头皮针短暂调解巴金森氏病患皮质应激性的作用*

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摘 要：对于巴金森氏病人而言，因针灸的安全性且其与抗巴金森药物无交互作用，所以常作为辅助性的疗法。然而针灸对巴金森氏病的临床疗效是有争议的，而且少有用电生理的研究来评估针灸对巴金森氏病的影响。因此，本文设计电生理试验以衡量巴金森氏病人的头皮针治疗，我们使用皮质应激性（经成双穿颅磁刺激所诱发）为电生理评估的工具，对 9 位巴金森氏病人进行头皮针的试验并分析前后电生理变化。经头皮针的短暂治疗后 6 位巴金森氏病人并未在肢体活动获得短期的改善，但无任何不适的并发症。但是在头皮针的治疗前后确有明显的电生理改变，于巴金森氏病人中发现，其于成双穿颅磁刺激中存在对运动皮质应激性抑制。因此，进一步长期临床与生理机制评估是必需的。

关键词：头皮针 针灸 皮质应激性 巴金森氏病
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Introduction

Parkinson's disease (PD) is one of the neurodegenerative disorders, which commonly causes disability among the elderly because of motor dysfunction. The clinical features of PD are mainly tremor, bradykinesia, rigidity and posture instability in a progressive course[1, 2]. PD has existed worldwide since the ancient time. In western views, the anti-parkinsonian drugs, such as levodopa, anticholinergics, dopamine agonists and monoamine oxidase inhibitors, have satisfactory efficacy in the initial treatment of PD[3]. But they provide relatively little benefit during the progression of the disease and may cause the patient to develop unsatisfactory symptoms, which is due to the side effects of increased dosage and the long-term therapy[4].

Because of safety, negligible side effects and no known interactions with medications, the acupuncture

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has been an alternative treatment for PD[3]. After receiving acupuncture, the PD symptoms may relieve and the needed dosage of anti-parkinsonian medicine may decrease according to many experiences of staves in clinics[4,5]. Nevertheless, certain commentaries consider that acupuncture is well tolerated but the symptoms of PD don't improve other than sleep benefit[6~7]. The most of researchers evaluated the therapeutic effects of acupuncture on PD by using the rating scales[5~7], such as Webster's PD Rating Scale (WPDRS), Unified PD Rating Scale (UPDRS), Hoehn and Yahr (H & Y) score, Sickness Impact Profile (SIP), et cetera[1,8]. However, few studies evaluate the effects of acupuncture in PD by electrophysiological methods although the electromyogram (EMG)[9] and auditory evoked brain stem potential have been applied in some studies[10]. Scalp acupuncture, a specialized acupuncture technique[11], is also a usual remedy combined with body acupuncture for PD[12]. The purpose of this study was to investigate whether scalp acupuncture induces changes in cortical excitability before and during acupuncture.

Material and Methods

1. Subjects

Nine patients with idiopathic Parkinson's disease stage Ⅰ Ⅲ (according to UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria[2], and Hoehn and Yahr staging scale) were included in the study. Patients with atypical Parkinsonism or with exhibiting signs of cognitive impairment were excluded. Other exclusion criteria included:(1) patients taking medication for anxiety, depression, psychosis, or other psychiatric disturbances; (2) prior history of stroke or dementia; (3) bleeding or coagulation disorders; (4) skin infections; (5) history of arrhythmias, pacemaker, or implanted defibrillator;(6) needle phobia. All subjects underwent experimentation in Neuroscience Laboratory of the Neurology department in China Medical University hospital. The protocol was approved by the local Institutional Review Board.

During the "off phase" (discontinuing anti-parkinsonian medication at least 12 hours before each examination), paired pulse magnetic stimulation and Unified Parkinson's Disease Rating Scale (UPDRS) were used to evaluate nine patients before and during acupuncture. While undergoing experimentation, each subject received scalp acupuncture on the chorea-trembling control and motor areas by a licensed Acupuncturist, and the treatment lasted approximately for one hour. All of the subjects completed the study and were given informed consents for the participation.

