



## The role of arginine vasopressin in electroacupuncture treatment of primary sciatica in human



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### ABSTRACT

It has been implicated that electroacupuncture can relieve the symptoms of sciatica with the increase of pain threshold in human, and arginine vasopressin (AVP) in the brain rather than the spinal cord and blood circulation participates in antinociception. Our previous study has proven that AVP in the brain played a role in the process of electroacupuncture analgesia in rat. The goal of the present study was to investigate the role of AVP in electroacupuncture in treating primary sciatica in human. The results showed that (1) AVP concentration of cerebrospinal fluid (CSF) ( $7.5 \pm 2.5$  pg/ml), not plasma ( $13.2 \pm 4.2$  pg/ml) in primary sciatica patients was lower than that in health volunteers ( $16.1 \pm 3.8$  pg/ml and  $12.3 \pm 3.4$  pg/ml), although the osmotic pressure in CSF and plasma did not change; (2) electroacupuncture of the bilateral "Zusanli" points (St. 36) for 60 min relieved the pain sensation in primary sciatica patients; (3) electroacupuncture increased the AVP level of CSF, not plasma in primary sciatica patients; and (4) there was the positive correlation between the effect of electroacupuncture relieving the pain and the AVP level of CSF in the primary sciatica patients. The data suggested that central AVP, not peripheral AVP might improve the effect of electroacupuncture treatment of primary sciatica in human, i.e., central AVP might take part in the electroacupuncture relieving the pain sensation in primary sciatica patients.

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### 1. Introduction

Sciatica is a set of symptoms including pain caused by general compression or irritation of one of the five spinal nerve roots of each sciatic nerve or by compression or irritation of the left or right or both sciatic nerves. Symptoms include lower back pain, buttock pain, and numbness, and pain or weakness in various parts of the leg and foot. Primary sciatica, also called piriformis syndrome, is a neuromuscular disorder that occurs when the sciatic nerve is compressed or otherwise irritated by the piriformis muscle causing pain, tingling and numbness in the buttocks and along the path of the sciatic nerve descending down the lower thigh and into the leg.

Arginine vasopressin (AVP), a nonapeptide posterior hormone of the pituitary, is mainly synthesized and secreted in the hypothalamic

paraventricular nucleus (PVN) and supraoptic nucleus (SON). This hormone, combined with an apparent carrier protein (neurophysin), is transported along the hypothalamo-hypophyseal pathway to the neurohypophysis, where it is stored for subsequent release (Antunes and Zimmerman, 1978). The remarkable functions of AVP include body fluid homeostasis, hormone regulation, cardiovascular control, and learning and memory influence (McEwen, 2004; Bao et al., 2014).

AVP has been proven as an important factor governing analgesia in both human and nonhuman species (Berkowitz and Sherman, 1982; Berson et al., 1983; Kordower and Bodnar, 1984; Kordower et al., 1982). In 1968, Aziz et al. observed that AVP could prevent lumbar puncture-induced headache (Aziz et al., 1968). Kendler et al. reported that pain interacted with plasma AVP concentrations in surgical emergency of men (Kendler et al., 1978). Some studies discovered that intraventricular injection (*icv*) of AVP increased the pain threshold (Bernson and Berson, 1980) and anti-AVP serum (*icv*) decreased the pain threshold (Bodnar et al., 1984), but neither intrathecal (*ith*) nor intravenous injection (*iv*) of AVP or anti-AVP serum influenced the pain threshold (Yang et al., 2006e, 2007a). The data indicated that AVP in the brain rather than the spinal cord and blood circulation participated in antinociception.

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**Table 1**

Arginine vasopressin concentration in the plasma and cerebrospinal fluid of primary sciatica patients.

	Health participants	Primary sciatica patients
Number	75	77
Plasma (pg/ml)	12.3 ± 3.4	13.2 ± 4.2
Cerebrospinal fluid (pg/ml)	16.1 ± 3.8	7.5 ± 2.5***

The data were expressed as mean ± standard error of the mean (SEM).

\*\*\*  $p < 0.001$  was used for the comparison of the arginine vasopressin concentration between health participants and primary sciatica patients.

Many studies have reported that acupuncture can relieve the symptoms of sciatica with the increase of pain threshold in human (Chen et al., 2009; Inoue et al., 2005). Our previous study showed that intraventricular injection (icv) of AVP enhanced electroacupuncture analgesia, whereas anti-AVP serum decreased; neither intrathecal nor intravenous injection of AVP or anti-AVP serum influenced electroacupuncture analgesia; electroacupuncture of “Zusanli” points (St. 36) changed AVP concentration in many brain nuclei, but did not change that in the pituitary, spinal cord and plasma (Yang et al., 2009a). The data suggested that AVP in the brain played a role in the process of electroacupuncture analgesia. The goal of the present study was to investigate the role of AVP in electroacupuncture in treating primary sciatica.

