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EXPERIMENTAL STUDY

Role of transient receptor potential vanilloid subetype 1 in the increase of thermal pain threshold by moxibustion

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Abstract

OBTECTIVE: To explore the role of transient receptor potential vanilloid subetype 1 (TRPV1) in the increase of the thermal pain threshold by moxibustion.

METHODS: Forty Kunming mice (20 ± 2) g were randomized into control group,capsaicin group, capsazepine group, moxibustion group and moxibustion + capsazepine (MC) group with 8 mice in each, and 16 C57BL/6 wild-type mice (18 ± 2) g were randomized into wild-type (WT) control group and WT moxibustion group with 8 mice in each, and 14 TRPV1 knockout mice (18 ± 2) g were randomized into knockout (KO) control group and KO moxibustion group with 7 in each. Each mouse in the capsaicin group was subcutaneously injected with the amount of 0.1 mL/10 g into L5 and L6 spinal cords; each mouse in the capsazepine group was intraperitoneally injected with the amount of 0.1 mL/10 g. Similarly, each mouse in the moxibustion group was given a suspended moxibustion with specially-made moxa-stick for 20 min on L5 and L6 spinal cords. Each mouse in MC group was intraperitoneally injected with the amount of 0.1 mL/10 g first, then after 15 min was given a suspended moxibustion for 20 min on L5 and L6 spinal cords. Each mouse in WT moxibustion group and KO moxibustion group was given a suspended moxibustion with specially-made moxa-stick for 20 min on L5 and L6 spinal cords. The control group, WT control group and KO control group were of no treatment in any way. After all treatments were completed, the digital-display measurement instrument for thermal pain was used to measure the threshold of thermal pain in each group respectively.

RESULTS: Compared with the control group, the thresholds of thermal pain in the moxibustion group and MC group were significantly increased (P <0.01); no significant changes in the thresholds in the capsaicin group and the capsazepine group (P > 0.05); compared with moxibustion group, he threshold of thermal in MC group was obviously decreased (P < 0.01). Compared with WT control group, the threshold of thermal pain in WT moxibustion group was significantly increased (P < 0.01); compared with KO control group, no changes in the threshold in KO moxibustion group (P > 0.05).

CONCLUSION: TRPV1 participated in the process of increasing the threshold of thermal pain by stimulating L5 and L6 of mice spinal cord with burning mosa-stick.

Key words: Moxa stick moxibustion; Pain threshold; Heat stimulation; Transient Receptor Potential Vanilloid subetype 1

INTRODUCTION

The transient receptor potential vanilloid (TRPV) 1 receptor is a nonselective cation channel, which is expressed on peripheral and central terminals of small and mediumsized primary sensory neurons.[1] Since the receptor could be activated by capsaicin of specificity, it is also known as capsaicin receptor,[2] which could also be activated by a wide range of noxious stimulations including protons and heat etc. When the temperature is higher than 43 ℃, TRPV1 will be activated as is recognised as one of the thermo-sensitive cation channels.[3] TRPV1 can also be sensitized by different stimulations,[1] and its sensitization is crucial in the development of pain,[4] which is an important property of pain signaling,[5] playing a key role in pain transmission and modulation.[6] Under certain nerve injury or inflammatory disease conditions, TRPV1 is up-regulated.[7] TRPV1 is a noxious signaling, which becomes the potential therapeutic target for developing analgesics.[4] Many studies show that, the expression of TRPV1 could be inhibited by virtue of TRPV1 antagonist to attenuate pain and heat hyperalgesia.[8-11] However, topical application of capsaicin is clinically effective in treating a variety of chronic painful conditions, including postherpetic neuralgia and HIV-associated peripheral neuropathies. Its analgesic action is considered a consequence of inhibition of TRPV1 function by desensitization.[7]

Moxibustion therapy is an important part of the acupuncture and moxibustion therapy in Traditional Chinese Medicine. It is a kind of external treatment using folium artemisiae argyi or moxa as the principal material to cauterize or warm and iron at the acupoint or diseased region on body surface after ignition for the purpose of prevention, healthcare and cure. The heat stimulation of ignited moxa will directly or indirectly effects at specific areas of human body surface, generate effects on local and distant regions through meridians, and it is also the key property and the one of the causes for curative effect.[12] Pain relief is one of the main effects of moxibustion therapy[12] which has been existed for over two thousand years with a wide range of indications, applicable for deficiency, excess and acute diseases.[13] There is a research shown that, moxibustion may increase the expressions of POMC mRNA and PDYN mRNA in hypothalamus of rats,as well as promote the analgesic potency of organism, suggesting the moxibustion has analgesic effect.[14]

TRPV1 is a temperature sensor which is a member of the TRP family, and may be in connection with the activation mechanism of warming and promoting effect from moxibustion. TRPV1 can be activated by heat stimulation of > 43 ℃, which is similar to the local skin temperature caused by moxibustion.[15] TRPV1 plays a basic role in the signal transduction of tissue injuries and pain reponses, regaeding the analgesic effect of moxibustion, therefore, whether TRPV1 participates in the analgesic process of moxibustion heat effect? This study shall try to discuss the role of TRPV1 in the increase of the thermal pain threshold by moxibustion.

MATERIALS AND METHODS

Experimental animals

Fifty Kunming (KM) male mice of 18-22g (Certificate No. of SCXK (Shanghai): 2007-0005, provided by Shanghai Slac Laboratory Animal Co., Ltd.,), 24 C57BL/6 wild-type male mice of 16-20 g [Certificate No. of SCXK (Jiangsu): 2010-0001, provided by Laboratory Animal Center of Nanjing University], and 21 J003770 TRPV1 knockout male mice of 17-20 g [Certificate No. SCXK (Jiangsu): 2010-0001, provided by Laboratory Animal Center of Nanjing University].

Reagent preparation

Capsaicin (50 mg),Capsazepine (25 mg), 500 mL absolute ethyl alcohol, Polyoxyethylene Sorbitan (Tween 80) (500 mL) and Dimethyl Sulfoxide (50 mL) were purchased from Sigma (St. Louis, MO, USA). Normal Saline (250 mL) was purchased from Guangdong Litai pharmaceutical Limited by Share Ltd. (Guangdong, China). Capsaicin in powder 50mg is dissolved in 10% polyoxyethylene sorbitan (Tween 80) and 10% ethanol before being mixed with 80% normal saline to obtain a capsaicin solution of 0.01 M;[16] Capsazepine in powder 25 mg is dissolved in 25 mL dimethyl sulphoxide and then diluted in normal saline to obtain a capsazepine solution of 0.01 M.[17]

Experimental apparatus

JL-F Digital-display type measurement instrument for thermal pain was purchased from Shanghai Precision Instrument Co., Ltd., (Shanghai, China), Special-made moxa-stick (5 mm × 200 mm) was purchased from Nanyang Hanyi Moxibustion Technology Development Co., Ltd., (Nanyang, China), 1 mL Disposable sterilized syringe was purchased from Changzhou Medical Appliances General Factory Co., Ltd., (Changzhou, China)

Experiment Ⅰ

Grouping: 40 KM mice (20 ± 2) g are randomized into 5 groups by random number table method: control group, capsaicin group, capsazepine group, moxibustion group and moxibustion + capsazepine (MC) group with 8 mice in each, and the rest 10 mice are backups without any treatment.