Barbiturate Anesthesia and Brain Proton Spectroscopy

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BACKGROUND AND PURPOSE: Thiopentone reduces CBF and metabolic rate. Still, it is widely used for sedation during MR spectroscopy. We investigated whether barbiturate anesthesia and preanesthetic fasting have an effect on metabolic ratios in proton MR spectroscopy of the brain.

METHODS: Eight healthy, consenting, male volunteers were studied twice in a random, crossover fashion. The study sessions were conducted during fasting (F) and nonfasting (nonF), with glucose infusion mimicking the fed state. During both sessions, two sets of spectroscopic data were collected, one during the awake state (F or nonF) and one under barbiturate anesthesia (F+B or nonF+B), using TEs of 135 and 270. Spectral areas of N-acetylaspartate (NAA), choline-containing compounds (Cho), and creatine plus phosphocreatine (Cr) were calculated, and the presence of lactate or lipid was noted. Venous blood samples for glucose, β-hydroxybutyrate, lactate, and electrolytes were collected.

RESULTS: Barbiturate anesthesia caused a 42% reduction in blood lactate levels during fasting, but not during glucose infusion. There were no differences in NAA/Cho, NAA/Cr, or Cho/Cr between the groups F, nonF, F+B, or nonF+B. No lactate or lipid resonances were detected.

CONCLUSION: Barbiturate anesthesia with preanesthetic fasting can be used for proton spectroscopy at TEs of 135 or 270 without interference from NAA/Cho, NAA/Cr, or Cho/Cr or from the appearance of lactate or lipid.

MR spectroscopy enables noninvasive in vivo measurement of brain biochemistry (1–4). Children and other uncooperative patients often need sedation or general anesthesia during the data collection. The metabolic state of the brain is affected by anesthetic agents (5) and possibly also by preanesthetic fasting (6). We wanted to determine whether the fasting preceding anesthesia, or barbiturate anesthesia itself, had any effect on the major spectral metabolites N-acetylaspartate (NAA), choline (Cho), creatine plus phosphocreatine (Cr), lactate, or lipids.

Methods

Subjects and Study Protocol

Eight healthy male volunteers (20 to 32 years old) were studied. None of them had a history of alcohol and/or drug abuse and none were currently using any medication. The study was approved by the Institutional Ethics Committee of Turku University Hospital and written informed consent was obtained prior to participation in the study. Each subject was examined twice in a random crossover fashion. The study sessions during fasting and nonfasting were 1 week apart. The person analyzing the spectra was kept unaware of the treatment.

At every session, baseline MR spectroscopy with the subject awake was performed first, after which anesthesia was induced with 5 to 8 mg/kg thiopentone IV and MR spectroscopy was repeated. The subjects were kept asleep by consecutive 50-mg doses of thiopentone. They were breathing spontaneously, and the adequacy of ventilation was monitored with pulse oximetry (SpO₂).

In the nonfasting session, food was allowed until 6 hours before the examination and an infusion of 10% glucose solution 100 mL/h was started 2 hours before the spectroscopy. In the fasting session, volunteers fasted for 18 to 20 hours before the examination and slow isotonic saline infusion was started for maintaining the IV line. Another IV cannula was inserted into the contralateral arm for blood sampling. Venous blood samples for analysis of glucose, β-hydroxybutyrate, lactate, and electrolytes were collected before the start of the glucose infusion, at the end of the spectroscopic examination performed with the subjects awake (F or nonF), and at the end of spectroscopic data collection with the subjects under anesthesia (F+B or nonF+B).

MR Spectroscopic Protocol

Imaging and spectroscopy were performed with a 1.5-T MR imager (Siemens Magnetom 63 SP 4000 and NUMARIS version A2.7, Erlangen, Germany) with a standard circular head coil and spectroscopic package. Transverse axial T2-weighted...
TABLE 1: Physiological data

<table>
<thead>
<tr>
<th></th>
<th>Glucose</th>
<th>β-hydroxybutyrate</th>
<th>Lactate</th>
<th>Plasma Sodium</th>
<th>Plasma Kalium</th>
<th>Serum Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>4.6 ± 0.2</td>
<td>0.28 ± 0.22</td>
<td>1.18 ± 0.33</td>
<td>142 ± 1</td>
<td>3.7 ± 0.3</td>
<td>2.4 ± 0.1</td>
</tr>
<tr>
<td>F+B</td>
<td>4.9 ± 0.6</td>
<td>0.26 ± 0.21</td>
<td>0.68 ± 0.28</td>
<td>142 ± 2</td>
<td>3.8 ± 0.2</td>
<td>2.3 ± 0.1</td>
</tr>
<tr>
<td>nonF</td>
<td>6.2 ± 0.9</td>
<td>0.10 ± 0.00</td>
<td>1.08 ± 0.36</td>
<td>140 ± 1</td>
<td>3.8 ± 0.2</td>
<td>2.4 ± 0.06</td>
</tr>
<tr>
<td>nonF+B</td>
<td>6.1 ± 1.8</td>
<td>0.11 ± 0.04</td>
<td>0.96 ± 0.19</td>
<td>141 ± 1</td>
<td>3.7 ± 0.3</td>
<td>2.4 ± 0.1</td>
</tr>
</tbody>
</table>

P value (F vs nonF) .03 .03 NS NS NS NS
(F+B vs nonF+B) .01 .04 NS NS NS NS
(F vs F+B) ... ... .01 ... ... ... 
(nonF vs nonF+B) ... ... NS ... ... ... 

