In Vivo Brain ^{1}H-MRS of Sodium Pentobarbital: Potential Contaminations to the Cerebral Metabolites Quantification

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Introduction

Sodium pentobarbital is widely used in clinic and medical research as anesthesia. In this study, the localized ^{1}H MRS was performed in the rat brain anesthetized by sodium pentobarbital with varied dose. The results indicate that in vivo ^{1}H MRS is sensitive to detect and monitor brain pentobarbital concentration via the resonance peak at 1.15 ppm. However, the resonance peaks between 3.3 to 4.0 ppm contributed from sodium pentobarbital and its solvents have potential complications to the cerebral metabolite quantification. It is crucial to account these resonance peaks in metabolite quantification for improving reliability of in vivo ^{1}H MRS for brain applications in the presence of sodium pentobarbital.

Method and Materials

Animal Study: Male Sprague-Dawley rats (210-350 g) (n = 6) were prepared at three different anesthesia depths with various doses of sodium pentobarbital for MRS scan. The first state was achieved by inhalation of 2% (vol-vol) isoflurane in nitrous oxide/oxygen (3:2). The second anesthesia state (Pen_30) was achieved by switching isoflurane to sodium pentobarbital with 30 mg/kg bolus complying constantly infusing 30 mg/kg/h. The last state (Pen_70) was obtained by directly increasing infusing rate to 70 mg/kg/h to completely shut off brain electric signaling (i.e. iso-electric state).

Phantoms Study: Anesthetic agent, sodium pentobarbital injection solution (PB), was obtained from Ovation Pharmaceuticals, Inc. Each mL of sodium pentobarbital solution contains 50 mg sodium pentobarbital, 40% (v-v) propylene glycol (PG) and 10% (v-v) alcohol. In order to identify MR resonances arising from anesthesia drugs, 5 mM sodium pentobarbital diluted from sodium pentobarbital injection solution, 1 mM glucose (Sigma-Adrich Company) and 4% (v-v) alcohol (CH3CH2OH) saline solutions were prepared with pH = 7.0.

MR Measurements: MR experiments were carried out at a 9.4 T/31 cm horizontal bore magnet. Anatomic imaging and spectroscopy were acquired by using an elliptical surface coil with a long axis of 2 cm and a shot axis of 1.2 cm. Scout images were acquired using a turbo fast low-angle shot (TurboFlash) sequence. The ^{1}H-MRS of 4×4×4 mm^3 voxel mainly covering the cortex was acquired by the point-resolved spectroscopy (PRESS) sequence with 5 kHz spectra width, 64 repeated scans, 2048 data points, 3 s repetition time and 13 ms echo time.

Results and Discussions

Figure 1 presents the in vivo ^{1}H MRS spectra from a rat brain acquired under three anesthesia conditions. In this figure, spectrum (d) demonstrates the subtracted spectrum between spectrum (c) and (a) (i.e., between high and zero dose of pentobarbital). The resonance peak at 1.15 ppm is elevated with the increased dose of sodium pentobarbital and it is well resolved from other proton resonance peaks. However, there are a number of new resonance peaks appearing in the range of 3.0 to 4.0 ppm. To identify these peaks, the substance solutions were scanned and presented in (e) 5 mM sodium pentobarbital, (f) 4% (v-v) alcohol and (g) 1 mM glucose saline solution, respectively. The substance concentrations of phantoms were similar with that in the rat brain.

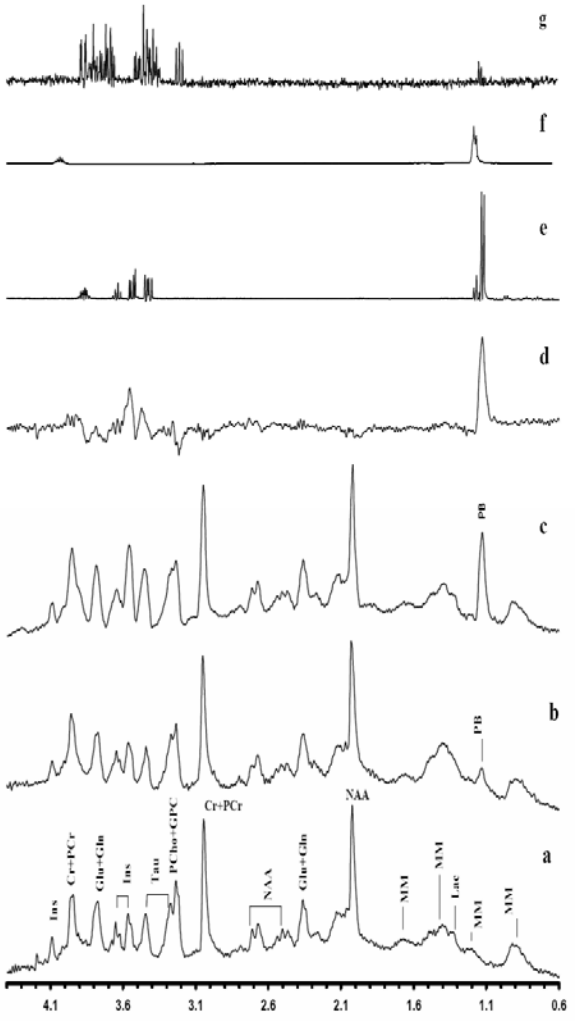

Figure 1. Representative in vivo ^{1}H MRS spectra acquired from a rat brain under three different anesthesia states and from phantoms, respectively. (a) isoflurane. (b) low dose pentobarbital (Pen_30). (c) high dose sodium pentobarbital (Pen_70). (d) (c)-(a). (e) 5mM sodium pentobarbital. (f) 4% (v-v) alcohol. (g) 1mM glucose.

The barbiturates are nonselective central nervous system depressants and substituted pyrimidine derivatives in which the basic structure common to these drugs is barbituric acid. The sodium pentobarbital injected solution used in this study was chemically designated as sodium 5-ethyl-5-(1-methylbutyl) barbiturate. The NMR peaks at 1.15 ppm and 3.0-4.0 ppm come from protons of -CH_3 and -CH_2/-CH_2CH_2- groups, respectively. These peaks possibly overlap with those of the solvents i.e. PG and alcohol. It has been found that the ^{1}H MRS spectrum of PG has a methyl doublet at 1.15 ppm and singlets at 3.4 and 3.6 ppm [1]. NMR peaks of alcohol solution were presented as the triplets partially overlapped with 1.15 ppm peak and multiplets at 3.80 ppm in the plot (1f). It was also found that alcohol NMR peak at 1.18 ppm appeared in the ^{1}H MRS of human brain of volunteers with alcohol consumptions [2]. Clearly these NMR peaks coming from sodium pentobarbital injection solution can potentially interfere with LCModel quantification of PCr/Cr, glycine, glucose and *myo*-inositol [2, 3]. They need to be considered in quantifying cerebral metabolites for improving the reliability of in vivo ^{1}H MRS in the presence of sodium pentobarbital.

Reference

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