## 2. Materials and methods

### 2.1. Materials

AVP was obtained from Peninsula Laboratories, San Carlos, CA, USA.  $^{125}$ Iodine was from Amersham Pharmacia, Buckinghamshire, UK. The other chemicals were from Sigma Co., St. Louis, MO, USA.

Rabbit anti-human arginine vasopressin (AVP) serum was made by the Department of Neurobiology, Second Military Medical University, Shanghai, China. The specificity of the antiserum was 100% cross-reactivity with arginine vasopressin and no cross-reactivity with oxytocin, vasotocin, lysine-vasopressin, vasoactive intestinal peptide, neurotensin, leucine-enkephalin, methionine-enkephalin,  $\beta$ -endorphin and dynorphin A<sub>1-13</sub>. The dilution of the antiserum was more than 1:40,000 for radioimmunoassay.

### 2.2. Participants

#### 2.2.1. Primary sciatica patients

Seventy-seven non-smoking habit, Chinese Han adult subjects including 40 males and 37 females (without pregnancy), 31–69 years, average  $49.7 \pm 8.4$  years, in Huaihai Hospital of Henan University, Jiangsu Su Bei People's Hospital, Henan Provincial Mental Hospital, 153 Hospital of People's Liberation Army, 101 Hospital of People's Liberation Army and 117 Hospital of People's Liberation Army, were asked to participate in the study between March 2010 and October 2013. They were diagnosed as primary sciatica by the history of the symptoms and physical examinations including the tenderness point, straight leg raising test (or Lasegue sign) and lower limb rotation test. The laboratory tests and imaging techniques including computed tomography (CT), magnetic resonance imaging (MRI), ultrasound and electromyogram (EMG) were used in excluding other conditions such as spinal disk herniation, spinal stenosis, pelvic injury (or fracture), tumors, facet arthropathy, lumbar muscle strain, severe back pain or a car accident extending to the hips and feet.

#### 2.2.2. Health volunteers

Seventy-five Chinese Han adult health volunteers including 37 males and 38 females (without pregnancy), 28–67 years, average  $46.1 \pm 10.3$  years, were asked to participate in the study between

March 2010 and October 2013. They were not suffering from any diseases related with pain.

### 2.2.3. Inclusion criteria

Inclusion criteria were as follows: (a) agreement to sign the informed consent form; (b) eligibility was checked in a uniform diagnostic procedure (exclusion criteria: pregnancy, psychiatric, endocrine, cardiovascular, or other chronic diseases, smoking, intake of psychoactive drugs); (c) participants were asked not to drink any alcohol or caffeine containing beverages during the experiment; (d) participants were asked not to eat anything over 12 h before collecting the blood and cerebrospinal fluid during the experimental day; (e) all experimental sessions were carried out between 09:00 am and 10:30 am; and (f) over 18 years old.

All experiments were approved by the hospital Ethics Committees and carried out according to the Declaration of Helsinki.

### 2.3. Procedure

#### 2.3.1. Primary sciatica patients

All experiments were carried out between 09:00 am and 10:30 am. The subjects undergone physical examinations including the tenderness point, straight leg raising test (or Lasegue sign) and lower limb rotation test, and asked not to drink any alcohol or caffeine containing beverages during the experiment, especially the subjects were inhibited to eat anything before the blood and cerebrospinal fluid (CSF) collection during the experimental day.

**2.3.1.1. Electroacupuncture treatment.** The stainless needles were placed at bilateral “Zusanli” points (St. 36). The stimulated electrical current was a dense-disperse wave (JSD-731-C electro-stimulator,  $f_1 = 10$  Hz, 1 min;  $f_2 = 20$  Hz, 1 min) for 60 min. The intensity was adjusted until the patient feels comfortable (10–15 mA).

**2.3.1.2. Sham treatment.** Except the stainless needles were not placed at bilateral “Zusanli” points (St. 36) and were not given electroacupuncture, the patients were treated as the electroacupuncture treatment.

#### 2.3.2. Health volunteers

All experiments were carried out between 09:00 am and 10:30 am. After signing the informed consent form, the participants' CSF and blood were collected.

### 2.4. Sample collection

All sample collections were carried out between 09:00 am and 10:30 am. The patients and health volunteers had 12 h or more of no eating before blood and CSF collection. Although the experiment has not put a limit to drinking, the patients and health volunteers were not allowed to drink more before blood and CSF collection.

#### 2.4.1. Blood sample

The blood (6 ml) was collected using the EDTA·Na<sub>2</sub>-treated vacutainer, and immediately placed on ice.

**Table 2**

Osmotic pressure in the plasma and cerebrospinal fluid of primary sciatica patients.

	Health participants	Primary sciatica patients
Number	75	77
Plasma (mmol/L)	315.6 ± 9.8	307.4 ± 8.4
Cerebrospinal fluid (mmol/L)	297.8 ± 7.2	301.2 ± 9.0

The data were expressed as mean ± standard error of the mean (SEM).

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