

Acupuncture in 21st Century Anesthesia: Is There a Needle in the Haystack?

Shu-Ming Wang, MD,* Richard E. Harris, PhD,† Yuan-Chi Lin, MD, MPH,‡ and Tong-Joo Gan, MD, FRCA, MHSS§

Acupuncture, a component of Traditional Chinese Medicine, has developed over a period of more than 3000 years and is based on the concept of “*天人合一*” unification of the human with his environment.¹ Acupuncture practice has constantly evolved throughout history and has been based on the knowledge and ideas garnered from astronomy, nature, science, and technology.^{2,3} In contrast to what was stated by Colquhoun and Novella,⁴ acupuncture consists of applying various stimuli (e.g., pressure, needle, heat, laser, suction cup, injection, and electrical stimulation⁵ as well as most recently ultrasound waves)⁶ on/into specific acupuncture points (acupoints) to restore a patient’s health. During the early 1970s, this traditional healing practice became more popular because of programs vigorously supported by the Chinese government⁷ leading to a greater international awareness of this therapeutic approach. A recent PubMed search of “acupuncture clinical trials” yields 3833 articles, demonstrating that acupuncture has been investigated as a treatment for many medical conditions. A potential reason for the popularity of acupuncture among patients may be the “individualistic” or “person-centered” approach.

Although >40 disorders have been recognized by the World Health Organization⁸ as conditions that can benefit from acupuncture treatment, many within the field of science view acupuncture as “quackery” and “pseudoscience,” and its effect as “theatrical placebo.”^{4,9–14} It seems somewhat naive to totally condemn the practice of acupuncture, while accepting orthodox medicine as the basis for treating all medical conditions. Herein, we describe evidence supporting the thesis that acupuncture, as part of anesthesia practice, can provide clinically meaningful benefits for patients. Postoperative nausea and vomiting (PONV),^{15–17}

postoperative pain,^{18,19} and chronic pain conditions^{20,21} are 3 clinical problems pertinent to anesthesia practice and yet cannot be adequately treated owing to the ineffective or only partially effective pharmacological interventions. Unsuccessful conventional treatments for these clinical entities have caused significant financial burden, health care cost, and patient dissatisfaction. As a result, acupuncture has been investigated as a treatment or a complementary treatment for these 3 clinical entities.

To validate acupuncture efficacy, multiple sham techniques and placebo instruments have been developed and are used in clinical trials and experimental conditions. These techniques and instruments are thought to control the “nonspecific” effect of acupuncture and are broadly termed “sham” or “placebo” acupuncture in the literature. Sham acupuncture is defined as an intervention, which mimics the sensation of acupuncture stimulation; however, it is thought to lack the analgesic and antiemetic effects of acupuncture. In both clinical and experimental trials, sham acupuncture can be classified based on whether the intervention penetrates the skin. Penetrating shams (minimal acupuncture) involve shallow insertion of acupuncture needles into actual acupuncture points with minimal stimulation or into sham point stimulation (applying same needling techniques but in areas where there is no documentation of acupuncture points or meridians). Nonpenetrating shams have also been developed, and these can either be sensorial sham (applying a toothpick or a filament on the skin surface of acupuncture points simulating needle sensations), or visual sham (applying placebo needles [e.g., Streitberger needle] that visually shorten when pressed onto the skin).

Using the above “controlling” techniques, acupuncture has been validated in various clinical trials. Thus far, the strongest evidence supporting acupuncture efficacy is pericardium-6 (PC-6) acupoint stimulation for PONV prophylaxis. The PC-6 acupoint Neiguan, translated as “inner gate,” is commonly used to treat nausea and vomiting in traditional Chinese medicine.^{1,5} This acupoint is located 5 cm proximal from the wrist between the palmaris longus and flexor carpi radialis. A meta-analysis²² has demonstrated the efficacy of PC-6 for the treatment of PONV in sham-controlled trials. Subsequently, a Cochrane Database article in 2004²³ showed that acupuncture stimulation at PC-6 is superior to pooled antiemetic prophylaxis in preventing nausea. An updated Cochrane review²⁴ surveyed 40 clinical trials (a total of 4858 participants) and found that compared with sham treatment, PC-6 acupoint stimulation is as effective as conventional antiemetics

From the *Department of Anesthesiology and Perioperative Care, University of California-Irvine School of Medicine, Irvine, California; †Department of Anesthesiology, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan; ‡Department of Anesthesia, Harvard Medical School, Boston, Massachusetts; and §Department of Anesthesiology, Duke School of Medicine, Durham, North Carolina.

