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Data supplement

Description of imaging, spectroscopy, pre-processing, fitting and quantification

Data were acquired with a 4.0 Tesla Varian (Palo Alto, California, USA)/Siemens (Erlangen, Germany) whole-body scanner with a Varian Unity Inova console, located at the Centre for Functional and Metabolic Mapping of the Robarts Research Institute, London, Ontario, Canada. A circularly polarised transmit-and-receive head coil was used. Global shimming was manually performed with linear and second-order shim coils and followed by T_1-weighted transverse anatomical images (three-dimensional (3D) magnetisation prepared fast low angle shot (MP-FLASH) sequence, repetition time (TR) 11 ms, echo time (TE) 6.4 ms, inversion time (TI) 500 ms, flip angle 30°, 64 slices, matrix 256×256, 0.78×0.78 mm resolution, field of view (FOV) 20 cm, slice thickness 2.75 mm). Using those T_1-weighted images, the $10 \times 15 \times 10$ mm^3 (right–left, anterior–posterior, inferior–superior direction) ^{1}H spectroscopy volumes were positioned at the left anterior cingulate gyrus (Brodmann Area, BA32) and the left thalamus.

Magnetic resonance spectroscopy data were obtained with a single voxel stimulated echo acquisition mode (STEAM) sequence (TE = 20 ms, mixing time (TM) 30 ms, TR = 2000 ms, dwell time 500 ms, eight-step phase-cycling). The power of the 90° radio frequency pulses and the CHESS water suppression pulses were optimised for each voxel. After local shimming, water suppressed data (256 averages) followed by water unsuppressed data (16 averages) were collected. Data post processing included zero order eddy current correction (ECC) and line shape correction with the QUECC technique.[34] The remnant water resonances in the water suppressed spectra were subtracted with the Hankel–Lanczos singular value decomposition algorithm.[35] Water suppressed spectra were fitted through an in-house software Fitman program[35,36] to the first 1024 data-points (512 ms) in the time domain using *a priori* knowledge. Our model is based on *in vitro* measurements from 12 metabolites plus literature values for 11 macromolecules added to the *a priori* knowledge.[37,38] Metabolite concentration levels were quantified with equations[8] that included the ratio to water concentration in each spectroscopy voxel. The voxel water concentration depends on the voxel fraction of grey matter, white matter, and cerebral spinal fluid (CSF) along with the water content of each of these tissues. The measured water signal was therefore corrected by the voxel's fractional tissue content and assumed literature values for the water content of each tissue type (grey matter 81%, white matter 71%, CSF 100%). Fractional tissue content was measured from semi-automated segmentation of the voxel location within the 3D T_1-weighted image set as in our previous study.[8]

Quality of each magnetic resonance spectrum was evaluated using the Visual Appreciation Scale (from 1 to 5) as well as the Baseline and Artefact Scale (from A to E), introduced by Théberge *et al*.[8] We excluded the spectra in which the gamma-glutamate peak (2.35 ppm) was not identified and/or severe hashing was seen in a part of the spectra (i.e. rating lower than 5B). Only metabolites with a group coefficient of variation (group CV = (group standard deviation / group mean) × 100%) less than 75% are reported. Group CV less than 75% in the normally distributed samples means that 10% of the samples have a chance to be negative values, which never emerge in our fitting procedure. This criterion protects the statistical analysis from the metabolites which reach the lower detection threshold. We elected not to use a criterion based on the lower bounds Cramér–Rao (CRLBs) since CRLBs are only a portion of the total inter-individual variability of the data. It is the total inter-individual variability (group standard deviation) that determines the final ability to distinguish between two groups (a.k.a. smallest detectable difference, SDD). Metabolites survived from the criterion are NAA, glutamate (Glu), glutamine (Gln), choline (Cho), total creatine (tCr), myo-inositol (Myo) in the anterior cingulate and the thalamus, taurine (Tau) and scyllo-inositol (Syl) in the thalamus only. The 'total glutamatergic metabolites' (tGL) refers to a sum of Glu and Gln levels measured individually. It should be noted that tGL is different from Glx, which is commonly used in the spectroscopy literature. Glx has an investigator-dependent definition which can refer to a variety of quantities. Often, it refers to the integrated spectral area encompassing the peaks from the 3C and 4C multiplets of Glu, Gln, GABA (gamma-aminobutyric acid), the aspartyl moiety of NAA and *N*-acetyl-aspartyl-glutamate (NAAG), the glutamate moiety of NAAG as well as signals from macromolecules. The concept of Glx was useful in the context of overlapping peaks at lower field strengths (1.5 T) and was used by many of the earlier studies where separate quantification of these metabolites may have been more difficult.

