



Metabonomic study of the effects of different acupuncture directions on therapeutic efficacy



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ABSTRACT

Posterior circulation ischemia (PCI) is a common clinical ischemic cerebrovascular disease that can endanger the lives of patients in severe cases. Our previous research found that needling the Fengchi (GB20) acupoint presents a significant effect on PCI and that different acupuncture directions can exert different effects. To investigate the biological mechanism of acupuncture directions, rapid resolution liquid chromatography coupled with quadrupole time-of-flight mass spectrometry-based metabonomic techniques are used to analyze the metabolic profiles of urine samples. The urine samples were obtained from 30 healthy control subjects, 60 PCI patients before and after treatment of different acupuncture directions. Six metabolites, including LPE (22:6), estrone, uric acid, vanillylmandelic acid, *N*-acetyl-L-tyrosine, and 4-hydroxyphenylacetylglutamine were identified as potential biomarkers of acupuncture treatment of PCI. Acupuncture treatment of PCI patients significantly changed the levels of these potential biomarkers. Moreover, different acupuncture directions showed different effects on the contents of these biomarkers. These results strongly support the belief that acupuncture direction performs an important function in acupuncture intervention. The findings provide new insights into the mechanism of acupuncture treatment and reveal that acupuncture manipulation results in various curative.

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1. Introduction

Posterior circulation ischemia (PCI) is a common cerebrovascular disorder. The posterior circulation of the brain includes the vertebral arteries, basilar artery, posterior cerebral arteries, and their branches [1,2]. Vertebrobasilar arteriosclerosis, blood hypercoagulation, or small infarcts caused by detachment of microthrombi result in blood circulation disorders and consequent symptoms, such as vertigo, nausea, and nystagmus [3]. Recurrent attacks often lead to infarction of the brain stem, cerebellum, and occipital lobe, functional disorders of the nervous system, and, eventually, life-threatening apoplexy. Three types of treatment are offered to patients with PCI, including medical, endovascular, and

surgical [4]. While modern medical treatments for PCI are palliative to some extent, the etiology of the problem is often difficult to solve. Most treatments can ease or even eliminate vertigo but are rarely effective when addressing concomitant symptoms and provide limited effects on alleviating hemorrhological indices and hypoperfusion after brain ischemia. Adverse reactions have also been reported for some treatments. As the risk and relapse rate involved in surgical treatments are fairly high, the disease is widely acknowledged to be difficult to treat by conventional clinical therapeutics.

Acupuncture is an ancient traditional Chinese medicine (TCM) technique that dates back at least 2500 years. Today, it is widely practiced in many parts of the world [5–8] for treating a variety of diseases, such as post-stroke impairment [9], migraine [10], chronic shoulder pain [11], osteoarthritis of the knee [12,13], nausea and vomiting [14], arterial hypertension [15], and so on. Previous research conducted in our hospital showed that needling the Fengchi (GB20) acupoint could improve symptoms of vertigo

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resulting from posterior circulation ischemia (PCIV) in a number of patients [16]. While most research on acupuncture efficacy, including our own, have shown positive results, others have not. The contradiction between these results may be due to several factors, such as the quality of randomization and blinding [17], sample size [17], placebo effect [18], acupoint selection [18], and acupuncture manipulation [19]. Among these factors, manipulation may be the most significant in influencing acupuncture efficacy.

The effects of acupuncture manipulation are often overlooked compared with other factors in both animal and clinical studies. According to the definition of acupuncture [20], adequate stimulation must be ensured to achieve appropriate physical stimulus. Acupuncture manipulation, which regulates the quality of stimulation, involves frequency, duration, depth, direction, and several other aspects. Direction, which reflects the location of the needle tip, is one of the most commonly used factors in regulating acupuncture manipulation. Our previous article demonstrated that the different acupuncture manipulations, including frequency and direction, exert a variety of therapeutic effects on patients with PCIV [21]. However, information on the direction of needle insertion, as well as explorations of its efficacy or related mechanisms, is relatively limited and requires further research. Knowledge of the mechanism of needle insertion direction may help provide new evidence for future acupuncture studies. Thus, new methods in the biomedical field must be applied to reveal the relevant underlying mechanisms.

