# Effects of Electro-acupuncture on A Chronic Mild Stress Model of Depression in Rat Studied by Magnetic Resonance Imaging

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### Introduction

Depression is a major mental disease threatening human health. Commonly-used antidepressants, however, exhibit beneficial effects only after long-term treatment, and often are associated with side effects<sup>[1]</sup>. It has been suggested that acupuncture, a form of traditional Chinese medicine, can be used as an alternative treatment for depression<sup>[2]</sup>, and the results from a growing number of studies have supported this view<sup>[3]</sup>. We investigated in this study the therapeutic effects of electro-acupuncture (EA) on a well-established chronic mild stress (CMS) model of depression in rat using in vivo magnetic resonance imaging (MRI) and behavioral tests.

#### **Materials and Methods**

Thirty male SD rats (180-200g) were divided into three groups (n=10 each): control group (C), CMS model group (M) and EA-treated group (A). The rats in Groups M and A had unpredictable mild stresses each day for 21 days<sup>[4]</sup>. The rats in Group A, in addition, received 20-minute EA at the Bai-Hui point and the Yin-Tang point each day right before receiving the stressors. For sucrose intake measurement, the rats were deprived of water and food for 24 hrs (as part of the CMS procedure) and then given a 100ml bottle of 1% sucrose solution for 1hr. The volume of sucrose solution consumed was measured. Five rats selected randomly from each group underwent MRI measurements carried out on a Bruker Biospec 4.7 T/30 cm spectrometer. T<sub>2</sub>-weighted and diffusion-weighted (DWI) imaging were performed on the second day after CMS/EA with FOV  $3.5 \times 3.5 \text{cm}^2$ , matrix size  $128 \times 128$ , slice thickness 0.8mm and TR 3s. Three b values (i.e., 14, 343 and  $1169 \text{s/mm}^2$ ) were used to calculate the apparent diffusion coefficient (ADC) map. Statistical analysis was carried out using ANOVA and student's *t*-test, and a *p*<0.05 was considered to be statistically significant. **Results** 

All rats had significant body weight gain after 21 days. However, the gains in Groups M and A were significantly lower than that in Group C (Table 1). Sucrose intake was similar among the three groups before the treatments. Compared to Group C, Group A had significant higher post-treatment sucrose intake, while that in Group M was significantly lower (Table 1). The results of MRI measurements were summarized in Table 1 and Fig. 1. Compared to Group C rats, the rats in Groups M and A had significantly higher  $T_2$  in periaquductal gray matter (PAG), and significantly lower ADC in hippocampus and temporal cortex, but not in striate cortex.

#### Discussion

Stress-induced decrease in sucrose intake, and anhedonia, is an indicator for development of experimental depression<sup>[5]</sup>. The Group M rats in this study had lower sucrose consumption than control after CMS treatment, suggesting that our model of depression is valid. The CMS procedure used this study induced significant morphological and structural changes in PAG, temporal cortex and hippocampus of the stressed rats, which are similar with those found in clinical depression<sup>[6]</sup>. Having no observable effects on reversing the MRI-detectable brain changes induced by CMS, EA seemed, however, to be able to release the depression symptom of anhedonia to some extent, as indicated by the results of sucrose intake measurements.

## Acknowledgement: Supported by Natural Science Foundation of China 10234070, 30370419 and 30400136.

**References** [1] Stahl SM, Grady MM. J Clin Psychiatry 2003; 64(S13):13-7; [2] Luo H, Meng F, Jia Y, Zhao X. Psychiatry Clin Neurosci 1998; 52:S338-40; [3] Han JS. Int J Neurosci 1986; 29(1-2):79-92; [4] Willner P, Muscat R, Papp M. Neurosci Biobehav Rev 1992; 16(4):525-34; [5] Willner P. Psychopharmacology 1997; 134:319-329; [6] Rabins P V, Pearlson G D, Aylward E, et al. Am J Psychiatry 1991; 148(5):617-620.



**Figure 1.** Comparison of  $T_2$ -weighted images of a slice at the level of middle brain (top row) and ADC maps of a slice at the level of hippocampus (bottom row) among the three groups.

		Group C	Group M	Group A
Body Weight (g)	before CMS	$210\pm18$	$217\pm16$	$223\pm11$
	after CMS	$338 \pm 31$	$308 \pm 14*$	$295 \pm 22*$
Sucrose Intake	before CMS	$96\pm7$	94±9	$90\pm8$
(ml/kg)	after CMS	$72\pm 8$	$59\pm8*$	80±5* <sup>,</sup> **
<b>ADC</b> (10 <sup>-3</sup> <b>mm<sup>2</sup>/sec</b> )	Hippocampus	$0.77\pm0.05$	$0.68\pm0.05*$	$0.65 \pm 0.06*$
	Temporal cortex	$0.64\pm0.04$	$0.57\pm0.05*$	$0.57 \pm 0.05*$
	Striate cortex	$0.68\pm0.07$	$0.66 \pm 0.05$	$0.64\pm0.02$
<b>T</b> <sub>2</sub> ( <b>ms</b> )	Hippocampus	$73.3 \pm 3.2$	$74.0 \pm 2.9$	$72.7\pm2.4$
	Temporal cortex	$67.9\pm2.8$	$68.4 \pm 3.1$	$68.6 \pm 1.8$
	Striate cortex	$66.7 \pm 3.4$	$68.3 \pm 2.7$	$68.0 \pm 5.3$
	PAG	$70.5 \pm 2.15$	$74.5 \pm 3.2*$	$75.2 \pm 1.6*$

**Table 1**. Body weight, sucrose intake and calculated ADC and  $T_2$  values of the rats in the three groups. \**p*<0.05, comparing with Group C; \*\* *p* <0.05, comparing with Group M.