

## Effect of Acupuncture on Hypothalamic–Pituitary–Adrenal System in Maternal Separation Rats

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**Abstract** The maternal separation (MS) animal model has been widely used to study early life stress and several psychiatric conditions such as depression and anxiety. In this study, we investigated the effect of acupuncture on anxiety-related behaviors and hypothalamic–pituitary–adrenal (HPA) system in MS-induced early life stress of Sprague–Dawley rat pups (14–21 postnatal days). For determining anxiety-related behaviors, the elevated plus-maze test was performed. The effects of acupuncture on the activation of stress were measured by assessing plasma levels of corticosterone (CORT) and adrenocorticotropin hormone (ACTH). The hypothalamic immunoreactivity (IR) of arginine vasopressin (AVP) was also examined. Acupuncture was conducted at acupoint HT7, which is used to treat mental disorders in Oriental medicine, for seven consecutive days. Acupuncture significantly decreased the frequencies of open arm entries and the amount of time spent in the open arms in MS rats. In addition, acupuncture reduced CORT and ACTH levels in plasma of MS rats, and AVP-IR in the hypothalamic paraventricular nucleus of MS rats. In conclusion, acupuncture reduced anxiety-related behaviors and modulated the HPA system. These findings suggest that acupuncture at HT7 may be useful as a therapeutic treatment in MS-induced early life stress.

**Keywords** Acupuncture · Maternal separation · Early life stress · Anxiety-related behavior · Hypothalamic–pituitary–adrenal system

### Introduction

Individuals with a history of early adverse experiences such as child abuse, social isolation, and parental loss often reveal antisocial personality symptoms with serious psychiatric problems like depression and anxiety disorders (Agid et al. 1999; Barnow et al. 2001).

Maternal separation (MS) in rats during the early postnatal period has been established as an animal model of early adverse experiences (Park et al. 2005; Veenema et al. 2006, 2007). MS rats are characterized as increase of anxiety- and depression-related behaviors (Kalinichev et al. 2002; Wigger and Neumann 1999) and dysfunction of the hypothalamic–pituitary–adrenal (HPA) system such as elevated plasma levels of corticosterone (CORT) and adrenocorticotropin hormone (ACTH) (Levine et al. 1991; Plotsky and Meaney 1993). In addition, MS has been shown to alter the activity of neuropeptide systems including arginine vasopressin (AVP) (Veenema et al. 2006, 2007).

Acupuncture therapy has long been practiced in East-Asian countries for treating various medical conditions, and has recently been considered a new alternative method of medicine in some Western countries (Cherkin et al. 2003; Kaptchuk 2002). We previously reported the effects of acupuncture at acupoint HT7 (Shenmen), which has been used to treat mental disorders in Oriental medicine (Lin 1995), on early life stress using the MS animal models. In our previous study, acupuncture at HT7 reduced anxiety-related behaviors, enhanced neuropeptide Y

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