Influence of Acupuncture on HPA Axis in a Rat Model of Chronic Stress-induced Depression

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DOI: 10.1007/s11726-007-0206-2

Abstract

Objective: To investigate the neurobiological mechanism of depression pathogenesis and reveal the mechanism of acupuncture treatment of depression. Methods: Wistar rats were selected for subjects. A rat model of depression was made by individually housing with unpredicted chronic moderate stimuli. Changes in behavior and hypothalamus-pituitary-adrenocortical axis were examined in rat models of stress-induced depression. Meanwhile, the intervening effect of acupuncture was evaluated and the curative effects of different acupuncture methods compared. Results: CORT and ACTH contents of serum were significantly higher in the model and normal saline groups than in the control group (P<0.05); hand acupuncture and electroacupuncture groups showed significantly lower CORT and ACTH contents than the model group (P<0.05); drug group showed significantly lower ACTH and CORT contents than the normal saline group (P<0.05). There were no significant differences between the hand acupuncture, electroacupuncture and medication groups. Conclusion: Acupuncture of Baihui (GV 20) and Taichong (LR 3) has a marked antidepressant effect. Its mechanism may be related to the regulation of HPA axis by acupuncture.

Key Words: Depression; Acupuncture Therapy; Hypothalamus-Pituitary-Adrenocortical Axis

CLC Number: R203

Document Code: A

Man or other creatures may have emotional reactions such as nervousness, anxiety and depression, when they are faced with abnormal stimuli or stress. However, chronic stress over a long time may cause hyperactivity of HPA axis through a series of neuro-biological mechanism, leading to organic impairment of the brain tissue, especially the hippocampus structure. These impairments may affect the hippocampus-dependant cognitive and emotional functions and trigger depression along with other factors such as gene. The RIA is adopted in this research to analyze the content changes of CORT and ACTH in individually housed rats, which were modeled under chronic stress depression. This study aims to investigate the pathogenesis of depression and action mechanism of acupuncture therapy, compare the therapeutic effects of different therapies and thus provide an effective way and scientific experiment basis for clinical treatment of depression.
Materials and Methods

1. Animals
Health male Wistar rats, weighed from 200 to 230 gram, clear class, provided by the animal center of Heilongjiang university of Traditional Chinese Medicine.

2. Reagent and apparatus
Major reagents: RIA kits of CORT and ACTH are provided by Beijing Beifang bio-tech institute.

Major apparatus: self-made exploration box(cube shape, 40cm high, 80 wide and long, black walls and floor, with the floor marked off into 25 equal squares by white lines), KWD808II multi-functional electro-therapeutic apparatus(Wujin Great Wall medical apparatus CO., Ltd. Jiangsu province); Low Temperature Freezer(Sanyo CO., Ltd Japan); LD-42 type Centrifuge(Beijing medical Centrifuge factory), FJ2003PS type Gamma radioimmunoassay counter (Xi'an nuclear apparatus factory)

3. Animal model preparation
The open field test was conducted first as behavior score. Animals with less than30 or more than 120 in the total scores of horizontal and vertical movement were excluded. 42 rats were selected, placed in quiet lab, providing light from 7 o'clock to 19 o'clock and darkness from 19 o'clock to 7 o'clock for one week to adapt surrounding before the experiment. Normal group was placed as 7 rats per cage with no stimulation. The model animal were randomly allocated into 5 groups: depression model group, saline group, hand acupuncture group, electroacupuncture group, and Amitriptyline group. Seven rats in each group were individually housed.

Chronic long-term moderate unpredictable stimuli was adopted according to Zurita[1,2] to get depression model of individually housing rats. In 21 days, various stimulus was used on rats, including ice water swimming(4℃, 5 min), heat stress(45℃, 5 min), 24-hours water deprived, tail clamp 1 min, foot electric shock(50 mV, one stimuli per min, stimuli lasting 10 seconds, totally 30 times), shaking (1/s, 15 min), 48-hours fasting, perversion of day and night, et al. One type of stimulus was picked randomly per day, and each stimuli was proceeded 2 or 3 times for unpredictably happening to rats. After 21 days, open-field scoring was used as behavior evaluation to prove if model duplication was successful.

4. Point selection and needling method
Baihui (GV 20) and right Taichong (LR 3) are selected, according to "acupoint map on experimental animal"(ShiYan DongWu ZhenJuXueWei TuPu), published by experimental acupuncture academic association of China association of acupuncture and moxibustion.

Location: Baihui(GV 20), in the middle of parietal bone, Taichong(LR 3), on the depression distal to junction of the first and second metatarsal bones.

Acupuncture method: Filiform needles of 0.25 mm in diameter and 15 mm in length were punctured 3 mm subcutaneously forward at Baihui (GV 20) and 1 mm perpendicularly at Taichong (LR 3). In hand acupuncture group the needles were twisted once per 5 min in treatment group, 0.5 min each time, even reinforcing-reducing manipulation, retaining 30 min. Electroacupuncture group after insertion, the needles were twisted 0.5 min, and then connected with KWD808II multi-functional electro-therapeutic apparatus (9V, disperse-dense waves, intensity without causing local cramp or screaming, retain 30 min. All above methods were lasted 21 days.

5. Intervention
Control group: In the same condition, normal feed, no intervention; model group: after modeling, tied up every day; normal saline group, after modeling, 1mL saline with intraperitoneal injection; Amitriptyline group, after modeling, Amitriptyline(Elavil),10 mg/kg, dissolved in 1ml saline, injected intraperitoneally, all of groups were intervened 21days. Hand acupuncture and electroacupuncture were intervened as what was described in above after modeling.

6. Open Field behavior score system
In a sound insulated room, animals behavior was recorded. Crossing one square was accounted one score as horizontal activity; rearing one time (both front paws lifted off floor) was accounted one score as vertical activity. Each animal was tested once a day, 3min for each testing time. The tests were proceeded three days to get information of behavior changes in rats, the day before modeling, the day after the modeling, and the day after treatment.

7. Evaluation
After 21 days and another 24 hours, the blood of all groups was obtained by decapitation quickly, standstill in water Bath Test Tube about 30 min, 4℃, 3000 × g Centrifuged 10 min, serum separating,