Accepted for publication February 1, 2013.

Funding: None.

The authors declare no conflicts of interest.

Reprints will not be available from the authors.

Address correspondence to Shu-Ming Wang, MD, Department of Anesthesiology, University of California-Irvine and University of Connecticut, 114 Woodland St., Hartford, CT 06105. Address e-mail to smwang800@gmail.com.

Copyright © 2013 International Anesthesia Research Society

DOI: 10.1213/ANE.0b013e31828f5efa

(e.g., droperidol,²⁵ ondansetron,²⁶ and others).²⁷ PC-6 acupuncture can also complement antiemetics in reducing PONV. More importantly, the side effects associated with PC-6 acupoint stimulation were minor and self-limiting.²⁴ Although the number needed to treat (NNT) for PONV with acupuncture ranged from 34 to 5 patients, this is similar to NNT for conventional antiemetics. For example, the NNT for nausea for IV droperidol 0.5 to 0.75 mg is 4.8 (95% confidence interval [CI], 3.0–12) and for vomiting is 10 (95% CI, 4.6 to –51).²⁸ Similarly, metoclopramide 10 mg IV, a commonly used drug to prevent nausea and vomiting in the perioperative period, has an NNT of 30.²⁹ Direct comparison between acupuncture and IV ondansetron reveals that the NNT for nausea (0–6 hours) is 4 (95% CI, 2.0–11.4) vs 5 (95% CI, 2.3–120.6), respectively, and for vomiting (0–6 hours) the NNT is 6 (95% CI, 3.0–84.7) vs 5 (2.9–21.0), respectively.³⁰ Comparing acupuncture versus IV ondansetron, the NNT for nausea (0–24 hours) is 20 (95% CI, 3.7 to –5.8) vs 27 (95% CI, 3.9 to –5.5) respectively, and the NNT for vomiting (0–24 hours) is 18 (95% CI, 3.7 to –6.4) vs 9 (95% CI, 3.1 to –11.2).³⁰

Acupuncture has also been investigated as an adjunct for acute postoperative pain and various chronic pain conditions. A recent review article³¹ included 15 randomized controlled trials that compared acupuncture with sham controls in managing postoperative pain. The investigators found that patients in the acupuncture group required less cumulative opioid consumption (the average cumulative opioid consumption was –3.14 mg [95% CI, –5.15 to –1.14], –8.33 mg [95% CI, –1.06 to –5.61], and –9.14 mg [95% CI, –16.07 to –2.22] at 8, 24, and 72 hours, respectively). As a result, acupuncture-treated patients had a lower incidence of opioid-related side effects, such as nausea (risk ratio [RR]: 0.67; 95% CI, 0.53–0.86), dizziness (RR: 0.65; 95% CI, 0.52–0.81), sedation (RR: 0.78; 95% CI, 0.61–0.99), pruritus (RR: 0.75; 95% CI, 0.59–0.96), and urinary retention (RR: 0.29; 95% CI, 0.12–0.74), as compared with sham control groups.³¹

Acupuncture analgesia also has been investigated as a treatment for chronic pain conditions. Another systematic review with 31 randomized controlled trials found that acupuncture may have a specific analgesic effect in treating chronic headache patients because the combined response rate in the acupuncture group was significantly higher compared with sham acupuncture either at the early (8 weeks) follow-up period (RR: 1.19; 95% CI, 1.08–1.30) or late (6 months) follow-up period [RR: 1.22; 95% CI, 1.04–1.43]. Acupuncture was also superior to medication therapy for headache intensity (weighted mean difference [WMD]: –8.54 mm; 95% CI, –15.52 to –1.57), headache frequency (WMD: –0.70; 95% CI, –1.38 to –0.02), physical function (WMD: 4.16; 95% CI, 1.33–6.98), and response rate (RR: 1.49; 95% CI, 1.02–2.17).³² A recent individual patient meta-analysis of 29 randomized control trials with 17,922 patients indicated that acupuncture was statistically superior to control for all analysis ($P < 0.001$).³³ In this report, effect sizes between acupuncture and sham were 0.37, 0.26, and 0.15 for musculoskeletal pain, osteoarthritis (OA), and chronic headache, respectively.³³ These significant differences between true and sham acupuncture indicate that acupuncture is more effective than placebo. The authors concluded that acupuncture is effective for the treatment of chronic pain and is therefore a reasonable treatment option.³³ Colquhoun and Novella⁴

