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# **Dense cranial electroacupuncture stimulation for neuropsychiatric disorders: rationale and clinical application**

**密集顱部電針刺激用于神經精神障礙：原理和臨床應用**

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# Neural acupuncture unit (NAU): 神經針刺單元

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*Review Article*

## **NAU: A New Concept for Interpreting Effects and Mechanisms of Acupuncture**

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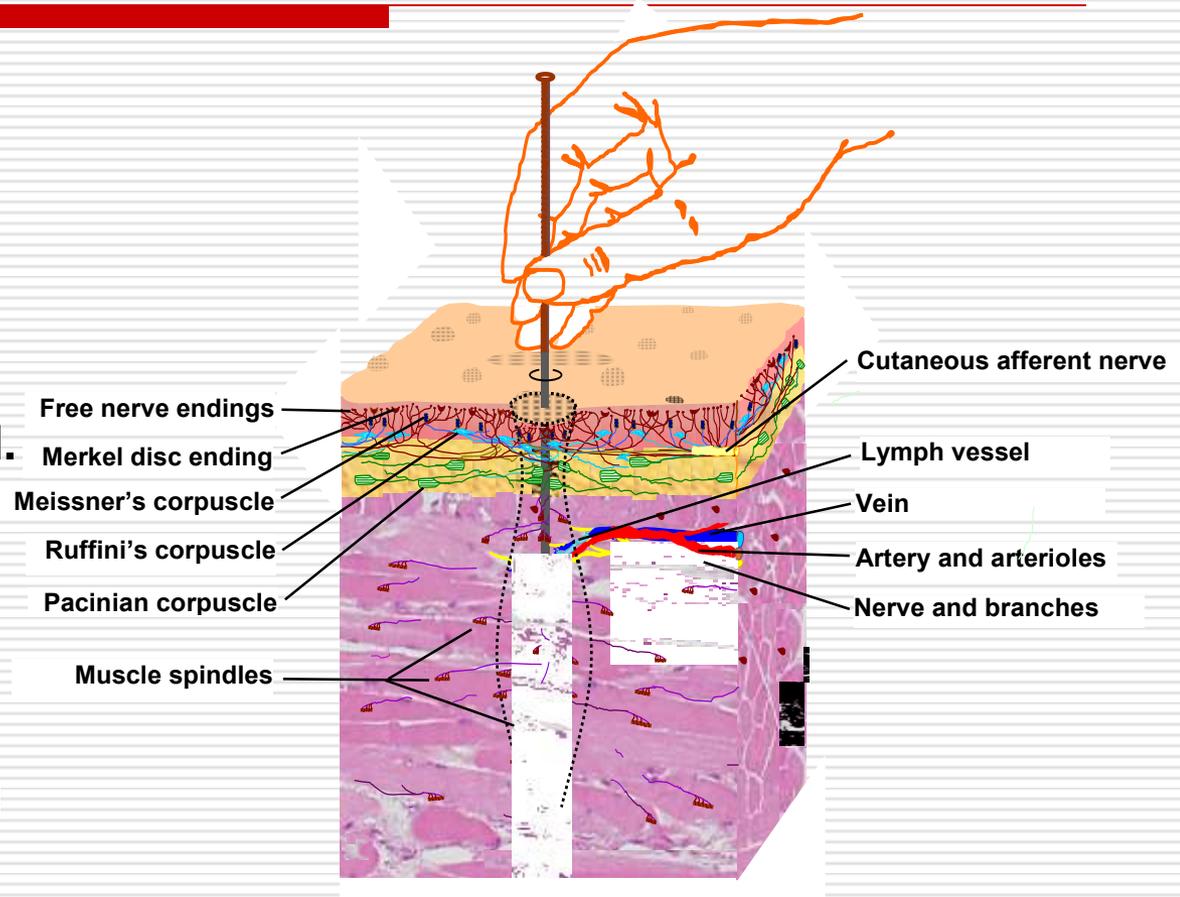
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# What is NAU

**When an acupuncture needle is inserted into a designated point on the body and mechanical or electrical stimulation is delivered, a variety of neural and neuroactive components are activated. A collection of the activated neural and neuroactive components distributed in the skin, muscle, and connective tissues surrounding the inserted needle is defined as a neural acupuncture unit (NAU).**



