

针刺对肥胖大鼠下丘脑腹内侧核作用的研究

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摘要 观察针刺对肥胖大鼠下丘脑腹内侧核(VMH)神经细胞自发放电和单胺类神经递质水平的影响。结果显示,肥胖组较正常组 VMH 中酪氨酸(Tyr)、多巴胺(DA)水平均低下,5-羟色胺(5-HT)和 5-羟吲哚乙酸(5-HIAA)水平升高;VMH 神经细胞自发放电频率显著低下。针刺在取得减肥效果的同时,可以显著提高 VMH 神经细胞自发放电频率;还可以升高 VMH 组织中 Tyr、DA、色氨酸(Trp)、5-HT/5-HIAA 水平,回降 5-HT 水平。提示针刺对 VMH 的良性调整作用可能是针刺减肥关键性因素之一。

主题词 下丘脑/针灸效应 肥胖症/针灸疗法

为进一步认识中枢神经系统在肥胖病发生机制中的作用以及针刺对肥胖机体中枢神经的作用。本文观察了实验性肥胖大鼠下丘脑腹内侧核(VMH)组织中单胺类递质水平及其神经细胞自发放电的状况以及针刺后发生的变化,揭示针刺减肥过程中针刺对肥胖机体中枢神经的作用机理。

1 材料与方法

1.1 实验动物:实验动物为刚断乳 SD 雄性大鼠,体重 50~60g,由南京铁道医学院实验动物中心提供。按文献^[1]制成单纯性肥胖病胃肠实热型大鼠动物模型,简称肥胖大鼠。本组肥胖大鼠随机分为肥胖对照组(简称对照组)29 只,不做任何治疗;针刺治疗组(简称治疗组)28 只,给予针刺治疗。正常对照组(简称正常组)29 只,以普通饲料喂养。

1.2 实验方法:用普通饲料喂养各组大鼠,自由摄食和饮水,放入大鼠固定器中每日 15 分钟。针刺组大鼠于第 15 天开始给予针刺治疗,针刺组针刺期间其他组操作同前 14 天。

针刺方法:将大鼠放入固定器中,用酒精消毒双侧后三里(相当足三里)和内庭穴,取 36 号美容针(0.19mm×10mm)分别刺入 4mm 和 2mm 深度,后三里采用平补平泻的手法运针 1 分钟,内庭穴用捻转泻法运针半分钟,然后均接通电针仪(6805-Ⅱ型,福建

省医疗器械厂),频率为 10Hz,强度为 1.5V 的连续波,每次治疗 10 分钟,每日 1 次,连续 12 天。

1.3 检测方法:实验前后观察大鼠的摄食量、饮水量、大小便、体重、体长及 Lee 氏指数等。实验结束后,每组各 22 只大鼠禁食过夜,次日上午断头处死,迅速分离心包、肾周、腹股沟脂肪,称重并记录。立即将分离的脑置于液氮中保存,测定前取出脑组织置于冰碟上分离出 VMH 组织,称重后制成 VMH 组织匀浆。VMH 组织中 Tyr、DA、去甲肾上腺素(NA)、Trp、5-HT、5-HIAA 含量等用荧光分光光度法^[2]。

VMH 神经细胞自发放电的观察:正常组、对照组各 7 只大鼠,针刺组 6 只大鼠实验结束后,室温 24±1℃的条件下,称重后先用乙醚麻醉作为基础麻醉,然后用 25%乌拉坦 1g/kg 体重腹腔注射进行复合麻醉,固定在实验台上,行气管插管术,以防窒息。随后取俯卧位固定在大鼠脑立体定位仪上,于颅顶正中中线切开皮肤,暴露颅骨,调整水平位,使前囟、中缝、人字缝在同一水平面,按照包新民等^[3]大鼠脑立体定位图谱所示,确定 VMH 区在颅顶的投射点,用动物骨钻钻开一直径约 1mm 的小孔,将玻璃微电极装在微推进器支架上,推至颅内 6.9~7.1mm 深处,通过神经信号放

表 1 各组肥胖指标的比较($\bar{x} \pm s$)

组别	样本数	体重(g)	体长(cm)	Lee 氏指数
正常组	22	396.78±15.63	41.85±0.63	0.2265±0.010
对照组	22	497.41±29.18 ^{△△}	44.36±1.17 ^{△△}	0.2528±0.012 ^{△△}
针刺组	22	445.15±29.13 ^{△*}	43.11±0.79 ^{△*}	0.2394±0.010 ^{△*}

与正常组比较,△P<0.05,△△P<0.01;与对照组比较 *P<0.05, **P<0.01,以下表同

表 2 各组脂肪量的比较($\bar{x} \pm s$)

组别	样本数	心包脂肪量(g)	腹股沟脂肪量(g)	肾周脂肪量(g)
正常组	22	0.21±0.02	1.66±0.86	2.15±0.80
对照组	22	0.28±0.05 ^{△△}	5.08±1.47 ^{△△}	4.35±1.06 ^{△△}
针刺组	22	0.22±0.03 [*]	2.85±0.83 [*]	3.03±0.85 [*]

表 3 各组下丘脑腹内侧核儿茶酚胺含量的比较($\bar{x} \pm s$)

组别	Tyr(μg/g)	NA(μg/g)	DA(μg/g)
正常组	0.725±0.116(6)	0.975±0.401(10)	1.028±0.298(10)
对照组	0.546±0.107 [△] (6)	0.906±0.254(10)	0.703±0.270 [△] (10)
针刺组	0.964±0.326 [*] (5)	0.974±0.355(10)	0.980±0.123 [*] (10)

括号内数字为样本数,下表同

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表4 各组下丘脑腹内侧核 5-HT 代谢的比较($\bar{x} \pm s$)

组别	Trp($\mu\text{g/g}$)	5-HT($\mu\text{g/g}$)	5-HIAA($\mu\text{g/g}$)	5-HT/5-HIAA
正常组	0.059 $\pm$ 0.038(5)	1.271 $\pm$ 0.281(13)	2.127 $\pm$ 1.626(13)	0.3598 $\pm$ 0.172(13)
对照组	0.047 $\pm$ 0.007(5)	1.625 $\pm$ 0.399 Δ (9)	3.737 $\pm$ 1.608 Δ (9)	0.434 $\pm$ 0.166 Δ (9)
针刺组	0.073 $\pm$ 0.018*(5)	1.233 $\pm$ 0.115*(11)	2.029 $\pm$ 1.817(11)	0.608 $\pm$ 0.175*(11)

大器和电生理仪逐级放大,引出 VMH 神经细胞自发放电,经微机处理,计数放电频率(Hz/s)。实验结束后,用 9V 直流电接负极通电 10 分钟,使蒽胺天蓝染液达到尖部,标记微电极记录部位,然后处死大鼠,取脑用 10% 甲醛固定,冰冻切片,进行组织鉴定。

2 结果

2.1 针刺对肥胖指标的影响:表 1 示,对照组肥胖指数均明显高于正常组(P 均 <0.01),证明造模成功。针刺组指数均显著低于对照组(P 均 <0.01)。说明针刺的减肥作用是肯定的。

2.2 针刺对脂肪量的影响:表 2 示,对照组 3 部位脂肪量均显著高于正常组(P 均 <0.01),针刺组 3 部位脂肪量均显著低于对照组(P 均 <0.01)。

2.3 针刺对 VMH 儿茶酚胺含量的影响:表 3 示,对

表5 肥胖指标与下丘脑腹内侧核神经细胞自发放电的关系($\bar{x} \pm s$)

组别	样本数	Lee 氏指数	自发放电(Hz/s)
正常组	7	0.2256 $\pm$ 0.0050	10.77 $\pm$ 4.70
对照组	7	0.2527 $\pm$ 0.0068 $\Delta\Delta$	5.49 $\pm$ 1.51 Δ
针刺组	6	0.2337 $\pm$ 0.0093**	19.35 $\pm$ 5.46 $\Delta\Delta$ **

照组 Tyr 和 DA 含量明显低于正常组(P 均 <0.05),针刺组 Tyr 和 DA 含量明显高于对照组(P 均 <0.05)。

2.4 针刺对 VMH 5-HT 代谢的影响:表 4 示,对照组 5-HT 和 5-HIAA 含量明显高于正常组(P 均 <0.05),5-HT/5-HIAA 比值明显低于正常组(P 均 <0.05);针刺组 5-HT 含量明显低于对照组(P 均 <0.05),Trp、5-HT/5-HIAA 明显高于对照组(P 均 <0.05)。

2.5 肥胖指标与 VMH 神经细胞自发放电的关系:表 5 示,对照组肥胖指标明显高于正常组,VMH 中神经细胞自发放电明显低于正常组,针刺组肥胖指标明显低于对照组,VMH 中神经细胞自发放电显著高于对照组,经统计学处理均具有显著性差异(P 均 <0.05 或 P 均 <0.01)。

3 讨论

下丘脑外侧区(LHA)——饥饿中枢和 VMH——饱中枢是调节摄食活动的关键部位,统称摄食中枢,功能

上两者相互拮抗。一般认为,LHA 是发动摄食的主要神经结构,VMH 对 LHA 有抑制作用。儿茶酚胺类神经递质与 5-HT 是参与摄食中枢调节的重要介质,两者对摄食中枢的影响也是相互制约的^[4~6]。本文结果证实,肥胖大鼠 VMH 中 Tyr、DA 均明显低于正常大鼠水平,5-HT 和 5-HIAA 明显高于正常大鼠水平。这一结果与我们另一项实验证明肥胖大鼠 LHA 中 NA、DA 升高而 5-HT 水平低下恰恰相反^[1]。提示 LHA 中 NA 的增加和 5-HT 的减少,提高了 LHA 的兴奋性致使大鼠摄食增强,而 VMH 中 DA、NA 减少和 5-HT 增加致使 VMH 兴奋性降低,对 LHA 的抑制减弱,使 LHA 增加摄食的作用更为失控。说明摄食中枢的功能失调是引起动物肥胖的重要原因之一。

针刺治疗后,肥胖大鼠不仅获得了良好的减肥效应,同时中枢 VMH 中 DA 含量明显回升,5-HT 含量明显回降。

本文结果表明,肥胖组大鼠 VMH 神经细胞自发放电频率显著低于正常组大鼠,针刺组大鼠 VMH 神经细胞自发放电频率明显高于肥胖组和正常组。进一步证实肥胖大鼠 VMH 兴奋性低下,而针刺可以增强肥胖大鼠 VMH 的兴奋性。从而加强了对 LHA 的抑制作用,有效控制亢进的食欲,减少能量摄入,最终产生减肥效应。

本文通过对肥胖大鼠 VMH 单胺类递质和神经细胞自发放电的观察以及针刺对其影响,提示肥胖大鼠 VMH 功能失调可能是肥胖的重要发病环节,针刺对 VMH 功能的良性调整作用可能是针刺实现减肥效应的一个重要因素。

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ABSTRACTS FROM ORIGINAL ARTICLES

Action of Acupuncture on Ventromedial Nucleus of Hypothalamus in the Rat of Obesity

Liu Zhucheng, Sun Fengmin, Su Jing, et al.

Effects of acupuncture on spontaneous discharges of nerve cells in ventromedial nucleus of hypothalamus (VNH) and levels of monoamine neurotransmitters in rats of obesity were observed. Results indicated that levels of tyrosine (Tyr) and dopamine (DA) were decreased, and the levels of 5-hydroxytryptamine (5-HT) and 5-hydroxyindole acetic acid (5-HIAA) increased in VNH; The frequency of spontaneous discharges of nerve cells in VNH lowered significantly in the obesity group as compared with those in the normal group; When acupuncture attained effect of weight reduction, the frequency of spontaneous discharges of nerve cells in the VMH increased obviously; the levels of Tyr, DA, tryptamine, and 5-HT/5-HIAA increased, and 5-HT level decreased in VMH tissue. It is suggested that the benign regulative action of acupuncture on VNH is possibly one of the crucial factors for acupuncture in reducing body weight.

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Key words: Hypothalamus/acupuncture effect, Obesity/acupuncture therapy

(Original article on page 25)

Clinical Observation on 107 Cases of Middle-Age and Old Patients of Coronary Heart Disease with Ventricular Premature Beat Treated by Qing Xin An Shen Prescription

Jia Yuhua, Sun Xuegang, Jia Manying, et al.

According to the pathological characteristics that simultaneous occurrence of phlegm, heat, blood stasis and deficiency are commonly seen in middle-age and old patients of coronary heart disease with ventricular premature beat, the principles of clearing away the heart—fire and tranquillizing were adopted, and 107 middle-age and old patients of coronary heart disease with ventricular premature beat were treated by self-formulated compound Qing Xin An Shen Prescription and the results were compared with that of the control group treated by mexilit plus compound Dan Shen Tablet. Results showed that the markedly effective rate was 85.1% and the total effective rate was 96.3% in the Qing Xin An Shen group, which were superior to those in the control group; And Qing Xin An Shen Prescription had better actions of reducing blood pressure, blood lipid and improving microcirculation and clinical symptoms.

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Key words: Tachycardia, ventricular/TCM therapy, Coronary

artery disease/TCM therapy, @Clearing away the heart—fire and tranquillizing method

(Original article on page 27)

Clinical and Experimental Studies on 180 Cases of Male Infertility Treated with Shou Wu Huan Jing Capsule

Zeng Jinxiong, Dai Xihu, Yang Jiahui, et al.

In order to further probe into the therapeutic effect and mechanisms of Shou Wu Huan Jing Capsule for treatment of male infertility, 180 patients were investigated. Results showed that the prescription had reliable therapeutic effect with no side-effect, and the effective rate was 93.89%. Effects of Shou Wu Huan Jing Capsule on human sperm moment velocity, index of vitality, capillary penetrativity test and sperm hypotonic expansion test were analysed for the application in improving the seminal quality of male infertility patients in culture of human sperm with extract of Shou Wu Huan Jing Capsule. The results revealed that it could promote motor ability and membrane function of sperm. Thus, it is of potential application value for treatment of male infertility and in auxiliary fertility technique as extrinsic additive.

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Key words: Infertility, Male/TCM therapy, @Shou Wu Huan Jing Capsule

(Original article on page 33)

Characteristics of Syndromes of Diabetic with Different Duration of Disease

Xu Zhengzheng

Preliminary analysis of TCM syndromes in the various groups indicated that pathogenic dampness (internal retention) Zheng was universal in the A group (who were just diagnosed with no treatment), B group (5-6 years after diagnosed without good control) and C group (over 10 years after diagnosed without good control). It is suggested that internal retention of pathogenic dampness is greatly related with protracted course of diabetes; Yin-deficiency in patients at early stage are universal; Blood stasis is commonly seen in the patient with over 10 years duration of illness and no good control. It is indicated that it is necessary in TCM treatment of diabetes to pay close attention to removing pathogenic dampness at any time, and to nourishing Yin and protecting Yin at the early stage, and to removing blood stasis for over 10 years duration of illness.

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Key words: Diabetes/Diagnosis, Syndrome

(Original article on page 44)