commented that real acupuncture was better than sham; however, by a small amount that lacked any clinical significance.⁴ While there is ongoing debate regarding the specific analgesic effect of acupuncture, the effect sizes reported are on par with standard accepted pharmacologic therapy for chronic pain. For example, a meta-analysis of 23 trials (10,845 patients) estimated that the analgesic efficacy of nonsteroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors, in osteoarthritic knee pain was 1.01 cm (95% CI, 0.74–1.28) on a 10 cm visual analog scale, just 15.6% better than placebo.³⁴ Thus, the effect size of nonsteroidal anti-inflammatory drugs versus placebo for pain reduction is similar to real acupuncture versus sham acupuncture in reduction of pain in OA knee pain patients. These data highlight the comparable effect sizes of acupuncture and conventional pharmacologic treatments for knee OA. Another aspect of therapeutic intervention that is as important, if not more so, is the potential to cause harm or adverse effects as a result of treatment. There is significant harm and the potential for even death caused by conventional medications leading to the withdrawal of some medications from use by regulatory authorities over the years.^{35,36} This is in sharp contrast to the safety record of acupuncture performed by trained acupuncturists.^{37–39}

Furthermore, epidemiologists have evaluated the cost effectiveness of acupuncture in the management of various chronic pain conditions.^{40–43} Acupuncture was found to improve health-related quality of life at a small additional cost and was relatively cost-effective compared with a number of other interventions.⁴⁰ A pragmatic trial evaluating the clinical and economic effectiveness of acupuncture for chronic low back pain demonstrated that acupuncture plus routine care was associated with marked clinical improvements and was relatively cost-effective.⁴¹ Acupuncture was also found to improve quality of life and was cost-effective as a treatment for other pain conditions (dysmenorrheal, OA, and neck pain).^{42,43} Moreover, neuroscientists have applied brain imaging techniques, e.g., functional magnetic resonance imaging (fMRI) and positron emission tomography to explore the neural correlates of acupuncture as an antiemetic and an analgesic. Using fMRI, neuroscientists have identified specific brain regions related to PC-6 stimulation that further suggest that the antiemetic effects of acupuncture may be distinct from sham or placebo effects.^{44,45}

Napadow et al.⁴⁶ demonstrated cortical amplification and altered primary somatosensory digit somatotopy in patients suffering from carpal tunnel syndrome that can be corrected or normalized by a series of acupuncture treatments. The results of this study demonstrate that acupuncture shows promise in inducing beneficial cortical plasticity manifested by more focused digital representations. After controlling for noncutaneous somatosensory and cognitive elements of acupuncture, a subsequent study further demonstrated that acupuncture treatment for carpal tunnel syndrome patients cannot be explained as merely a placebo effect.⁴⁷

Dhond et al.⁴⁸ found verum stimulations produced more extensive modulation of limbic and paralimbic regions than sham stimulations in healthy volunteers. Pariente et al.⁴⁹ explored brain processing during verum, covert sham and overt sham needling at acupoint LI-4 in pain patients using positron emission tomography. These investigators suggested that activity within the insular cortex may be