# Re-definition of acupoints

## 穴位的重新定義

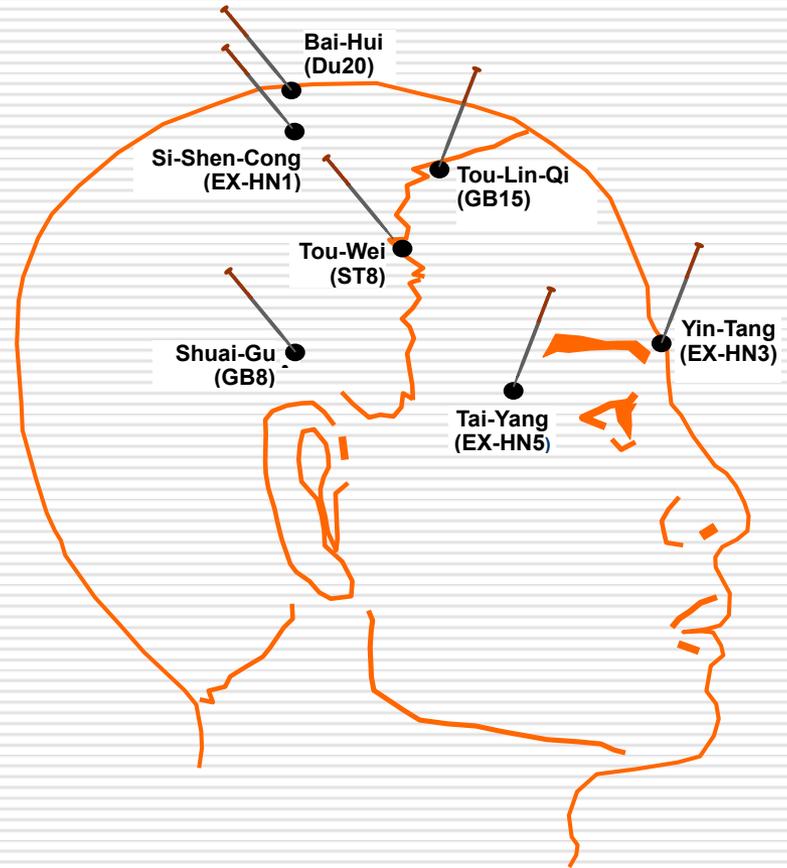
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**The traditional acupoint system represents an anatomical landmark system that indicates local sites where NAUs may contain relatively dense and concentrated neural and neuroactive components, upon which acupuncture stimulation would elicit a more efficient and effective therapeutic response at local and systemic level.**

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# Dense cranial electroacupuncture stimulation (DCEAS)

**DCEAS is a novel stimulation mode in which electrical stimulation is delivered on dense forehead acupoints. It could more efficiently modulate activity of NAU neural and neuroactive components.**



# Why DCEAS is more efficient?

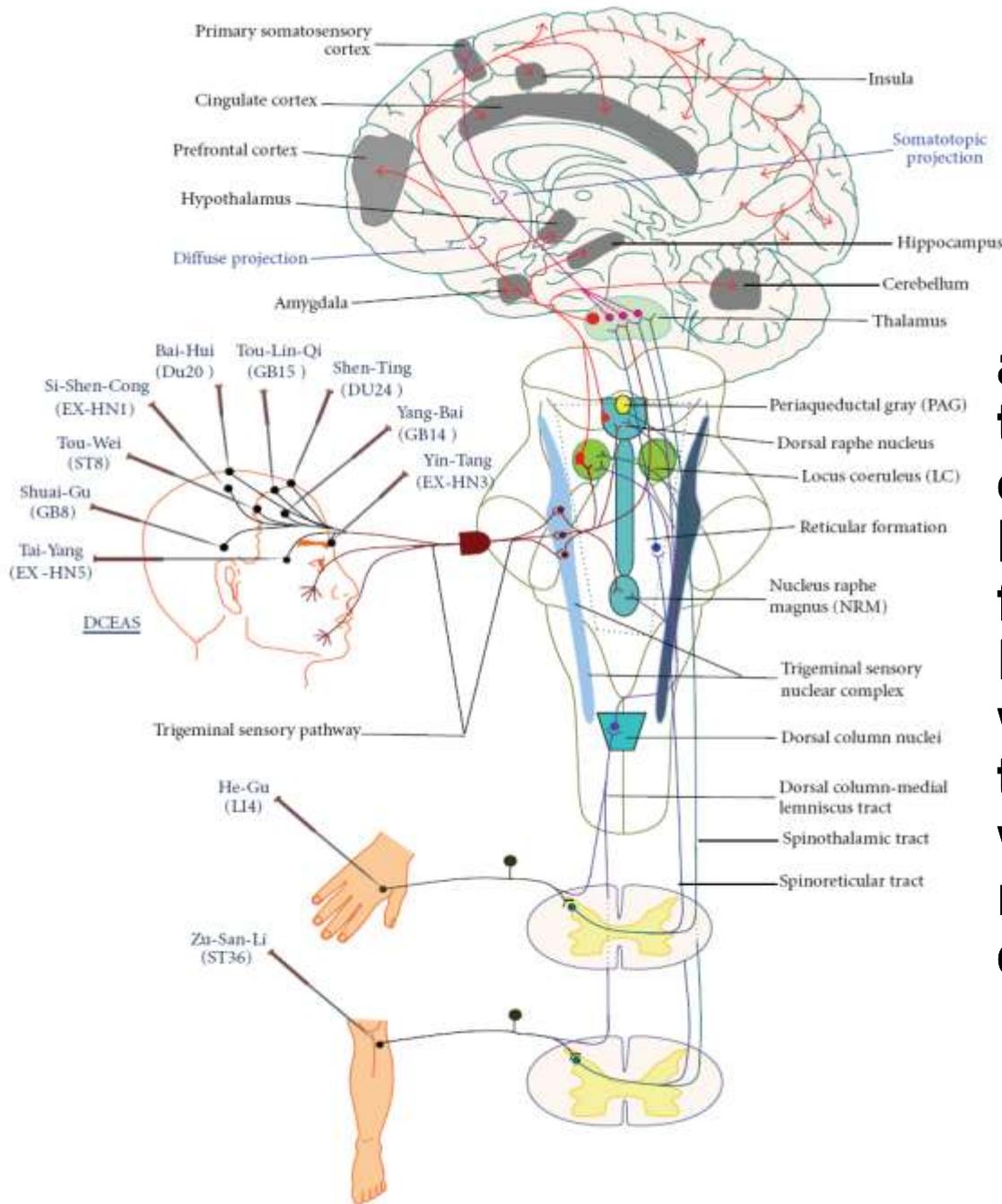
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- **Neural and neuroactive components are much richer in forehead acupoint-based NAUs than other acupoint-based NAUs.**
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# Why DCEAS is specific for neuropsychiatric disorders