2. Cortical Excitability Experimentation

Subjects were initially evaluated with UPDRS and paired pulse magnetic stimulation before acupuncture. The scalp acupuncture was implemented with well preparedness of skin sterilization. The gauge-30 filiform needles were inserted with 1cm in length subcutaneously to motor area (anterior oblique line of vertex-temporal with the upper limit, being 0.5cms posterior to the midpoint of the anterior-posterior line, and the lower limit, intersecting the eyebrow-occiput line at the anterior border of the natural hairline on the temple) and chorea-trembling control area (parallel to anterior 1.5cms in front of the motor area). After achieving needling sensations and then maintaining the needle under scalp around 20 minutes, the subjects, they underwent again paired pulse magnetic stimulation and UPDRS before removing needles from scalp.

3. Paired pulse magnetic stimulation (cortico-cortical inhibition as cortical excitability)

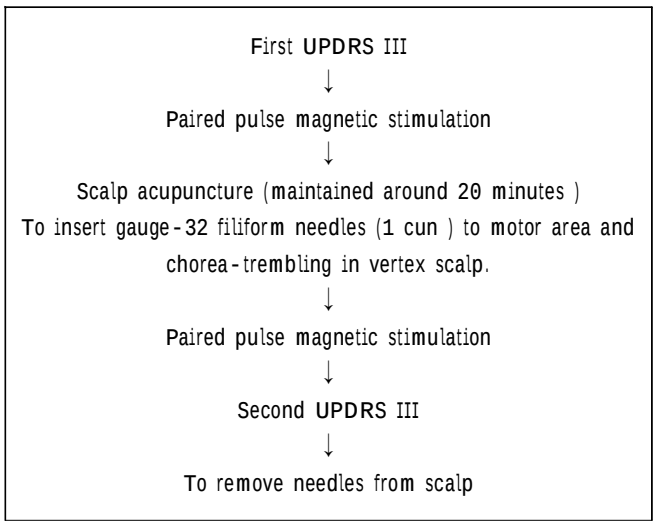

Fig. 1 Following chart of acupuncture experimentation

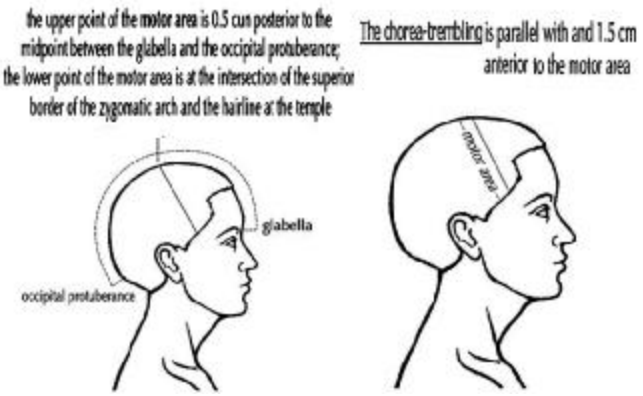

Fig. 2 Scalp points

Surface EMG signals recording from the first dorsal interosseous (FDI) were amplified by Nicolet IIIP, filtered from 3Hz to 2KHz, digitized (sampling rate 1kHz per channel), processed with CED 1401 plus (Cambridge Electronic Device, UK), and stored on a computer. The impedance between the cathode and anode was kept below 5 kΩ during the study.

The motor cortex in left hemisphere was stimulated to use a MAGSTIM 200 (Whitland, Dyfed UK) with a figure-of-8 coil placed at the optimum scalp position to elicit motor responses in the contralateral FDI. Stimulating intensities were expressed as a percentage of the maximum output of the stimulator. Resting threshold was determined during complete electrical muscle silence; active threshold was determined during a tonic contraction of 5% maximum voluntary contraction. Thresholds were defined as the stimulus intensity required to produce a motor evoked potential (MEP) of at least 100 μV peak-to-peak amplitude in at 50% of consecutive trials with the tested muscle.

Two magnetic stimuli converged onto a Bistim module (Whitland, Dyfed, UK) were delivered through the same stimulating coil over the motor cortex. The study was performed with the target muscle at rest. Paired-pulse TMS (Conditioned stimulus) was performed with the first (conditioned) stimulus intensity, set 5% (of stimulator output) below the active threshold, and the second (test) stimulus, adjusted to evoke a muscle response over the relaxed FDI with a peak-to-peak amplitude of approximate 1 mV. Interstimulus intervals (ISIs) between 1 and 17 msec (2, 3, 4, 5, 6, 8, 11 and 16, as eight ISI statuses) were investigated. Conditioned and unconditioned stimuli were randomly intermixed, by programmed pulses from CED 1401 plus, and given every 10 s. At least 10 conditioned and 10 unconditioned trials were collected in each subject for each ISI. The peak-to-peak amplitudes of magnetic conditioned MEPs were compared with the average amplitudes of unconditioned MEPs and expressed as a percentage of the size of the amplitude of the unconditioned response. Kujirai et al. reported that the cortical excitability in this modal of paired pulse magnetic stimulation presents the condition of cortico-cortical inhibition, especially in short ISIs less than 5 msec. This interaction is due to the activation of circuits in the cerebral cortex[13].

4. Statistical Analysis for data

For each experimentation and groups, Student's t tests were also capable of measuring the alteration between responses in some ISIs of paired pulse magnetic stimulation before and during acupuncture. The parametric one-way analysis of variance (ANOVA) was used for the measure of difference among ISIs in each procedure of paired pulse magnetic stimulation. Significance was set at $P<0.05$ for all tests. Data are expressed as means ±S.D. (standard deviation) in the text and are illustrated as means ±S.E.M. (standard error of the mean).

Results

All patients didn't feel predominant improvement in motor symptoms through acupuncture although no adverse events developed. Also there were no differences in UPDRSIII (the motor section of UPDRS).

Cortico-cortical inhibition (CCI)

Ipsilateral ortico-cortical inhibition was investigated over ISIs from 2 to 16 msec. A comparison between the mean data of response percentages before and during acupuncture from nine patients was shown on Figure 3 (Data of eight ISI statuses are illustrated as average percentage means +S.E.M).

In gross vision of Figure 3, two curves (solid and dotted lines) are close. But according to the ANOVA used

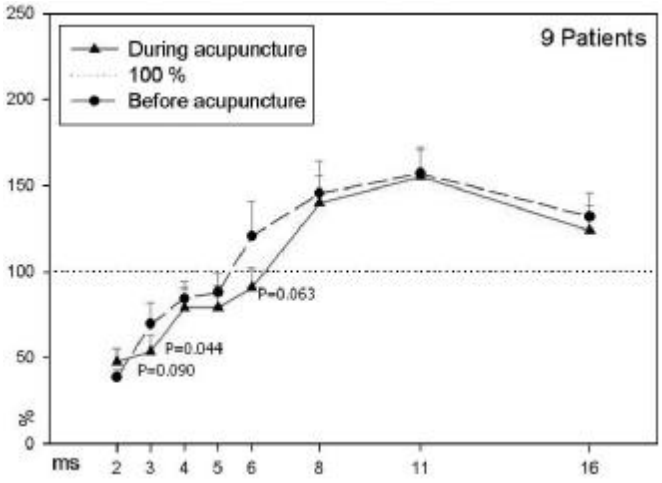

Fig. 3 Solid line: during acupuncture, and dotted line: before acupuncture

for the measure of difference among ISIs reflecting cortical excitability, analysis of variance discovers that there was significantly enhanced inhibition at ISIs of 3 msec ($P<0.05$) whereas relatively less inhibition at ISI of 2 msec. So the result hints increased cortico-cortical inhibition produced by the treat of scalp acupuncture.

Discussion

The use of alternative therapies is common in patients with Parkinson's disease. Forty percent of patients reported the use of at least one form of alternative therapy in a systematic survey of 201 patients with Parkinson's disease. Acupuncture was among the most frequently used treatment modalities. The majority of patients had not discussed the use of alternative treatments with their treating physician[7].

A non-blinded, pilot trial was conducted to assess the safety, tolerability and efficacy of acupuncture for the symptoms of Parkinson's disease[6,7]. Twenty patients received 10 to 16 sessions of acupuncture therapy by a licensed acupuncturist. Broad batteries of tests were used to evaluate the response, including quantitative tests of motor function, UPDRS, H & Y, Beck Depression and Anxiety Inventories, and the SIP. Although 85% of patients reported subjective improvement of individual symptoms, the only objective improvement of significance was in the sleep and rest subcategory of the SIP. Acupuncture was well tolerated, and no adverse effects were reported. No statistically significant differences in UPDRSIII, Parkinson's Disease Questionnaire and Geriatric Depression Scale between controls and patients from a double-blind pilot study for evaluation of acupuncture in the treatment of Parkinson's Disease[17]. But the lasting periods of acupuncture treatments (usual for 3 months) were longer in observational studies of groups of patients reported in the Chinese medical literature [5,10,12], and above trials had lack of individualization of the treatments. In our study, there was neither alteration in UPDRSIII, nor subjective improvement in motor symptoms for all patients through acupuncture although no any adverse event happened. But it does not demonstrate that there is no evidence of long-term benefit according to the result in our study designed for short-term acupuncture influence.

