and 2, respectively. Fig. 4 presents an example of acquired data, showing an overlap of all acquisitions. This shows similar stability for data acquired without motion and data with motion with correction. Data acquired with motion without correction show some outliers for PRESS but more severe instabilities for HERMES are observed likely due to the increased echo time.

Second, retrospective outlier detection was performed. For PRESS without motion, 1.5% of all acquisitions were removed. For PRESS with
motion with correction, 1.6% and 1.1% of all acquisitions were removed for session 1 and 2, respectively. For PRESS with motion without correction, 2.1% of all acquisitions were removed. For HERMES without motion, 0.5% of all acquisitions were removed. For HERMES with motion with correction, 0.8% and 1.6% of all acquisitions were removed for session 1 and 2, respectively. For HERMES with motion without correction, 8.4% of all acquisitions were removed. After outlier removal, data was summed up to generate the input data for the spectral fitting routines (Fig. 5).

3.3. Spectral quality

The coefficient of variation of the spectral quality measures is shown in Table 2. Variability in spectral quality measures for PRESS (after retrospective data correction) was similar, except an increased coefficient of variation in the linewidth was observed in the second motion with correction experiment. For HERMES, the coefficient of variation for the linewidth was stable, but for creatine, GABA+ and GSH, an increase in the coefficient of variation was seen between the baseline case without motion and the case with the motion corrected states. A larger increase in the coefficient of variation was seen in the case with motion without correction in Cr, GABA+ and GSH.

The mean and standard deviations of the spectral quality values are shown in Fig. 6. Repeated-measures ANOVA determined that mean CRLB of tCr and FWHM of PRESS did not significantly differ across the four scans ($F_{3, 51}=0.541$, $p=0.656$ and $F_{1,523}=2.883$, $p=0.280$, respectively). Mean CRLB of tCr and FWHM of HERMES did not significantly differ across the four scans ($F_{4,147}=2.605$, $p=0.116$ and $F_{1,526}=2.737$, $p=0.516$ respectively). Mean CRLB of GABA+ and GSH of HERMES did not significantly differ across the four scans ($F_{2,091}=3.055$, $p=0.058$ and $F_{1,371}=2.675$, $p=0.364$, respectively).
4. Metabolite level estimates

Repeated-measures ANOVA determined that mean tNAA/tCr, tCho/tCr, mlNs/tCr and Glx/tCr measured with PRESS did not significantly differ across the four scans (F<sub>2,102</sub>.37.414=2.193, p = 0.123; F<sub>1.449</sub>.26.079=0.324, p = 0.657; F<sub>3.54</sub>=2.407, p = 0.077; F<sub>3.54</sub>=2.916, p = 0.420, respectively).

Mean GABA+/tCr measured with HERMES differed across the four scans (F<sub>3.54</sub>=4.278, p = 0.009). Post-hoc pairwise comparisons determined a difference between GABA+/tCr acquired without motion and GABA+/tCr acquired with motion without correction (p = 0.031).

Mean GSH/tCr measured with HERMES did not significantly differ across the four recordings (F<sub>1.165</sub>.20.976=3.238, p = 0.081).

For HERMES, metabolite levels measured with motion without correction showed higher CV’s than the other three scans (Table 2, Fig. 7).

4. Discussion

Using MR spectroscopy, both the major inhibitory neurotransmitter GABA+ and the dominant antioxidant GSH can be detected in vivo. However, the signal intensities of the metabolites are generally low, and the detection techniques are sensitive to subject motion during the relatively long scans. In this study we investigated the use of navigator-based motion correction in detection of low-sensitive neurochemicals GABA+ and GSH using novel simultaneous spectral editing techniques. Motion sensitivity of HERMES for simultaneous GABA+ and GSH detection was examined and compared to a short-TE PRESS sequence for detection of metabolites of higher sensitivity (tNAA, tCho, mlNs, Glx).

The stability of spectra acquired with motion correction was higher compared to spectra acquired without motion correction, and similar to spectra acquired without motion. This was observed from the retrospective outlier removal, where for spectra acquired with correction a similar amount of data was removed as compared to spectra acquired without motion, and less data was removed compared to scans with motion and without correction. This resulted in smaller amounts of post-hoc rejected data.

