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EXPERIMENTAL STUDY

Bloodletting at Jing-well points decreases interstitial fluid flow in the thalamus of rats

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Abstract

OBJECTIVE: To investigate the changes in the neuronal microenvironment of the middle cerebral artery (MCA) territory induced by Jing-well points bloodletting acupuncture (WPBA) and to explore the neuroprotective mechanism of WPBA in stroke.

METHODS: Adult male Sprague Dawley (n = 32) rats were randomly divided into four groups of eight animals each: WPBA-thalamus group (WT), WPBA-caudate nucleus group (WC), sham-control thalamus group (ST) and sham-control caudate nucleus group (SC). Animals in the WT and WC groups received 2 μL of the extracellular tracer gadolinium-diethylene triamine pentaacetic acid (Gd-DTPA) injected into the thalamus or caudate nucleus, respectively, and 12 Jing-well points in the distal ends of the rats' digits were used for WPBA. Although 2 μL of Gd-DTPA was injected into the thalamus or caudate nucleus, respectively, for animals in the two sham groups (ST and SC), no acupuncture or bloodletting was performed. Brain extracellular space and interstitial fluid flow parameters were measured using Gd-DTPA-enhanced magnetic resonance imaging.

RESULTS: The brain interstitial fluid flow speed was decreased in the thalamus after WPBA, with a significantly lower Gd-DTPA clearance rate and longer half-life of Gd-DTPA in the thalamus of treated rats than those in sham-control rats [WPBA-treated rats'

clearance rate, (7.47 ± 3.15) × 10^{-5}/s (P = 0.009); half-life, (1.52 ± 0.13) h, P = 0.000]. By contrast, no significant changes in brain extracellular space and interstitial fluid flow parameters were detected in the caudate nucleus after WPBA (P = 0.649). In addition, no differences in the morphology of the brain extracellular space or the final distribution of the traced brain interstitial fluid were demonstrated between the WT and WC groups (P = 0.631, P = 0.970, respectively).

CONCLUSION: The WPBA decreased the speed of the local thalamic ISF flow in rats, which is assumed to be a beneficial protection by down-modulated the metabolic rate of the attacked neurons under stroke.

Key words: Bloodletting; Extracellular space; Gadolinium ethoxybenzyl DTPA; Interstitial fluid; Magnetic resonance imaging

INTRODUCTION

Jing-well points bloodletting acupuncture (WPBA) is an ancient therapy in traditional Chinese medicine that has been used to treat stroke. The positive therapeutic effects observed following WPBA include a reduction in swelling and the removal of the obstruction in the meridian-collateral channels.[1,2] Recent evidence also indicates that WPBA effectively promotes blood circulation and modulates ion channel activity on neuronal membranes.[3-7] According to Traditional Chinese Medicine theory, meridians and collaterals compose a network of passages through which energy or *Qi* circulates and on which most acupuncture points are distributed.[8] Therefore, the network is equivalent neither to the vascular system nor to the nervous system. The extracellular space (ECS), surrounding neurons and capillaries in the brain tissue, has long been neglected in anatomical studies. However, by using a newly developed method based on magnetic resonance imaging (MRI), the interstitial fluid (ISF) flow can be dynamically visualized with the tracer gadolinium-diethylene triamine pentaacetic acid (Gd-DTPA) injected into the space.[9-12] In the present study, changes in the neuronal microenvironment were quantitatively measured after WPBA. Two sites commonly damaged during stroke were selected as the regions of interest, the thalamus and the caudate nucleus, which were supplied by the middle cerebral artery.[13] The neuroprotective mechanism of WPBA against cerebral stroke injury is discussed based on the findings.

METHODS

Animals

Thirty-two healthy, age-matched, adult male Sprague Dawley rats (250-300 g) of SPF grade were supplied by the laboratory animal center of Peking University Health Science Center (Certificate of quality No. SCXK [jing] 2011-0012). The experimental protocols were approved by the Ethics Committee of Peking University Health Center (No. LA2012-016).

Animal treatment and grouping

Thirty-two rats (n = 8 per group) were randomly divided into the following four groups by using a random number table: WPBA-thalamus group (WT), WPBA-caudate nucleus group (WC), sham-control thalamus group (ST), and sham-control caudate nucleus group (SC). Animals in the WT and WC groups received 2 μL of Gd-DTPA injected into the thalamus or caudate nucleus, respectively, and 12 Jing-well points in the distal ends of their digits were used for WPBA. Although 2 μL of Gd-DTPA was injected into the thalamus or caudate nucleus, respectively, for animals in the two sham groups (ST and SC), no acupuncture or bloodletting was performed.

Drugs and reagents

The Gd-DTPA solution was prepared using 10 mmol/L of Gd-DTPA (Magnevist; Bayer Schering Pharma AG, Berlin, Germany) diluted with 0.9% NaCl solution (Double-Crane Pharmaceutical Company Limited, China Resources, Beijing, China).

Intraparenchymal microinjection of Gd-DTPA into the brain

The skin overlying the calvaria of anesthetized rats was shaved and disinfected using iodinated alcohol. An incision was made on the scalp along the sagittal suture, from the midpoint of interaural line to the middle of the interocular line, and the skull was exposed by scraping away the skin and underlying tissues. The rats were placed in a stereotaxic instrument (Lab Standard Stereotaxic-Single, Stoelting Co., Wood Dale, Illinois, USA), and 2 μL of Gd-DTPA was administered by intracranial microinjection into the thalamus or caudate nucleus over 10 min. The stereotaxic coordinates for the thalamus were bregma − 2 mm, lateral − 2 mm, vertical − 5.5 mm, and those for the caudate nucleus were bregma+1 mm, lateral − 3 mm, and vertical − 4.5 mm. Rats were kept on a heating pad set at 38 ± 0.5 ℃ to maintain body temperature and the core temperature was monitored with a rectal thermometer.

Jing-well points bloodletting acupuncture

The 12 Jing-well points used for bloodletting were located in the distal ends of the digits and at the acupoints of Shaoshang (LU 11), Shangyang (LI 1), Zhongchong (PC 9), Guanchong (TE 1), Shaochong