Acute restraint stress-induced change in glutamate neurotransmission in rat brain: An in vivo 1H-MRS study

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INTRODUCTION

It is well known that a variety of stressors induces a significant alteration in various putative neurotransmitters in the mammalian CNS [1]. However, relatively little attention has been paid on the alteration of central glutamate neurotransmission, which is a major excitatory neurotransmitter in mammalian brain, following the application of various stresses. The present study investigated to determine whether acute restraint stress causes the changes in neurotransmitter level, especially glutamate, in rat brain and whether the acute stress-induced changes in brain metabolism can be recovered during the rest.

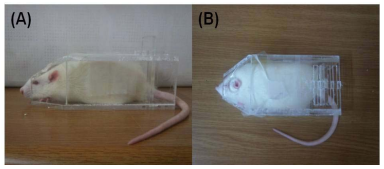

Fig.1. The animal exposed to acute restraint stress for 1 hour is shown. (A) front view (B) top view

MATERIALS AND METHODS

Animal Male Sprague Dawley rats (180-200 g, N=29) were divided into three group (Control, N=8; Stress, N=10; Stress+1h recovery, N=11). The stress group was exposed to restraint stress for 1 hour before the MRI/MRS measurement (Fig. 1). To assess the recovery effect, the stress+1h recovery group was given 1 hour restraint stress followed by 1hour rest. The control group was not given any stress.

In vivo ^{1}H-MRS acquisitions and quantification *In vivo* MR experiments were conducted using a 4.7 T BIOSPEC scanner (Bruker Medical GmbH, Ettlingen, Germany). The position of the VOI was carefully selected based on multislice RARE images (TR/TE= 5000/22 ms, mm, NEX = 2) (Fig. 2). *In vivo* ^{1}H-NMR spectra were acquired from prefrontal cortex (PFC) and hippocampus (Hip) using PRESS (TR/TE=4500/20 ms, NEX=384) and analyzed using LCModel [2] including 15 metabolites (Ala, Asp, Cr, GABA, Glc, Glu, Gln, GPC, PCho, mIns, Lac, NAA, NAAG, PCr, Scy, and Tau). Total Cr signal assuming 8 umol/kg was used for absolute concentrations. One-way ANOVA test with Bonferroni corrections (SPSS software) was used to compare the metabolic differences between three groups.

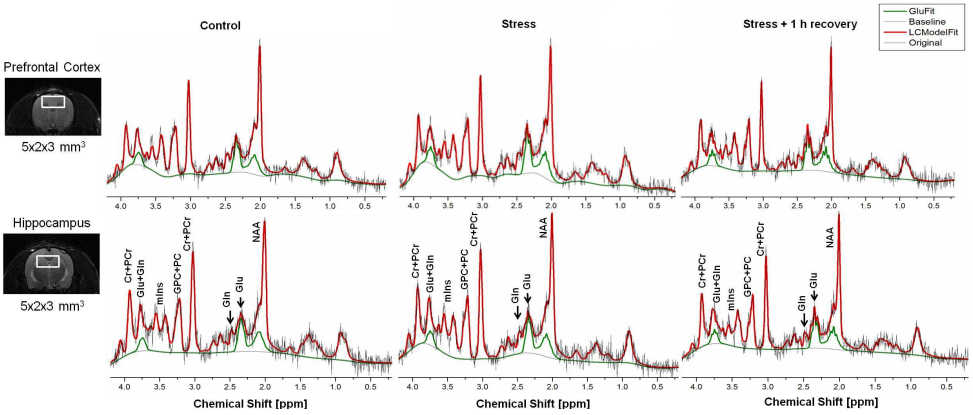

Fig.2. Typical multi-slice RARE images of rat brain and corresponding *in vivo* ^{1}H-NMR spectra for each group are shown. Proton spectra were acquired with conventional PRESS sequence (TR/TE = 4500/20 ms, NEX = 384) using 4.7 T animal MRI.

RESULTS

In vivo proton spectra acquired from both brain regions (prefrontal cortex, hippocampus) of each group are shown in Fig.2. The resulting high spectral resolution enabled us unambiguous signal assignment. Most of major metabolites in both brain regions were quantified within the CRLBs range of 20 %, except for GABA. The Glu concentrations obtained from PFC and Hip were significantly increased in rats exposed to acute restraint stress ($P < 0.05$). However, the increased Glu level in both brain regions could not be recovered during 1 hour rest (Control vs. Stress + 1 hour recovery, $P < 0.05$).

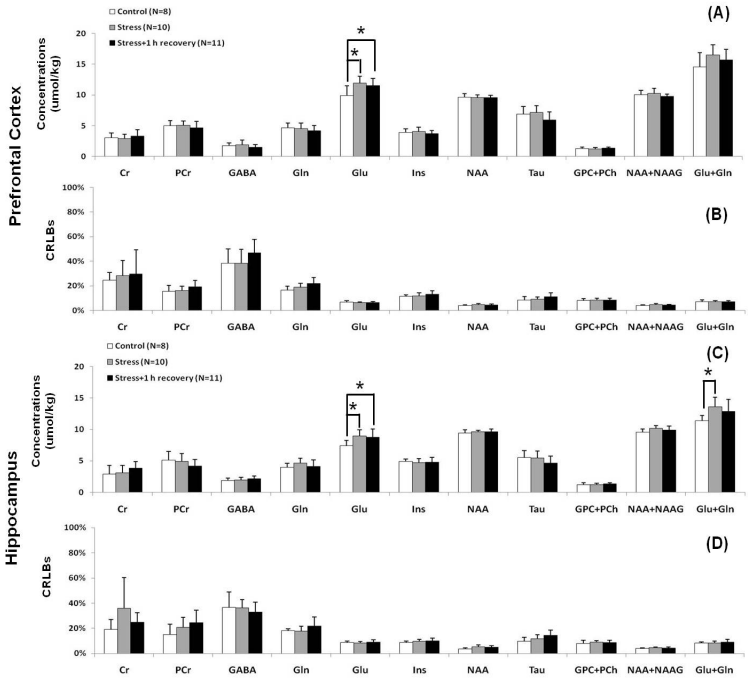

Fig.3. Absolute metabolite concentrations quantified in the prefrontal cortex (A) and in hippocampus (C) of each group. Averages of the Cramer-Rao lower bounds (CRLBs) for the corresponding metabolites are shown in (B) and (D). All data are expressed as the mean±SD. *Significance level: One-way ANOVA, $P < 0.05$

DISCUSSION AND CONCLUSION

The present study is the first *in vivo* ^{1}H-MRS study to measure the altered neurotransmitter level induced by acute restraint stress. Our results suggest that glutamate neurotransmission in both PFC and Hip be strongly implicated in regulating of stress response. Further study is needed to test pharmaceutical interventions that modulate glutamate, testing their potential use to treat the stress responses.

ACKNOWLEDGEMENT

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