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RESEARCH ARTICLE

Acupuncture Reduces Memory Impairment and Oxidative Stress and Enhances Cholinergic Function in an Animal Model of Alcoholism

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Abstract
Currently, the therapeutic strategy against memory deficit induced by alcoholism is not satisfactory and is expensive. Therefore, an effective, low-cost strategy is required. On the basis of the memory-enhancing effect of stimulation of the HT7 acupoint, we aimed to determine whether acupuncture at the HT7 acupoint can reduce alcoholism-induced memory impairment. The possible underlying mechanism was also explored. Alcoholism was induced in male Wistar rats weighing 180—220 g. The alcoholic rats received either acupuncture at HT7 or sham acupuncture for 1 minute bilaterally once daily for 14 days. Their spatial memory was assessed after 1 day, 7 days, and 14 days of treatment. At the end of the study, the malondialdehyde level and the activities of catalase, superoxide dismutase, glutathione peroxidase, and acetylcholinesterase enzymes in the hippocampus were determined using colorimetric assays. The results showed that acupuncture at HT7 significantly decreased the acetylcholinesterase activity and the malondialdehyde

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level, but increased the activities of catalase, superoxide dismutase, and glutathione peroxidase in the hippocampus. These results suggest that acupuncture at HT7 can effectively reduce the alcoholism-induced memory deficit. However, further studies concerning the detailed relationships between the location of the HT7 acupoint and the changes in the observed parameters are required.

1. Introduction

At present, drinking alcohol beverages is regarded as a common feature of social gatherings. However, alcohol consumption is the world's third largest risk factor for mortality and disability-adjusted life years [1,2]. Alcohol use has been estimated to account for approximately 3.8% of deaths globally and 4.6% of disabilities. In addition, the estimated cost for this burden is equal to >1% of the gross national product in high-income and middle-income countries [3]. Therefore, alcohol-related problems are important issues of concern.

Excessive and long-term use of alcohol has long been recognized as a cause of memory loss. Alcohol-mediated memory impairments are characterized by a "continuum of effects" ranging from the short-term memory impairments seen in social drinkers to blackouts in some alcoholics [4–6]. Accumulative lines of evidence have demonstrated that memory impairments of chronic alcoholics are often associated with alcohol-induced brain damage, particularly damage to the hippocampus [7–9], and with the impairment of cholinergic function [10,11].

Alcohol-induced brain damage is reported to be associated with the elevation of oxidative stress. Repetitive consumption of alcohol increases oxidative stress both via the increased oxidative stress formation and via the decreased activities of scavenger enzymes [12], leading to the effects of oxidative stress on various cell organelles and resulting in neurodegeneration.

Acupuncture has been used for a long time to treat at a low cost disorders associated with the use of alcohol and drugs. It can successfully induce detoxification and improve the withdrawal symptoms [13]. Recent findings showed that acupuncture at some acupoints could decrease oxidative stress, leading to neuroprotection [14,15], and that acupuncture could modify neurotransmission [16,17]. In addition, data obtained from functional magnetic resonance imaging study demonstrate that the stimulation of HT7 could activate brain regions involved in learning and memory [18], improving the cholinergic function and spatial memory [19]. Based on the roles of oxidative stress and the hypocholinergic function in neurodegeneration and memory impairment induced by alcohol consumption and on the beneficial effect of HT7 stimulation on oxidative stress, cholinergic function, and memory improvement mentioned earlier, we hypothesized that stimulation at the HT7 acupoint might reduce oxidative stress, improve cholinergic function, and reduce memory impairment in patients suffering from disorders induced by the use of alcohol. Owing to the limitation of available scientific evidence, this study was carried out to determine the effect of acupuncture at HT7 on spatial memory in an animal model of alcoholism. In addition, changes in the oxidative stress and the cholinergic function in the hippocampus were explored to investigate the possible underlying mechanism.

2. Materials and methods

2.1. Animals

Adult male Wistar rats, 8 weeks old, were used as experiment animals. They were obtained from the National Laboratory Animal Center, Salaya, Nakornpatom, Thailand. The weight of the animals on the 1st day of the experiment ranged from 180 g to 220 g. They were randomly housed at six per cage and maintained in a 12-h:12-h light:dark cycle and given access to food and water *ad libitum*. The experiments were performed to minimize animal suffering, and the experiment protocols were approved by the Institutional Animal Care and Unit Committee, Khon Kaen University, Thailand. All treatments in this study were performed once daily between 9:00 AM and 6:00 PM.

2.2. Chemicals

Absolute ethanol was purchased from VWR International, LLC (USA). Thiopental sodium sterile was purchased from Jagsonpal Pharmaceuticals Ltd. (Haryana, India). Acetylthiocholine iodide, 2-thiobarbituric acid (4,6-dihydroxypyrimidine-2-thiol; TBA), cytochrome *c*, catalase (CAT), and other chemicals were purchased from Sigma-Aldrich Pte Ltd. (Singapore).

2.3. Experimental protocol

Alcoholism was induced in the animals using a semi-voluntary intermittent intake method [20]. In brief, rats were exposed to alcohol in their drinking water. The alcohol concentration in the drinking water was gradually increased in a stepwise fashion from 5% to 10%, 15%, and 20% in the first 4 weeks (5%/wk) in order to allow the rats to get used to the taste of alcohol. The alcohol concentration was further increased to 30% in the 5th week; then, it was kept unchanged until the completion of 15 weeks. Rats that showed increased responses to environmental stimuli, such as easily being startled, irritability, hypervigilance, and ataxia, were regarded as alcoholic rats. Then, the alcoholic rats were randomly assigned to four groups of six animals each as follows: