

# Acupuncture in the Treatment of Parkinson's Disease

Yan Jiang, MD, PhD, Kenneth K Kwong, PhD, Jing Liu, MD

## Abstract

Many studies have shown the potential benefits of the acupuncture for Parkinson's disease although lack of the solid scientific data in clinic. To understand the mechanism of acupuncture is not easy, but many clues in this review would be helpful for the study in the future. As we know today that acupuncture may affect multiple factors of the brain activities, which may involve in the pathogenesis and the development of Parkinson's disease. They include Dopamine, Dopaminergic neurons, Dopaminergic metabolites, Dopamine D2 receptors, Cyclooxygenase-2 (COX-2), inducible Nitric Oxide Synthase (iNOS), brain-derived Neurotrophic factor (BDNF), Superoxide Dismutase (SOD) and Lipids Peroxides (LPO) in the striatum, substantia nigra (SN), and ventral tegmental area (VTA). Different techniques of acupuncture stimulation seem induce the different responses of the neural activities on the animal model.

[N A J Med Sci. 2009;2(1):32-34.]

**Key words:** *Acupuncture, Parkinson's disease, Dopamine, Striatum, Substantia nigra*

## Introduction

Parkinson's disease (PD) is an extrapyramidal chronic neurodegenerative disease of brain mainly characterized by a progressive degeneration and necrosis of dopaminergic neurons in substantia nigra of brain. The disease affect people mostly in the middle and old-aged.<sup>1</sup> There are about one in every 100 people above the age of 65 years are diagnosed as PD in the world.<sup>2</sup> The causes of the PD is not clear, but the progressive degeneration and necrosis of dopaminergic neurons and the oxidative stress-free radicals seem to play an important role in the deterioration of dopaminergic neurons. The results from a numbers of studies support that

dopaminergic function stimulation and the anti-oxidant therapy may be helpful to halt the progression of PD.<sup>2,3</sup> In the passed years, more advanced therapeutic techniques have been attempted to treat the disease, including neuroprotective strategies,<sup>3</sup> gene therapy, and neural transplantation.<sup>2</sup> So far, the synthetic drugs, such as atropine, levodopa, and medopa, have shown limited effects because they can only bring temporary relief of the symptoms.<sup>2</sup> Many attempts on searching complementary therapies have opened up a new vision in treating PD. Acupuncture, herbs, physical therapy and biofeedback are most frequently used in the clinical practice for PD in the whole world, especially in China. Among them, the potential benefits of acupuncture on the PD patients and the promising results in animal models have gained increased attention.<sup>4</sup>

According to the ancient theory of traditional Chinese Medicine, the cause of PD is mainly from the deficiency of the energy in the kidney system (root) and excess in the liver system(branch).<sup>5</sup> As the result, no enough Qi and blood flow to nourish the certain area of brain. In addition, the harmful wastes cannot be cleansed out in the situation of the poor circulation, which aggravates the damage and the degenerations of the brain. In conclusion, deficiency and congestion constitute the basis of the pathology of PD.<sup>5</sup> By integrating the traditional Chinese medicine and the modern medical science, many clinical practitioners and researchers have tried to reevaluate the effects of acupuncture on PD and find out the scientific explanations behind such effects.

## 1. Clinical Research in PD Patients

Although the clinical studies of acupuncture have been lack of required statistical control, such as placebo comparison,<sup>6</sup> many of the studies showed at least the potential likelihood that acupuncture have beneficial effects for patients and deserve further research.<sup>7-14</sup> A few reports stated that acupuncture helped only PD-related sleep disturbance.<sup>6</sup>

### 1.1. Effect of acupuncture on the symptoms of PD

The results from treating 29 cases of PD with acupuncture showed that acupuncture induced significant therapeutic effectiveness for PD. In this study, the treatment group (n=29) was treated with acupuncture every other day for 3 months, the control group (n=24) was administered the drugs, including L-dopa and dopaminergic receptor stimulants. The results indicated that acupuncture can improve the clinical symptoms and signs of tremor and twitch.<sup>7</sup>