By regulating energetic imbalances within the organism, the insertion of acupuncture needles in specific acupoints have a therapeutic benefit on nearby or distant organs via "meridians"(经络), as a network of channels to connect functional organic systems according to traditional Chinese medicine. According to recent neuropharmacological and neuroimaging data, many of the effects of acupuncture might be mediated by the activation of disease-related areas within the central nervous system. For example, the releases of different kinds of opioid neuropeptides are induced by stimulation of analgesic acupoints, causing the activation of many areas of the limbic/paralimbic systems involved in pain mediation. Furthermore, stimulation of eye-related and language-related acupoints has been shown to activate cortical areas implicated in vision, auditory and language processing, respectively[14].

Changing afferent input by peripheral somatosensory afferent can influence motor cortical organization[15]. Motor-evoked potentials evoked by transcranial magnetic stimulation(TMS) could be increased in the hand muscles innervated by the repetitively stimulated nerve[16]. If multiple brain areas are activated by acupuncture, this may be the consequence of the stimulation of somatosensory afferent fibres, produced by needle insertion. According

to measuring MEP by TMS, C. Maioli and associates[17] demonstrate that simple insertion of the acupuncture needle, which produces only a very mild, localized and short-lasting somatosensory stimulation, is sufficient to induce a significant modulation of excitability of the motor pathways that depart from the primary motor cortex; acupuncture effects can hardly be ascribed to nonspecific changes in whole-system excitability; changes in MEP amplitude following acupuncture depend on the stimulation point and on the investigated muscle so the elicited responses strongly depend on the needling point. Also the change of cortical excitability through acupuncture was noticed in our study, which enhanced cortico-cortical inhibition, at ISIs on 3msec and longer, developed on the motor cortex.

The abnormality of motor cortical inhibition in patients with PD was demonstrated by a significant decrease in the amount of corticocortical inhibition, which improved after L-dopa intake[18] because dopamine might contribute to the associative long-term potentiation-like effect in the motor cortex[19]. In our study, there was no short-term benefit in our patients regardless of relatively strong cortico-cortical inhibition at ISIs on 3msec.

In initial request, the scalp needle should be rotated about 200 times per minute during therapy approach[11], which may give rise to strong somatosensory stimulation in order to enhance certain activity in central nerve system, such as modulation of excitability of the motor pathways via organisational change within the motor and sensory cortex. In our study, scalp needles were maintained subcutaneously without other management after achieving needling sensations, which might be difficult to reach requested strength for acupuncture. The electro-acupuncture may be a stable tool instead of strong manual management and considered to be used further study.

Conclusion

Acupuncture is safe and well tolerated without adverse effects for alternative therapy in patients with Parkinson's disease. It is an argument if (scalp) acupuncture improves motor symptoms of PD before of ambiguous evidences in clinical trials. According to our finding, all patients didn't feel predominant improvement in motor symptoms although none take marked discomfort during acupuncture. Anyway, there were some electrophysical effects in distant for patients. So it is essential to arrange further and long-term studies to ascertain the clinic efficacy and physical mechanism in scalp acupuncture.

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The Short-term Modulation of Scalp Acupuncture on the Cortical Excitability in Patients with Parkinson's Disease: A Pilot Study

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Abstract: Acupuncture was frequently used for alternative treatments in Parkinson's disease because of its safety, but there was an argument whether acupuncture improves motor symptoms or not. Besides, few electrophysiological studies were designed for acupuncture combined with Parkinson's disease Using the technique of paired transcranial pulse magnetic stimulation, we measured the excitability of corticocortical inhibitory circuits to investigate effects of scalp acupuncture from 9 patients with Parkinson's disease. Although patients didn't take any short-term benefit in motor symptoms through the treatment of scalp acupuncture, there was no any adverse event, and some electrophysical effects developed in patients. The enhanced corticocortical inhibition on motor cortex possibly developed at longer interstimulus intervals, and there was a relatively increase in later part of motor-related cortical potentials on the central part and right-side near vertex around over sensory cortex, but was not significant in early potentials. So a further long-term study is essential to ascertain the physical mechanism and clinical effects in scalp acupuncture.

Keywords: scalp acupuncture, acupuncture, cortical excitability, corticocortical inhibition, Parkinson's disease

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