**NAUs of forehead acupoints in trigeminal territory have intimate connection with the brainstem reticular formation of NA and 5-HT neuronal systems, which are major transmitters associated with the pathogenesis of major neuropsychiatric disorders.**



# DCEAS for OCD

## Electroacupuncture for Refractory Obsessive-Compulsive Disorder *A Pilot Waitlist-Controlled Trial*

Zhang-Jin Zhang, MD, PhD,\* Xue-Yi Wang, MD,† Qing-Rong Tan, MD,‡ Gui-Xing Jin, MD,†  
and Shao-Min Yao, MD†

**Abstract:** A large proportion of obsessive-compulsive disorder (OCD) patients are refractory to pharmacological and cognitive-behavioral therapy. The aim of this pilot, waitlist-controlled trial was to evaluate the effectiveness of electroacupuncture (EA) as add-on therapy for treatment-resistant OCD. Nineteen patients with treatment-resistant OCD were assigned to EA treatment for 12 sessions (5 sessions per week,  $n = 10$ ) or waitlist for controls ( $n = 9$ ) while continuing their current anti-OCD medications. The clinical outcomes were measured using the Yale-Brown Obsessive-Compulsive Scale and the Clinical Global Impression-Severity at baseline and end point. EA additional treatment produced significantly greater improvements at end point compared with the waitlist group in reducing both Yale-Brown Obsessive-Compulsive Scale ( $10.2 \pm 4.2$  vs.  $18.8 \pm 7.4$ ,  $p = 0.004$ ) and Clinical Global Impression-Severity scores ( $3.0 \pm 1.1$  vs.  $4.4 \pm 1.1$ ,  $p = 0.002$ ). As an additional therapy, EA is effective in alleviating OCD symptoms of treatment-resistant patients. A large-scale controlled study is warranted.

**Key Words:** Electroacupuncture, obsessive-compulsive disorder, pilot trial.

(*J Nerv Ment Dis* 2009;197: 619–622)

gery-related anxiety, and posttraumatic stress disorder (Hollifield et al., 2007; Pilkington et al., 2007). There also have been several studies reported in Chinese journals, showing positive results of electroacupuncture (EA) in patients with OCD, although the studies lacked methodological details and rigorous designs (Su and Zhu, 2004). In addition, EA therapy has been found to alleviate obsession symptoms in female subjects with obesity (Cabioglu et al., 2007). These observations have led us to believe that acupuncture may be also beneficial for OCD. The purpose of this waitlist-controlled pilot trial was to evaluate the effectiveness of EA additional therapy in the treatment of refractory OCD.

### METHODS

Male and female patients were eligible for the study if they met all of the following criteria: (1) aged 12 to 65 years; (2) had a primary DSM-IV diagnosis of OCD; (3) had a documented treatment-resistant status, as defined by the absence of clinically significant improvement after treatment with at least 2 anti-OCD medications at usually effective doses and/or cognitive-behavioral therapy for a time generally sufficient to demonstrate symptom relief; (4) had persistent OCD symptoms, as evidenced by the

# DCEAS for postpartum depression



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Research report

## Randomized non-invasive sham-controlled pilot trial of electroacupuncture for postpartum depression

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# DCEAS similar approach for insomnia

## ELECTROACUPUNCTURE FOR INSOMNIA ASSOCIATED WITH DEPRESSION

10.5665/SLEEP.1056

### Electroacupuncture for Residual Insomnia Associated with Major Depressive Disorder: A Randomized Controlled Trial

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<sup>1</sup>Department of Psychiatry, University of Hong Kong, Hong Kong SAR, China; <sup>2</sup>School of Chinese Medicine, Hong Kong Baptist University, Hong Kong SAR, China; <sup>3</sup>School of Chinese Medicine, University of Hong Kong, Hong Kong SAR, China; <sup>4</sup>Department of Community Medicine, University of Hong Kong, Hong Kong SAR, China.

**Study Objectives:** To evaluate the efficacy and safety of electroacupuncture as an additional treatment for residual insomnia associated with major depressive disorder (MDD).

**Design:** Randomized, placebo-controlled.

**Setting:** A psychiatric outpatient clinic.

**Participants:** 78 Chinese patients with DSM-IV-diagnosed MDD, insomnia complaint, a Hamilton Rating Scale for Depression (HDRS<sub>17</sub>) score ≤ 18, and fixed antidepressant dosage.

**Intervention:** Electroacupuncture, minimal acupuncture (superficial needling at non-acupuncture points), or noninvasive placebo acupuncture 3 sessions weekly for 3 weeks.

**Measurements and Results:** Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), HDRS<sub>17</sub>, 1 week sleep diaries, and 3 day actigraphy were administered at baseline, 1 week post-treatment, and 4 week post-treatment. There was significant group by time interaction in ISI, PSQI, and sleep diary-derived sleep efficiency (mixed-effects models,  $P = 0.04$ ,  $P = 0.03$ , and  $P = 0.01$ , respectively). Post hoc pairwise comparisons revealed that electroacupuncture and minimal acupuncture were more efficacious than placebo acupuncture in ISI and PSQI at 1 week and 4 week post-treatment. Minimal acupuncture resulted in greater improvement in sleep diary-derived sleep efficiency than placebo acupuncture at

# DCEAS for major depression

OPEN ACCESS Freely available online



## Dense Cranial Electroacupuncture Stimulation for Major Depressive Disorder—A Single-Blind, Randomized, Controlled Study

Zhang-Jin Zhang<sup>1\*</sup>, Roger Ng<sup>1</sup>, Sui Cheung Man<sup>1</sup>, Tsui Yin Jade Li<sup>1</sup>, Wendy Wong<sup>1</sup>, Qing-Rong Tan<sup>3</sup>, Hei Kiu Wong<sup>1</sup>, Ka-Fai Chung<sup>4</sup>, Man-Tak Wong<sup>2</sup>, Wai-Kiu Alfert Tsang<sup>2</sup>, Ka-chee Yip<sup>2</sup>, Eric Ziea<sup>5</sup>, Vivian Taam Wong<sup>5</sup>

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### Abstract

**Background:** Previous studies suggest that electroacupuncture possesses therapeutic benefits for depressive disorders. The purpose of this study was to determine whether dense cranial electroacupuncture stimulation (DCEAS) could enhance the antidepressant efficacy in the early phase of selective serotonin reuptake inhibitor (SSRI) treatment of major depressive disorder (MDD).

# Previous studies of acupuncture for depression

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Review

The effectiveness and safety of acupuncture therapy in depressive disorders: Systematic review and meta-analysis

Zhang-Jin Zhang<sup>a,\*</sup>, Hai-Yong Chen<sup>a</sup>, Ka-chee Yip<sup>b</sup>, Roger Ng<sup>b</sup>, Vivian Taam Wong<sup>c</sup>

- **Enhancing antidepressant efficacy in MDD and PSD.**
- **Improve mild depression.**
- **Improve sleep and other comorbide symptoms.**
- **Reduce adverse effects.**

# Inclusion criteria

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- 1. Aged 25–65 yrs**
  - 2. DSM-IV diagnosis of MDD;**
  - 3. HAMD-17 score >18**
  - 4. Clinical Global Impression-Severity (CGI-S) score  $\geq 4$  (moderately ill).**
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# Treatment and assessment

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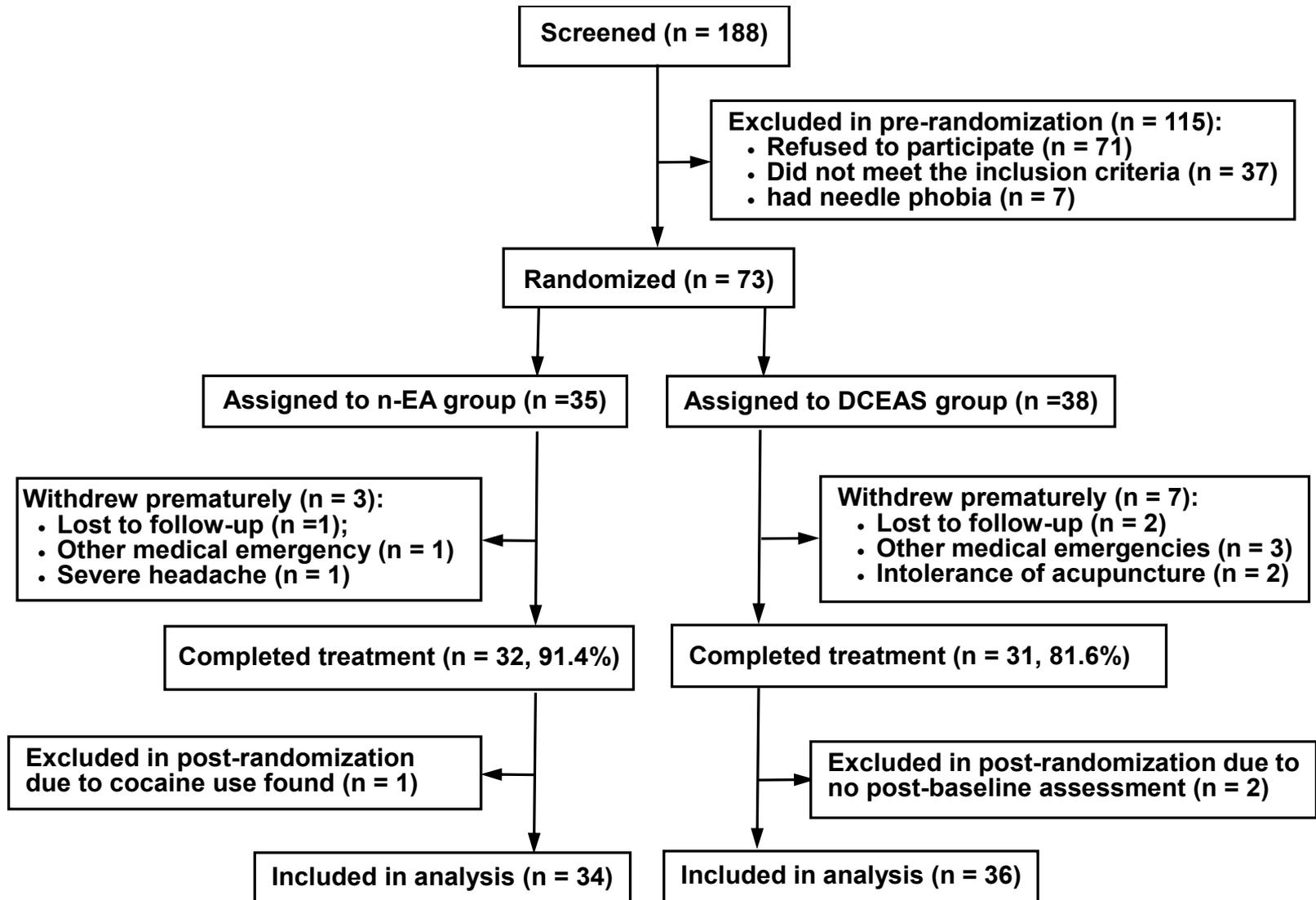
- **73 patients were randomized to receive 9 sessions of DCEAS (n = 38) or noninvasive EA control procedure (n-EA, n = 35) combined with fluoxetine (FLX) for 3 wks (3 sessions per wk).**
  
  - **Clinical assessment:**
    - **HAMD-17**
    - **Clinical Global Impression-severity (CGI-S),**
    - **Self-rating Depression Scale (SDS)**
    - **Clinical response: > 50% reduction in HAMD-17**
    - **Remission rate: <7 in score on HAMD-17.**
-

# Credibility of sham and DCEAS

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- After the completion of 9-session treatment, patients were asked: “As we informed you that you had an equal chance of receiving sham or active acupuncture treatment, which do you think you had received?”**
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# Recruitment and allocation



# Baseline characteristics of patients

| Variables  | Sham<br>(n = 34) | DCEAS<br>(n = 36) | P values<br>(t or $\chi^2$ ) |
|--|------------------|-------------------|------------------------------|
| Female, n (%)  | 33 (97.1)        | 25 (69.4)         | 0.006                        |
| Age (yrs) <sup>a</sup>   | 48.2 ± 9.8       | 46.3 ± 9.9        | 0.414                        |
| Duration of MDD (yrs) <sup>a</sup>                                   | 7.3 ± 7.1        | 7.9 ± 8.0         | 0.744                        |
| No. of previous depressive episodes <sup>a</sup>                     | 3.6 ± 4.4        | 4.9 ± 6.1         | 0.332                        |
| No. (%) of patients with first-onset MDD                             | 3 (8.8)          | 2 (5.5)           | 0.669                        |
| No. (%) of patients with previous psychiatric admission              | 8 (23.5)         | 7 (19.4)          | 0.901                        |
| No. (%) of patients with family members having mental illnesses.     | 9 (26.5)         | 13 (36.1)         | 0.800                        |
| No. (%) of patients with previous acupuncture treatment <sup>b</sup> | 22 (64.7)        | 24 (66.7)         | 0.937                        |
| No. (%) of patients receiving psychotropic medications at study      | 6 (17.6)         | 7 (19.4)          | 0.909                        |
| SSRIs  | 3                | 3                 |                              |
| SNRIs  | 1                | 1                 |                              |
| Mood stabilizers   | 1 <sup>d</sup>   | 1                 |                              |
| Benzodiazepines  | 2                | 2                 |                              |
| Baseline HAMD-17 score <sup>a</sup>                                  | 23.1 ± 3.6       | 23.9 ± 3.8        | 0.321                        |
| Baseline CGI-S <sup>a</sup>  | 4.3 ± 0.5        | 4.4 ± 0.5         | 0.760                        |
| Baseline SDS score <sup>a</sup>                                      | 40.6 ± 14.5      | 41.9 ± 14.0       | 0.704                        |

# FLX doses taken

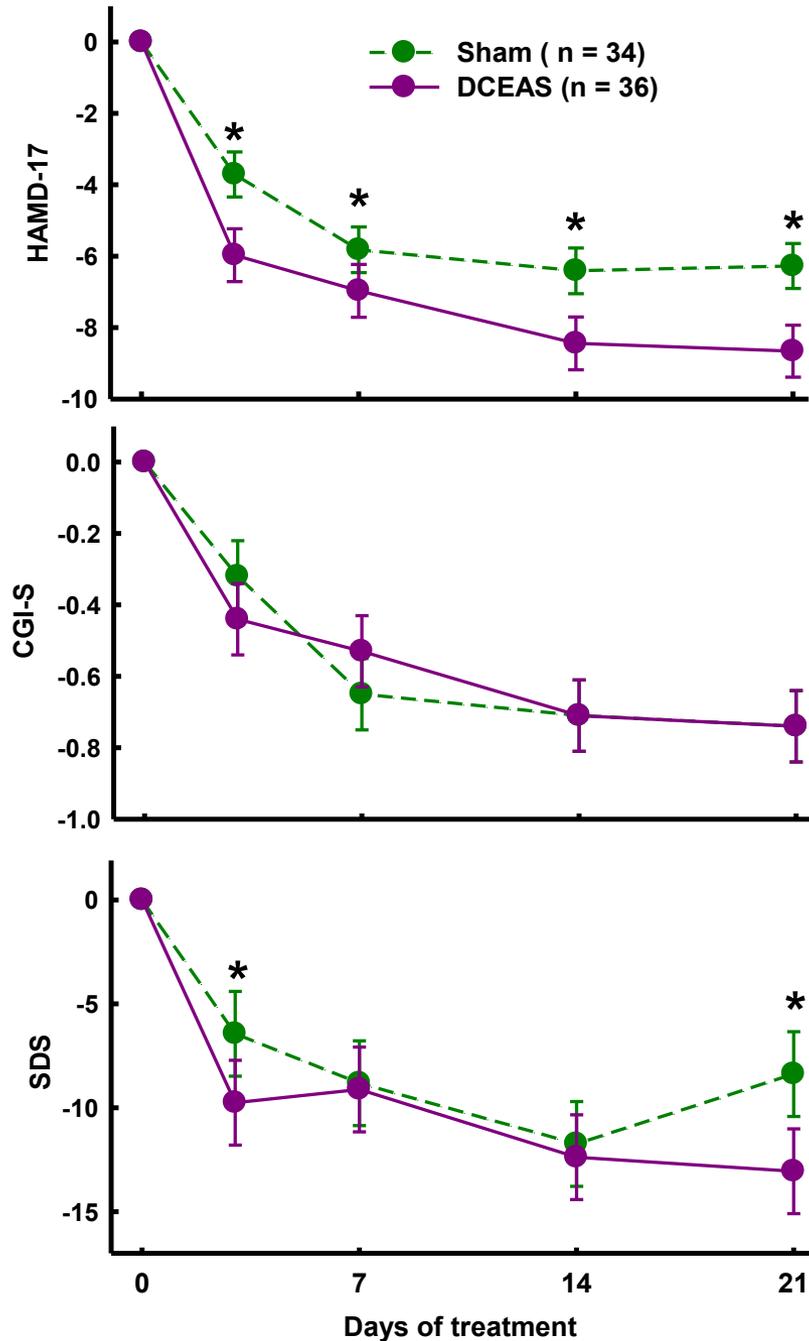
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- **The average dose of FLX in DCEAS group was similar to that in control group:**
    - **23.0 +/- 3.2 mg/day vs.**
    - **23.4 +/- 2.4 mg/day**
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# Efficacy

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- DCEAS-treated group had significantly greater improvement on both HAMD-17 and SDS.**
  - There were significant differences in HAMD-17 between the two groups at Day 3 through Day 21 and in SDS at Day 3 and Day 21.**
  - DCEAS produced a higher clinical response rate compared to sham group (19.4% vs. 8.8%), but similar in remission rate (2.7% vs. 2.9%).**
-



**Mean changes from baseline in score on HAMD-17, CGI-S, and SDS over time**

# Safety and tolerability

The incidence of any adverse events was not significantly different between the groups

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| Event                                | Sham (n = 34) | DCEAS (n = 36) | $\chi^2$ | P value            |
|--------------------------------------|---------------|----------------|----------|--------------------|
| Dizziness                            | 15 (44.1)     | 11 (30.6)      | 0.858    | 0.354              |
| Tiredness                            | 10 (29.4)     | 15 (41.7)      | 0.672    | 0.412              |
| Nausea                               | 10 (29.4)     | 10 (27.8)      | 0.013    | 0.910              |
| Excessive sweating                   | 9 (26.5)      | 6 (16.7)       | 1.403    | 0.236              |
| Headache                             | 8 (23.5)      | 10 (27.8)      | 0.018    | 0.894              |
| Transient tachycardia                | 8 (23.5)      | 9 (25.0)       | 0.018    | 0.892              |
| Insomnia                             | 7 (20.6)      | 9 (25.0)       | 0.024    | 0.877              |
| Uncomfortable for needling sensation | 7 (20.6)      | 14 (38.9)      | 1.985    | 0.159              |
| Vomiting                             | 4 (11.8)      | 3 (8.3)        |          | 0.706 <sup>a</sup> |
| Unsteadiness                         | 2 (5.9)       | 6 (16.7)       |          | 0.266 <sup>a</sup> |
| Somnolence                           | 2 (5.9)       | 6 (16.7)       |          | 0.266 <sup>a</sup> |

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# Results of credibility

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- 45.5% (15/33) of patients in sham EA perceived to have received DCEAS, while 23.5% (8/34) of patients in DCEAS believed to have control treatment. It was not significantly different ( $P = 0.103$ ).**
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# **A pilot PET study of DCEAS in depressed patients (1)**