**Yan Jiang, MD, PhD**

Beijing University of Chinese Medicine, Beijing, China

**Kenneth K Kwong, PhD**

**Jing Liu, MD, PhD\*** (corresponding author)

Department of Radiology

Mass General Hospital

Harvard Medical School

Charlestown, MA, 02129, USA

In a non-blinded controlled pilot study, a group of 20 cases of PD patients were treated with acupuncture twice a week; 7 patients received 10 treatments and 13 patients received 16 treatments. The safety, tolerability and efficacy of acupuncture (ACUPX) were evaluated by the Sickness Impact Profile (SIP), Unified Parkinson's Disease Rating Scale score (UPDRS), Hoehn and Yahr(H&Y), Schwab and England (S&E), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI) and quantitative motor tests. There were no changes in the UPDRS, H&Y, BAI, BD, quantitative motor tests, total SIP and the two SIP Dimension scores. On the other hand, 85% of patients reported improvement of the symptoms including tremor, walking, handwriting, slowness, pain, sleep, depression and anxiety.<sup>8</sup> In a clinical study, 24 cases of scalp acupuncture on PD were observed. The acupuncture needles were inserted from Qianding (GV-21) to Baihui (GV-20) along the central line of scalp. Another 12 needles were inserted to either sides of the central line. The electro-stimulation was applied for 40 minutes every other day for 10 times. The improvement of the tremor was observed in 2/3 of the patients.<sup>10</sup> A report showed that 56 patients with PD obtained clear therapeutic effects with acupuncture. In this study, scalp acupuncture was applied to the dancing trembler zone. The body acupoints included Fengchi (GB20), Quchi (LI11), Waiguai (SJ5), Yanglingquan (GB34), Taichong (LR3).<sup>11</sup>

The specificity of the acupuncture points for PD has been always questioned. An acupuncture study selected EX-HN-1 point on the head as the major point to compare with points on the limbs (arms and legs). As the result, acupuncture could increase the The point of EX-HN-1 showed significant stronger effect on reducing the tremor and improving the blood circulation to the affected parts of the brain of PD patients ( $p<0.05$ ).<sup>9</sup>

So far, there is no satisfactory methodology design for clinical trials of acupuncture in the world because of the special feature of acupuncture. This may be part of the reason for unclear conclusion in evaluating the effects of acupuncture for PD treatment. On the other hand, many successes have been achieved on finding the mechanism of acupuncture treatment on PD. Since it is well known that PD is caused by progressive degeneration and necrosis of dopaminergic neurons, many of the acupuncture studies have been targeted on dopamine neurons, dopamine transporter (DAT) in basal ganglia (BG), superoxide dismutase (SOD) and lipids peroxides (LPO).

### **1.2. Effect of acupuncture on regulating dopaminergic system**

By using single photon emission computed tomography (SPECT), the effect of electro-scalp acupuncture (ESA) on cerebral dopamine transporter (DAT) in basal ganglia (BG) of patients with PD was investigated.<sup>12</sup> PD patients (n=10) were randomly divided into ESA group and the Medopa group. ESA were treated by acupuncture. The subjects in the Medopa group took medopa. The DAT, analyzed by ratio of basal ganglia/occipital (BG/OC), were examined by 99m Tc-TRODAT\_1 SPECT before and after 6 weeks of acupuncture

treatments. The result showed that the uptake of 99m Tc-TRODAT\_1 SPECT increased after the treatment in both groups. ESA reduced the loss of DAT and improved its activity in basal ganglia but showed no difference from the Medopa group ( $p>0.05$ ). The values of contralateral BG/OC were significantly different before and after treatment in each group.<sup>12</sup>

The auditory evoked brain stem potential (ABP) examination showed that the latent period of V wave, the intermittent periods of III-V peak and I-V peak were evidently shortened in PD patients after acupuncture treatment (N=29). The increase of brain dopamine and the dopamine neuron excitability after acupuncture strongly indicate the potential therapeutic effect of acupuncture treatment on PD.<sup>13</sup>

### **1.3. Effects of anti-oxidant with acupuncture**

The superoxide dismutase (SOD) and lipids peroxides (LPO) before and after EA treatment were tested in a clinical study with scalp electroacupuncture (SEA) on PD patients (n=76). Patients were randomly divided into two groups, the SEA group (n=37) and the Medopa group as control group (n=39). The result of the treatment showed that the effective rate of the improvement of SOD and LPO was 97.3% in the treatment group with acupuncture and 61.5% in the control group respectively ( $p<0.01$ ).<sup>14</sup>

## **2. Experiment Research on Animal Model**

The effects of acupuncture on dopamine and its metabolite dihydroxy-phenyl acetic acid (DOPAC) of brain were observed in the MPTP C57BL mice. DA in Caudate nucleus (CN) and midbrain DA level was increased after 30 minutes of acupuncture stimulation. On the other hand, acupuncture showed less effective on DOPAC level.<sup>15</sup>

It was reported that electric acupuncture(EA) at Taichong (LR3) and Fengfu (GV16) may increase the dopamine in the striatum of brain, prevent injury of dopaminergic neurons in the substantia nigra, and decrease NOS in the cortex and Glu of PD rats.<sup>16,17,18,19</sup>