Metabonomics is a technique commonly used to study metabolic pathways in biological systems by observing changes in the metabolites of the biological system with time or after stimulation or interference [22]. Metabolic models are established mainly through acquisition of metabolite information as a function of time or space, internal relations are discovered through chemometrics and bioinformatics, and changes in metabolic mechanisms caused

by biological disturbances may be evaluated. By detecting the blood or urine metabolism of patients with a certain disease under the influence of certain drugs or other interventions through metabolomics, specific metabolic components related to the disease may be determined, metabolic pathways and metabolic conditions of the disease process may be revealed, and biomarkers of the disease may be found to aid clinical diagnosis and treatment. As a systematic biological approach, metabolomics has long been used in studies on brain ischemia, infarction, stroke, and other diseases related to PCI and important results have been achieved [23,24]. Metabolomics has yielded new insights into the mechanism of acupuncture and can help researchers investigate the biological effects, understand the pathophysiological processes, and identify the potential biomarkers of acupuncture. Several researchers have used metabolomics to investigate the effects of acupuncture on acute gouty arthritis [25] and functional dyspepsia [26] and determine the relevant mechanisms. Although basic research on acupuncture has achieved considerable progress over the last 10 years, the mechanism of acupuncture has yet to be understood completely [27]. To the best of our knowledge, no study has yet used metabolomics to explore the mechanisms of different acupuncture manipulations, particularly in terms of needle insertion direction. Thus, development of methods and techniques that can provide comprehensive knowledge conforming to the essence of TCM is necessary to explain the mechanisms of acupuncture and promote its development.

In the present study, we applied rapid resolution liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (RRLC-Q-TOF-MS) technology to study the metabolic mechanism of acupuncture direction. The roadmap of this study is shown in Fig. 1. The objectives of this article are to (1) compare the urine metabolic profiles of PCI patients treated by different acupuncture directions with those of healthy control subjects, (2)

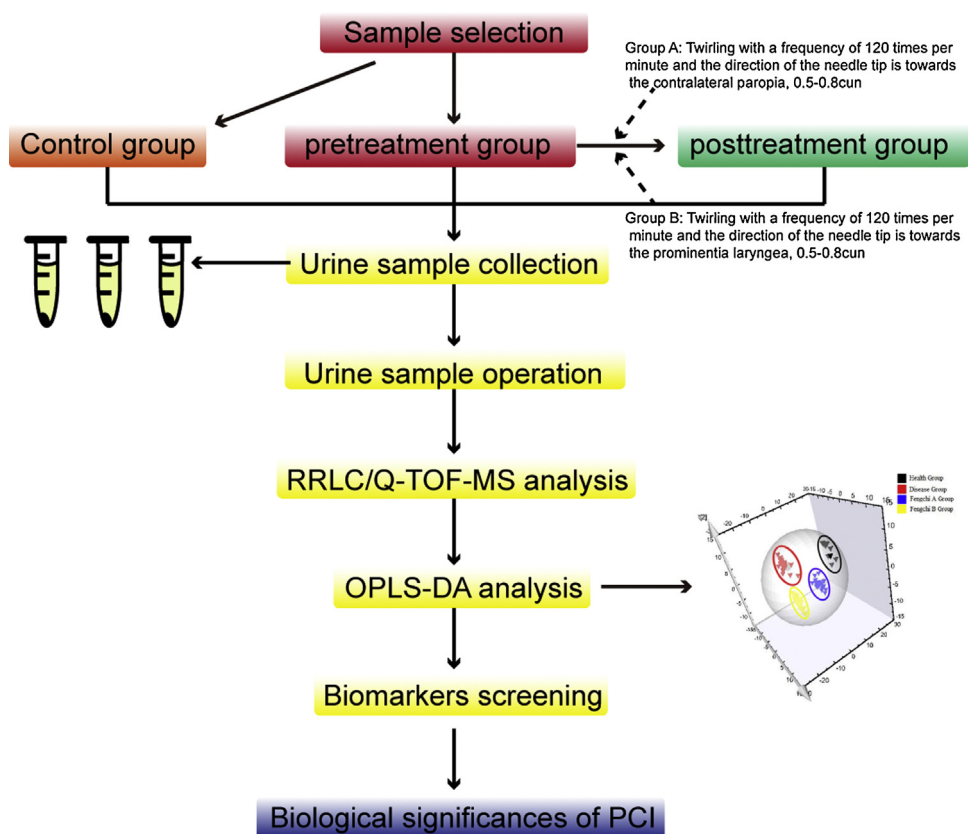


Fig. 1. The roadmap of this study.

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