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- 12 MDD patients received 12 sessions of DCEAS treatment in 3 weeks. PET scanning was conducted at baseline and endpoint. 6 healthy volunteers were included to serve as PET scan control.**
  - The four regions displaying significant response were identified: dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC), caudate nucleus, and posterior cerebellar cortex.**
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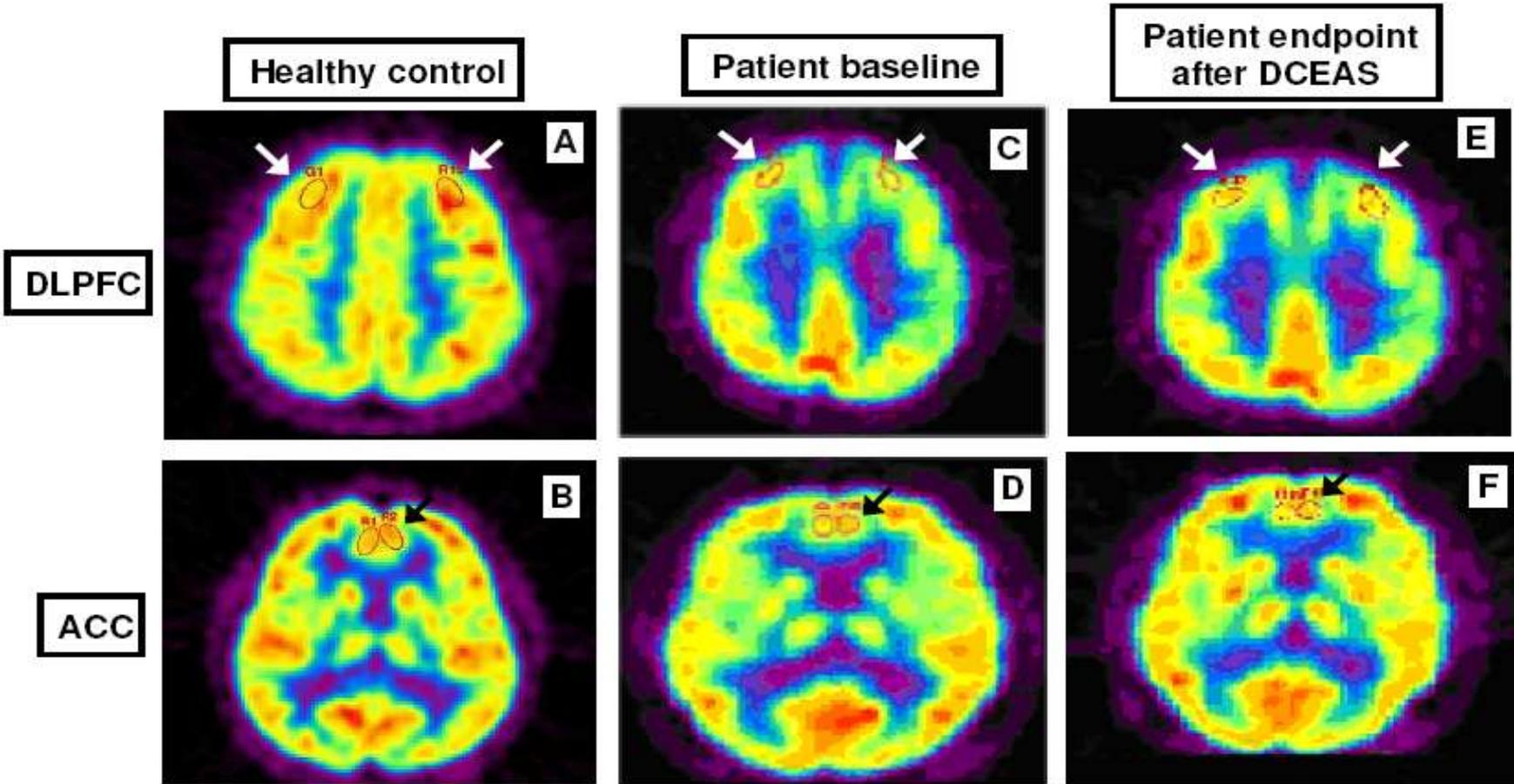
# A pilot PET study of DCEAS in depressed patients (2)

**Table 1. Changes in glucose metabolic levels measured using PET (<sup>18</sup>F)-Fluorodeoxyglucose (FDG) scan in the related brain regions following 3-week DCEAS intervention in MDD patients with compared to healthy controls**

|                                | Healthy controls (n = 6) |           | MDD subjects (n = 12)  |                        |
|--------------------------------|--------------------------|-----------|------------------------|------------------------|
|                                | Baseline                 | Endpoint  | Baseline               | Endpoint               |
| Dorsolateral prefrontal cortex |                          |           |                        |                        |
| L                              | 3.0 (0.1)                | 3.1 (0.1) | 2.5 (0.4) <sup>a</sup> | 3.0 (0.3) <sup>b</sup> |
| R                              | 2.9 (0.1)                | 3.1 (0.1) | 2.5 (0.3) <sup>a</sup> | 2.9 (0.3) <sup>b</sup> |
| Anterior cingulated cortex     |                          |           |                        |                        |
| L                              | 2.7 (0.3)                | 3.0 (0.2) | 2.4 (0.4)              | 2.7 (0.4) <sup>b</sup> |
| R                              | 2.8 (0.3)                | 2.8 (0.2) | 2.3 (0.3) <sup>a</sup> | 2.7 (0.2) <sup>b</sup> |
| Caudate nucleus                |                          |           |                        |                        |
| L                              | 2.8 (0.3)                | 3.0 (0.2) | 2.5 (0.2)              | 2.7 (0.6)              |
| R                              | 2.7 (0.3)                | 2.8 (0.1) | 2.4 (0.3)              | 2.6 (0.4) <sup>b</sup> |
| Posterior Cerebellar cortex    |                          |           |                        |                        |
| L                              | 2.3 (0.2)                | 2.5 (0.1) | 2.3 (0.2)              | 2.6 (0.2) <sup>b</sup> |
| R                              | 2.4 (0.1)                | 2.4 (0.1) | 2.3 (0.3)              | 2.5 (0.3) <sup>b</sup> |