It was reported that PD Wister rats were treated by 2Hz EA on points of Taichong (LR3) and Fengfu (GV16). The dopamine and its metabolite in striatum were tested by radiographic analysis, HPLC and ECD after 7days of the treatment. The results showed that dopamine, DOPAC, and homovanillic acid (HVA) were significantly increased in striatum in EA group compared with the control group ( $p<0.05$ ).<sup>16</sup> On a apoptosis of dopaminergic neurons of the substantia nigra model, The numbers of DA neuron apoptosis were lower in the EA treatment group, compared with that of the control group at 7<sup>th</sup> day and 14<sup>th</sup> day ( $p<0.05$ ).<sup>17</sup>

The immunohistochemical double-labeling method was used to observe the proliferation and differentiation of nerve stem cells. In this study, the numbers of nerve stem cells and transformed neurons in the destroyed substantia nigra and the striatum were increased in the acupuncture group with a specific Shuanggu Yitong needling technique ( $p<0.01$ ).<sup>20</sup> It

was reported that acupuncture treatment at Yanglingquan (GB34) and Sanjian (LI3) group significantly reduced the motor deficit (14.6+/-13.4 turns/h), enhanced survival of dopaminergic neurons in the substantia nigra and their terminals in the dorsolateral striatum. Acupuncture treatment also increased the expression of trkB (35.6% increases) in the ipsilateral SN.<sup>21</sup> It was reported that acupuncture at the ST36 for 14 days significantly inhibited rotational asymmetry in the rats with PD.<sup>22</sup>

EA treatment could increase the DA level to some extent and prevent D2 receptor's upregulation in rats with PD. The results of a study showed that the content of dopamine (DA) and metabolites such as DA, HVA, DOPAC in striatum after EA treatment were all increased comparing with the control group ( $P < 0.05$ ).<sup>23</sup> Acupuncture can increase not only dopamine (DA), but also noradrenalin (NA) and hydroxytryptamine (5-HT). It was showed that the head cupionts (GV20, GV14) were more potent than body acupoints (LI4, LR3) on promoting the DA and 5-HT production in striatum of PD rat. Interestingly, moxibustion on head acupoints significantly increase DA and NA. On the other hand, EA stimulation was more effective on 5-HT and DA in this research.<sup>24</sup> On a C57BL/6 PD mice model, acupuncture at GB34 and LR3 inhibited the decrease of the tyrosine hydroxylase (TH) and immunoreactivity (IR), suggesting that acupuncture may have neuroprotective effects in the striatum and the substantia nigra. Acupuncture also increased macrophage antigen complex (MAC-1), a marker of microglial activation, reduced expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthases (iNOS). Striatal DA increased 78% in the acupuncture group, compare with 46% in the control group.<sup>25</sup>

Long-term high-frequency electro-acupuncture not only halt the degeneration of dopaminergic neurons in the substantia nigra (SN), but also upregulated the level of brain-derived neurotrophic factor (BDNF) mRNA in the subfields of the ventral midbrain, and stimulate the regeneration of the injured dopaminergic neurons.<sup>26</sup> Different frequencies of EA stimulation (0, 2, 100Hz) were tested. The results of this study showed that about 60% of the tyrosine hydroxylase (TH)-positive neurons remained on the PD lesions of the SN. 100Hz EA stimulation significantly increased the levels of BDNF mRNA in the SN and ventral tegmental area (VTA). Whereas, zero Hz and 2Hz EA stimulation had no effect. It seems that long-term high-frequency electro-acupuncture stimulation may prevent the neuron degeneration.<sup>26</sup>

