Differential neurochemical responses in the rat striatum with isoflurane or ketamine/xylazine anesthesia: In vivo proton MRS study at 16.4 T

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Introduction

Since the small animal imaging generally requires anesthesia, anesthetic agents can induce unintended effects on animal physiology that may confound the results of imaging studies [1]. The use of isoflurane and ketamine/xylazine anesthesia is popular in imaging studies of laboratory animals. The striatum is the major input station of the basal ganglia system. It is involved in Parkinson's disease, Huntington's disease, choreas, choreoathetosis and dyskinesias [2]. Recently, ^{1}H-MRS studies of common and severe neuropsychiatric disorders (e.g., obsessive-compulsive disorder, schizophrenia, etc.) have reported abnormal metabolite levels in the striatum (cudate and putamen nuclei) [3]. The purpose of this study was to evaluate alterations in striatum metabolites of rats between anesthetized with isoflurane and with ketamine/xylazine in proton magnetic resonance spectroscopy (^{1}H-MRS), and to investigate the appropriateness of anesthetic agents for ^{1}H-MRS study.

Materials and Methods

Ten Sprague-Dawley rats divided by two groups, isoflurane (n = 5) and ketamine (100 mg/kg)/xylazine (10 mg/kg) (n = 5) were used to investigate different anesthetic effect. Ketamine/xylazine was administrated intramuscularly without seducing with isoflurane to investigate pure anesthetic effect. All experiments were performed on a horizontal 16.4 T/26 cm magnet (Bruker BioSpin GmbH, Ettlingen, Germany) using a 14 mm diameter quadrature surface coil as a transceiver. Combined module, consisted of seven water suppression pulses interleaved with three modules of outer volume saturation (OVS) was conducted before the localization scheme. The ultra-short STEAM sequence, TR 5000 ms, TE 1.7 ms, TM 20 ms, 256 averages and 2048 data points, was applied to place a rectangle volume-of-interest (VOI) in striatum (7.7 x 3.0 x 3.0mm^3). During measurements, body temperature was maintained at 37 ± 0.5 ^{0}C by an electric heating pad with monitoring through a rectal temperature sensor. *In vivo* ^{1}H spectra were quantified using LCModel with basis set composed numerically calculated metabolite spectra and simulated MM components.

Results and Discussion

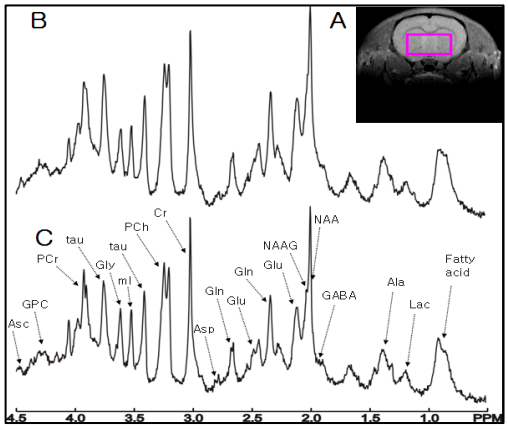

Fig1. Voxel localized striatum for 1H MRS (A), the spectra of ketamine / xylazine induced (B) and isoflurane administered rats (C).

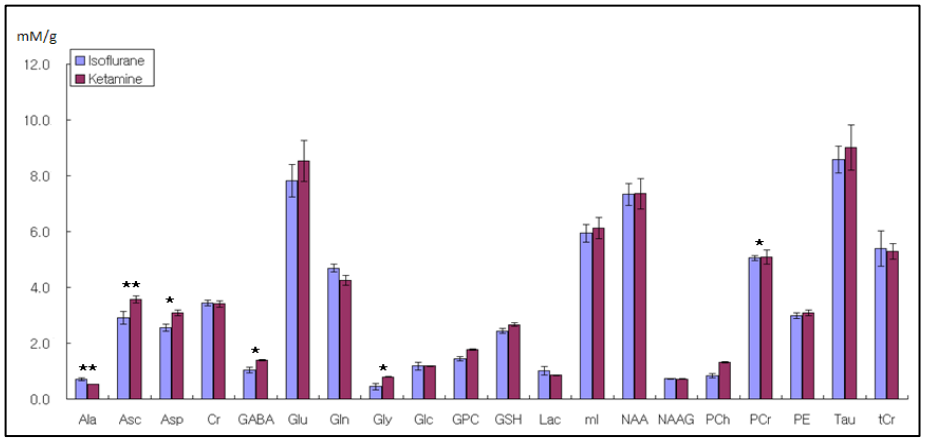

Fig.2 Metabolic concentrations of rat brain at the striatum. Ala, Asc, Asp, GABA, Gly and PCr are significantly different in both isoflurane/ xylazine and ketamine induced at the striatum. (; *P* < 0.005, *; *P* < 0.05)**

Fig1. illustrates a voxel localized striatum of rat brain for in vivo 1H MRS and the spectra of isoflurane/ xylazine and ketamine induced rats. Fig2. shows the brain metabolite concentrations of anesthesia isoflurane (C_i) and ketamine/xylazine ($C_{k/x}$), respectively. All of metabolite concentrations were calculated by absolute quantification method. The concentrations of Ala, Asc, Asp, GABA, Gly and PCr were significantly different between isoflurane and ketamine/xylazine induced groups at the striatum. The concentrations of Ala (C_i = 0.534 vs. $C_{k/x}$ = 0.074, $P < 0.005$), Asc (C_i = 3.572 vs. $C_{k/x}$ = 2.912 $P < 0.005$), Asp (C_i = 3.085 vs. $C_{k/x}$ = 2.563, $P < 0.05$), GABA (C_i = 1.390 vs. $C_{k/x}$ = 1.043, $P < 0.05$), Gly (C_i = 0.794 vs. $C_{k/x}$ = 0.451, $P < 0.05$) and PCr (C_i = 1.328 vs. $C_{k/x}$ = 0.837, $P < 0.05$) were evaluated by statistical analysis.

Studies in neuroscience and anesthesiology have focused on the modulation of synaptic communication that involves neurotransmitters induced by anesthetic drugs [4]. These anesthetics modify the release and concentration of neurotransmitters at specific regions in the brain [5]. We have demonstrated that metabolites in a specific brain region can be differentially influenced according to anesthetic agents. This study showed that the choice of anesthetic is significant in the setting of ^{1}H-MRS. Appropriate anesthetic choice should be pursued in order to exclude the effect of anesthetic agents on the target area.

References

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