Data are expressed as mean  $\pm$  standard deviation (SD) and analyzed using repeated measure two-way ANOVA with Student-Newman-Keuls multiple comparisons: <sup>a</sup>  $p < 0.05$ : vs. corresponding values of healthy controls; <sup>b</sup>  $p < 0.05$ : vs. baseline values within groups.

# A pilot PET study of DCEAS in depressed patients (3)



# What we are doing for DCEAS

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- We are currently applying both PET and fMRI to identify central neural network in response to DCEAS in 40 MDD patients in a randomized controlled design. The project was supported by HK Research Gant Council.**
  - We are also investigating behavioral and neurochemical effects of DCEAS in animal models of depression.**
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# Conclusions

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- ❑ **DCEAS is effective in reducing OCD, depression, and insomnia symptoms.**
  - ❑ **DCEAS also could improve neuroimaging-measured brain activity in depressed patients.**
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# Acknowledgements

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  - ❑ **We thank the following colleagues at Department of Psychiatry of Kowloon Hospital for help recruit MDD patients: Ka-Lik Kwan, Chun-Ting Chan, Man-Lui Chan, Chi-Kwan Cheung, Janice Chik, Lung-Kit Hui, Man-Man Kwan, Chee-Kin Lee, Kwok-Chuen Ng, Yin-Ting Ng, Ting-Keung Poon, Fu-Yin Tong, Wai-Ching Yan, Kam-Hing Yeung, Tin-Yan Yeung, Mei-Kuen Frieda Shiu, Cheuk-Kin Tang, Pui-Shan Tse, Ngar-Fong Lam, See-Cheuk Fu, Chui-Lin Carol Ching, Ka-Fai Ho, Sau-Lai Tai, Sau-Ming Chan, Yiu-Kwun Law, Yuk-Kwan Yvonne Kwong.**
  - ❑ **We thank Professor Yong Huang in Guangzhou Nanfang Medical University for PET study.**
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## EAST-WEST PERSPECTIVES

China's rapid development has attracted academic interest from around the world, and at the same time ignited interest within China in international collaborations. This has given a boost to HCU's traditional role as a meeting point of East and West. Our academics are pursuing research that reflects on developments in China and are also entering into joint research with academics there.

Our scholarship on China covers a wide range of topics. For example, in 2010-11 the book *Mao's Great Famine: The History of China's Most Devastating Catastrophe, 1958-1962* was published by C. Hart Professor of Humanities Frank Dikötter and won the 2011 BBC Samuel Johnson Prize for Non-Fiction; studies by the School of Chinese Medicine showed how traditional Chinese medicine and modern treatments interacted in patients suffering from schizophrenia, asthma and depression; and the largest-ever survey of child victimisation in China was carried out by the Department of Social Work and Social Administration.

Similarly our collaborations with mainland universities are diverse. Examples in 2010-11 include the Department of Physics' participation in the Daya Bay Reactor Neutrino Experiment in Guangdong, a major international project; studies of the endangered Chinese white dolphin by scientists in the Sowe Institute of Marine Science and colleagues in Taiwan and Guangdong; and the publication of a report linking climate change with large-scale human crises by academics in the Department of Geography and contributors from three universities in China.

HCU has made collaborations with Mainland China one of its main research strategies. We have a Strategic Research Theme on China Studies, which covers China business and economics, China-West studies and contemporary China. We also promote research and collaborations through such units as the Wah Ching Centre of Research on Education in China, the Centre for Chinese Law, and the Institute for China and Global Development. Our activities in China received a boost in 2010-11 with the announcement of new HCU-affiliated research centres there and new resources from the central government to support our research (see main article, Breaking Down Boundaries).

## MEDICINE AND MENTAL HEALTH

*Traditional Chinese medicine is increasingly being used in the medical mainstream, including in mental health. Two clinical studies led by Dr Zhang Zhanjin (right) of the School of Chinese Medicine investigated acupuncture treatment for depression and interactions between Chinese medicine and antipsychotic drugs in schizophrenia. Electroacupuncture was found to augment the effectiveness of antidepressants in depressed patients in the early stage of their treatment, while schizophrenia had mixed outcomes from taking a combination of Chinese medicine and antipsychotic drugs – a majority benefited but a significant minority had a worsened outcome. The findings contribute to evidence-based alternative medicine and the development of Chinese medicine.*



# Thank you!