## References

- Li G. Clinical analysis of Parkinson's disease treated by integration of traditional Chinese medicine and western medicine. *J Tradit Chin Med.* 1995;15(3):163-169.
- Neha S, Viness P, Choonara YE. Advances in the treatment of Parkinson's disease. *Neurobiology.* 2007;81(1):29-44.
- Hodaie M, Neimat JS, Lozano AM. The dopaminergic nigrostriatal system and Parkinson's disease: molecular events in development, disease, and cell death, and new therapeutic strategies. *Neurosurgery.* 2007;60(1):17-28.
- Manyam BV, Sanchez-Ramos JR. Traditional and complementary therapies in Parkinson's disease. *Adv Neurology.* 1999;80:565-574.
- Zhang QJ, Zhang YY, Huang WY. Traditional Chinese Medicine in treatment of Parkinson's disease. *Zhong Xi Yi Jie He Xue Bao.* 2004;2(1):75-77.
- Rabinstein AA, Shulman LM. Acupuncture in clinical neurology. *Neurologist.* 2003; 9(3):137-148.
- Huang Y, Jiang XM, Li DJ. Effects on electro-scalp acupuncture on cerebral dopamine transporter in patients with Parkinson's disease. *Zhongguo Zhong Xi Yi Jie He Za Zhi.* 2006;26(4):303-307.
- Wang L, He C, Liu Y, Zhu L. Effect of acupuncture on the auditory evoked brain stem potential in Parkinson's disease. *J Tradit Chin Med.* 2002;22(1):15-17.
- Wang S, Cai YY, Shang YJ, Jin-rong L. Effects of head point-through-point electroacupuncture on SOD and LPO in the patient of Parkinson's disease. *Zhongguo Zhen Jiu.* 2006;26(4):240-242.
- Zhuang X, Wang L. Acupuncture treatment of Parkinson's disease - a report of 29 cases. *J Tradit Chin Med.* 2000; 20(4):265-267.
- Shulman LM, Wen X, Weiner WJ, Bateman D, Minagar A, et al. Acupuncture therapy for the symptoms of Parkinson's disease. *Mov Disord.* 2002;17(4):799-802.
- Wang L, et al. Influence of acupuncture on brain blood flowing state in Parkinson's patients. *Chinese Acupuncture and Moxibustion.* 1999;2:115-116.
- Xi Guifang, et al. Impact of electrostimulation at scalp points on tremor-myoelectropotential in Parkinson's disease patients. *Shanghai Journal of Acupuncture and Moxibustion.* 1996;15(3):5-6.
- Xie Y. Clinical observation on 56 cases of Parkinson's disease with Chinese medicine. *Zhongguo Zhong Xi Yi Jie He Za Zhi.* 1993;8(5):490.
- Zhu W, Xi G, Ju J. Brain Dopamine Level of MPTP C57BL Mice. *Zhenci Yanjiu.* 1997;1(1):89.
- Zhu S, Ma J. Effects of the dopamine and its metabolite in striatum of Parkinson's disease in rat with electric acupuncture. *Journal of Jiangnan University(Natural sciences).* 2005;33(2):72-73.
- Ma J, Wang YC, Gan SY. Effects of electroacupuncture on behavior and dopaminergic neurons in the rat of Parkinson's disease. *Zhongguo Zhen Jiu.* 2006;26(9):655-657.
- Ma J. Effects of acupuncture on the amount of NOS in cortex in the rat of Parkinson's disease. *Hubei Chinese medicine Xuebao.* 2000;2(1):104.
- Ma J. Effects of acupuncture on the amount of Glu in striatum in the rat of Parkinson's disease. *Shanghai Zhen Jiu Za Zhi.* 2003;10(1):165.
- Wang YC, Ma J, Wang H. Effects of Shuanggu Yitong needling method on proliferation and differentiation of nerve stem cells in the Parkinson's disease model rat. *Zhongguo Zhen Jiu.* 2006;26(4):277-282.
- Park HJ, Lim S, Joo WS, et al. Acupuncture prevents 6-hydroxydopamine-induced neuronal death in the nigrostriatal dopaminergic system in the rat Parkinson's disease model. *Exp Neurology.* 2003;180(1):93-98.
- Kim YK, Lim HH, Song YK, et al. Effect of acupuncture on 6-hydroxydopamine-induced nigrostriatal dopaminergic neuronal cell death in rats. *Neurosci Lett.* 2005;384(1-2):133-138.
- Lin Y, Lin X. Comparative study of D2 receptor and content of DA in striatum before and after electroacupuncture treatment in the Parkinson's disease rats. *Zhong Hua He Yi Xue Za Zhi.* 1999;19(2):69-71.
- He C, Wang L, Dong H. Effects of acupuncture on monamine(MA) neurotransmitter in the rat of Parkinson's disease. *Zhongguo Zhong Yi Yao Ke Ji.* 1998;5(2):65-68.
- Kang JM, Park HJ, Choi YG, et al. Acupuncture inhibits microglial activation and inflammatory events in the MPTP-induced mouse model. *Brain Research.* 2007;1131(1):211-219.
- Liang XB, Liu XY, Li FQ, et al. Long-term high-frequency electroacupuncture stimulation prevents neuronal degeneration and up-regulates BDNF mRNA in the substantia nigra and ventral tegmental area following medial forebrain bundle axotomy. *Brain Res Mol Brain Res.* 2002;108(1-2): 51-59.