Additional references

34 Bartha R, Drost DJ, Menon RS, Williamson PC. Spectroscopic lineshape correction by QUECC: combined QUALITY deconvolution and eddy current correction. *Magn Reson Med* 2000; **44**: 641–5.

35 Bartha R, Drost DJ, Williamson PC. Factors affecting the quantification of short echo in-vivo 1H MR spectra: prior knowledge, peak elimination, and filtering. *NMR Biomed* 1999; **12**: 205–16.

36 Bartha R, Drost DJ, Menon RS, Williamson PC. Comparison of the quantification precision of human short echo time (1)H spectroscopy at 1.5 and 4.0 Tesla. *Magn Reson Med* 2000; **44**: 185–92.

37 Kauppinen RA, Kokko H, Williams SR. Detection of mobile proteins by proton nuclear magnetic resonance spectroscopy in the guinea pig brain ex vivo and their partial purification. *J Neurochem* 1992; **58**: 967–74.

38 Behar KL, Ogino T. Characterization of macromolecule resonances in the 1H NMR spectrum of rat brain. *Magn Reson Med* 1993; **30**: 38–44.

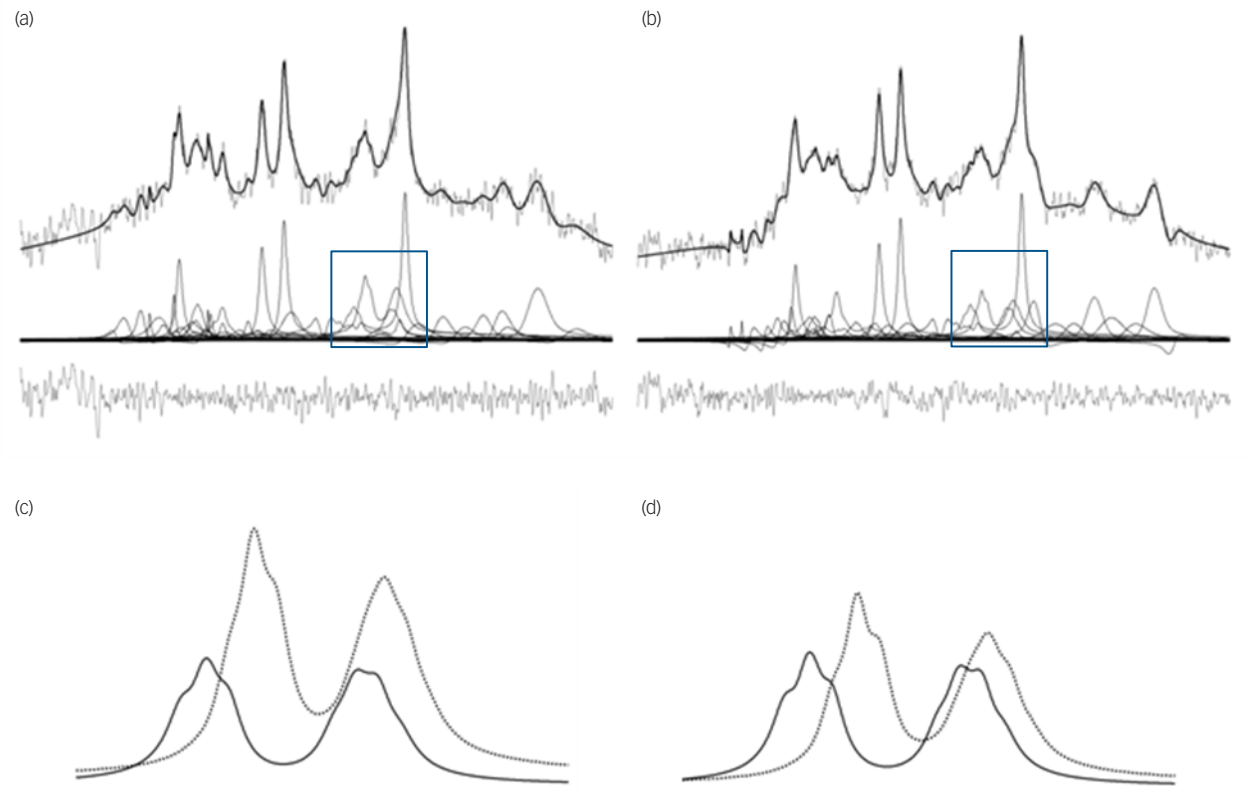

Fig. DS1 Fitted *in vivo* magnetic resonance spectra with 2 Hz line broadening collected from the left thalamus in a patient with schizophrenia at (a) never-treated assessment and (b) 80-month assessment.

Preprocessed spectrum (grey line) with fit (solid line) on the top, corresponding metabolite components in the middle, and the residual shown below. The boxed regions indicated in (a) and (b) are magnified in (c) and (d), showing the glutamate (dotted line) and glutamine (solid line) components.