Note.—Blood chemistry in the four treatment groups in mmol/L. F indicates fasting; F+B, fasting and barbiturate; nonF, glucose infusion; nonF+B, glucose infusion and barbiturate; NS, not significant. The relevant differences between the treatment groups were tested with paired t-test using \( P = 0.05 \) as the limit of significance.

Spin-echo images 2700/22,90/1 (TR/TE/excitations) with 5-mm section thickness, 192 × 256 matrix size, and 250-mm field of view were collected for localization of the 8-cm³ spectroscopic volume in the left basal ganglia, avoiding the CSF spaces. A double spin-echo sequence with chemical-shift selective water suppression was performed with parameters of 1500/135,270 (TR/TE), 256 acquisitions, and 1024 data points to acquire the spectra from a cubic 8-mL volume. Four spectra were acquired during each session with the two TEs and with the volunteer awake and under barbiturate anesthesia (Fig 1).

Data Postprocessing

Data postprocessing was performed with the NUMARIS A2.7 spectroscopic software package, and the integrated areas of each metabolite spectral line, the CH₃ group of NAA at 2.0 ppm, the N-CH₃ group of Cr at 3.0 ppm, and the N-CH₃ group of Cho at 3.2 ppm, were determined manually. The baseline of the spectrum was corrected with a second-order polynomial spline function. Metabolic ratios were calculated from the integrated peak areas of spectra recorded with TEs of 135 and 270.

Statistical Analysis

A paired t-test was used to compare the differences in blood glucose, β-hydroxybutyrate, and lactate between the F and nonF; and F+B and nonF+B sessions, respectively. A single-factor ANOVA was used to compare the differences in the other blood parameters and in spectroscopic metabolite ratios between the four treatment groups: fasting and awake (F), fasting and under anesthesia (F+B), glucose infusion (mimicking nonfasting) and awake (nonF), and glucose infusion and under anesthesia (nonF+B).

Results

There were no differences between the total doses of thiopentone administered during the two sessions (F+B vs nonF+B, 738 mg vs 778 mg). No significant decrease in SpO₂ occurred during any of the study sessions.

Physiological Data (Table 1)

The 10% glucose infusion resulted in a slightly elevated blood glucose at the end of the infusion (nonF and nonF+B). Prolonged fasting induced significant elevation of blood β-hydroxybutyrate (F and F+B). The induction of barbiturate anesthesia caused a 42% decrease in blood lactate in the F group, whereas in the nonF group blood lactate remained unchanged during anesthesia. Plasma so-
dium, plasma kalium, and serum calcium remained unchanged during the experiment.

**Spectroscopic Data (Table 2)**

There were no differences in the mean NAA/Cho, NAA/Cr, or Cho/Cr (P > .33) between the four treatment groups. No lactate or lipid resonances were detected.

**Discussion**

Selection of anesthetic agents for sedation during MR spectroscopy has been based mainly on anesthetic considerations (7, 8). To what degree these agents may affect the results has not been ascertained. We studied thiopentone because it is widely used for sedation during MR imaging, especially in children, who form the largest patient group for metabolic MR spectroscopic studies. For ethical reasons we were restricted to young adults as study subjects. Because of the obvious risks, we could not feed the subjects before the nonfasting sessions. Instead, we decided to use a continuous glucose infusion to mimic the postprandial state; glucose was infused at a rate corresponding to the average infusion to mimic the postprandial state; glucose and thus to potentially affect the metabolic state of the brain (6). The 18-hour fast used in this study was 4 to 6 hours prior to the examination. Fasting is known to alter blood levels of several substrates and thus to potentially affect the metabolic state of the brain (6). The 18-hour fast used in this study resulted in elevated plasma \( \beta \)-hydroxybutyrate levels, indicating fat oxidation typical for prolonged fasting (Table 1). Reduced brain lactate levels during barbiturate anesthesia have been linked to inhibition of phosphofructokinase activity (12). Our finding of the 42% reduction in blood lactate during barbiturate infusion is in line with this; however, we were unable to discover why blood lactate reduction did not occur in the nonfasting group. This difference in blood lactate between the awake state and barbiturate anesthesia is not reflected in brain tissue lactate, at least with the present sensitivity of the method.

**Conclusion**

Our study shows that if fasting is needed in a spectroscopic study for anesthetic reasons, the results will be comparable to those measured during the fed state. Also, barbiturate anesthesia does not interfere with the main NMR-visible brain metabolites measured during long-TE proton spectroscopy. These results may be important in spectro-
scopic studies of patients with mitochondrial disease, in which detection of brain lactate is crucial.

References