After retrospective outlier removal, across PRESS scans, spectral quality and metabolite estimates were not significantly different and variability was similar. This is surprising, as data from scans with motion without correction were at least partially acquired from different locations than the originally planned voxel location. In the current study, voxels were originally planned in the medial ACC and motion presumably did not result in the voxel overlapping the skull or cerebrospinal fluid (CSF). With voxel locations closer to the skull or CSF, effects of motion on spectral quality and estimated metabolite levels have been observed (Zaitsev et al., 2010). Also, the data was scaled with an internal reference (tCr). Therefore, overall signal loss would not be observed in the metabolite estimates, but would still have resulted in increases in the CRLB. Concluding we can say that in the PRESS case, the retrospective outlier removal performed sufficiently well, and resulting SNR after outlier removal was still sufficient to accurately quantify the metabolites.

The HERMES findings suggest that spectral editing sequences are more sensitive to motion than short-TE MRS sequences, which is likely due to the longer TE and the use of spectral editing RF pulses (MG Saleh et al., 2020). Similar amounts of data were retrospectively removed for HERMES spectra without motion and spectra with motion correction. We observed no significant difference in the spectral quality measures for HERMES between motion cases, but did observe a moderate increase in the variability of the CRLB, when comparing cases with motion and correction to cases without motion, indicating there was still some impact of motion on the CRLB measures. This was not reflection in the GABA+ and GSH concentration estimates. Lack of prospective correction in the presence of motion led to more retrospective data removal, showed a much variability of the CRLB and resulted in lower GABA+ estimates compared to conventionally acquired GABA+ estimates And largely increased variability in both the GABA+ and GSH estimates. As the subjects were left free to choose how to perform the consecutive motions (sneezing, coughing, deep breathing, nodding) at the instructed time points, some variation was seen in performance in individual motion traces (e.g. Fig. 3). However, the average motion scores between scans was similar leading to comparable motion between the different experiments. The motion load in this study was high compared to normal daily practice as motion was instructed every 25 s. This may have caused relatively high average motion scores for scans recorded with motion and long scan times for scans recorded with correction due to reacquisition of about 40% of the data. In clinical practice, the amount of time required for reacquisition will vary with a fixed threshold, but (depending on patient groups) will likely be shorter than this 40%, but even this increase is shorter than a repeat of a corrupted scan. When looking at the amount of retrospective outlier removal, it can be concluded that the chosen reacquisition threshold of 1 mm (as used for high
Fig. 6. Bar plots of spectral quality measures for PRESS and HERMES for scans acquired without motion (NoMo), scans acquired with motion with correction (first session: MoCo1, and second session: MoCo2), and scans acquired with motion without correction (NoCo). LW of PRESS was computed by LCModel, whereas all other spectral quality measures were derived from the tCr signal. CRLB: Cramér-Rao lower bound, GABA: gamma-aminobutyric acid, GSH: glutathione, HERMES: Hadamard encoding and reconstruction of MEGA-edited spectroscopy, LW: linewidth, PRESS: point-resolved spectroscopy, tCr: total creatine.

Fig. 7. Bar plots of metabolite level estimates for scans acquired without motion (NoMo), scans acquired with motion with correction (first session: MoCo1, and second session: MoCo2), and scans acquired with motion without correction (NoCo). The first four plots represent estimates measured with PRESS; the last two plots represent estimates for GABA+ and GSH measured with HERMES. GABA+: macromolecule-unsuppressed gamma-aminobutyric acid, Glx: glutamate + glutamine, GSH: glutathione, HERMES: Hadamard encoding and reconstruction of MEGA-edited spectroscopy, mIns: myo-inositol. PRESS: point-resolved spectroscopy, tCho: total choline, tCr: total creatine, tNAA: total N-acetyl aspartate.
resolution brain imaging) was sufficient to regain a similar level of retrospective data rejection in scans with motion with correction compared to scans without motion. The threshold was based on a previous study (Andersen et al., 2019), where other studies by Bogner et al. (2014) and Zaitsev et al. (2010) on MRS using reacquisition have used lower thresholds on 0.4 mm or degree and 0.5 mm, respectively. Choosing a higher reacquisition threshold would allow shorter scan times due to less reacquisition and could still result in acceptable spectral quality and accurate metabolite level estimates. However, determining an appropriate reacquisition threshold depends on several factors, including voxel position and size, neighboring anatomical structures and available scan time. An alternative is to order spectra on their motion score, and then allocate a fixed amount of time for reacquisition where only the spectra with highest motion score are reacquired (Tisdall et al., 2012).

Also, we observed that a certain level of retrospective outlier removal is necessary even in scans without motion, as some spectral artifacts can arise from motion during the TE of the MRS scan. This can for example be caused by heartbeat and is not detectable with navigator-based motion detection. As was observed by the retrospective data rejection, these artifacts arise more in HERMES data as the TE is longer. Our findings confirm the assumption that spectral editing sequences are more sensitive to motion as compared to short-TE MRS sequences and benefit even more from real-time motion correction. This is attributed to the combined use of editing pulses and long echo time.

A limiting factor of the study is the use of metabolite-to-T2 ratios instead of water ratio-based concentration estimates. We encountered complications when estimating the water signal in case of motion, as there was no reacquisition implemented for the single water acquisition. Therefore, we estimated metabolite concentrations from ratios with the internal reference Creatine. For MRS without prospective motion correction, acquisition of multiple water spectra spread throughout the metabolite acquisition is recommended (Saleh et al., 2020). However, careful quality control should be employed by e.g. using data removal for water acquisitions similar to data removal for metabolite acquisitions.

In this study we chose to perform a control experiment without motion and without correction, but with the navigators included, in order to have a measure on how much motion still occurred during the control measurement without motion. One could additionally perform an experiment without motion and with correction to investigate if performing motion correction could have a negative impact on the MRS acquisition due to errors in motion updating. We chose not to include such a control due to time limitations and because previous work (Andersen et al., 2019) has shown that 3D imaging sequences were not negatively impacted by motion correction using the same methodology. Furthermore, one can perform a control MRS experiment without motion and navigators to investigate possible effects of the navigator RF excitations on the MRS steady-state magnetization. From the signal model and average T1 value of the metabolites, we expected this to have an impact of around 1% on all metabolites. Due to T1 differences between resonances this amount can vary slightly, but induced differences in metabolite or water ratios would only be minor.

Apart from using navigator-based motion correction, several other technical solutions exist (e.g. optical cameras, Zaitsev et al., 2010; or NMR probes, Wilm et al., 2014) for detection and correction of motion. Although such systems allow for fast and accurate motion updating, it requires the installation and calibration of additional hardware. The advantage of navigator-based motion correction is that it only requires software changes to the MRI system. And although the method requires some dead time in the MRS sequence this is almost always available in relatively long TR used for MRS.

Recommendations for motion correction of spectral editing sequences based on the current study are applicable not only to sequences editing for GABA+ and GSH, but also for sequences editing for other (combinations of) metabolites (Oeltzschner et al., 2019) and sequences editing for only one metabolite at a time (Mescher et al., 1998).

In conclusion, HERMES data showed to be more sensitive to motion than PRESS data, most probably due to the longer scan time (Bogner et al., 2014), the use of spectral editing (Edden et al., 2016), the use of a four-step Hadamard-scheme, and the longer TE. When applying prospective frequency and motion correction combined with retrospective outlier removal, spectral quality of HERMES data acquired with instructed motion was improved to almost the level of data acquired without motion. Prospective frequency and motion correction using MRI-navigators is thus beneficial for spectral quality of edited MRS and eliminates the need for additional external equipment for frequency and motion correction.

Data and code availability statement

Due to Danish data handling legislation data will only be available upon request and only after finalizing a formal data sharing agreement.

Credit authorship contribution statement

Anouk Marsman: Conceptualization, Methodology, Formal analysis, Writing - original draft. Anna Lind: Software, Formal analysis, Investigation. Esben Thade Petersen: Conceptualization, Writing - review & editing. Mads Andersen: Software, Methodology, Writing - review & editing. Vincent Olman Boer: Conceptualization, Methodology, Software, Formal analysis, Writing - original draft.

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