responsible for the specific effect of acupuncture, whereas modulation of the dorsolateral prefrontal cortex, rostral anterior cingulate cortex, and periaqueductal gray may be related to expectation.⁴⁹ Kong et al.⁵⁰ used both behavior assessment and fMRI to examine patient expectations and the physiological effect of acupuncture in a group of healthy volunteers. They found that conditioning positive expectation can amplify acupuncture analgesia as detected by subjective pain sensory rating changes and objective fMRI signal changes in response to calibrated noxious stimuli. In addition, while both verum and sham acupuncture can have analgesic effects, only verum acupuncture significantly inhibited the brain responses to calibrated pain stimuli.⁵⁰ The researchers indicated that acupuncture stimulation (a peripheral to central modulation) may inhibit incoming noxious stimuli, while a top-down modulation, expectancy (placebo/sham) may work through the emotional circuit.⁴² Furthermore, Harris et al.⁵¹ found that while both verum and sham acupuncture produced similar levels of pain relief in fibromyalgia patients, the brain pathways of the 2 effects were quite different. The data were consistent with sham acupuncture evoking an increased release of endogenous opioids (consistent with mechanisms operative in placebos), whereas verum acupuncture increased receptor affinity and/or number.⁵¹ In aggregate, these neuroimaging studies provide strong evidence that verum and sham acupuncture stimulations have very different neural correlates, although they both can engender analgesic effects.

In conclusion, clinical trials support the efficacy of acupuncture in reducing PONV and postoperative pain; however, evidence supporting acupuncture as a treatment for chronic pain conditions is mixed. It should be noted that acupuncture trials in chronic pain have concluded that acupuncture treatment is often superior to standard of care or wait list controls and that acupuncture has minimal side effects and is cost effective.^{37–43} Brain imaging studies have demonstrated that there are different neural correlates between verum and sham acupuncture stimulation.^{44–51} Additionally, all clinical trials and many research studies have assumed that the acupuncture effect is equal to the “needle” effect, failing to recognize that factors in addition to specific effects of needling are also important contributors to the therapeutic effect of acupuncture in the setting of chronic pain.

Last, acupuncture is an ancient medical intervention first developed in an era when there were no laboratory tests, technology, or science of anatomy. The reason that the practice of acupuncture has survived for thousands of years is because it has evolved over time, with changes ranging from the number of acupuncture points to the practice techniques. Instead of criticizing this ancient art with arguments culled from modern medicine and science, physicians and scientists should try to integrate current knowledge into this ancient, yet ever-evolving practice so it may be used to treat conditions for which pharmaceutical interventions are ineffective and/or potentially dangerous.^{35,36} Over the last decade, there has been a growing green movement and eco-sustainability trend as well as an increased awareness that the same medication may not be effective in treating every patient with the same biomedical diagnosis. This

“new age-integrative medicine”^{52–55} in Western culture promotes a patient-oriented medical practice that complements the ancient Chinese theory behind acupuncture practice. Overall, acupuncture practice should not be seen as a placebo intervention or merely a needle therapy, but a medical option that not only treats disorders but also fosters a greater awareness of how harmonic interactions between self, family, work, and environment play a role in promoting health and restoring order. ■

DISCLOSURES

Name: Shu-Ming Wang, MD.

Contribution: This author helped write the manuscript.

Name: Richard E. Harris, PhD.

Contribution: This author helped write the manuscript.

Name: Yuan-Chi Lin, MD, MPH.

Contribution: This author helped write the manuscript.

Name: Tong-Joo Gan, MD, FRCA, MHS.

Contribution: This author helped write the manuscript.

This manuscript was handled by: Steven L. Shafer, MD.

REFERENCES

1. Liu G, Akira H. Basic principle of TCM. In: Liu G, Akira H, eds. Fundamentals of Acupuncture and Moxibustion. Tianjin: Tianjin Science and Technology Translation and Publishing Corporation, 1994:1-10
2. Ulett GA, Han J, Han S. Traditional and evidence-based acupuncture: history, mechanisms, and present status. *South Med J* 1998;91:1115–20
3. Han JS. Acupuncture analgesia: areas of consensus and controversy. *Pain* 2011;152:S41–8
4. Colquhoun D, Novella S. Acupuncture is probably no more than a theatrical placebo. *Anesth Analg* 2013;116:1360–3
5. Xinnong C, ed. Chinese Acupuncture and Moxibustion. 5th ed. Beijing: Foreign Language Press, 1999
6. Srbely JZ, Dickey JP, Lowerison M, Edwards AM, Nolet PS, Wong LL. Stimulation of myofascial trigger points with ultrasound induces segmental antinociceptive effects: a randomized controlled study. *Pain* 2008;139:260–6
7. Taylor K. Chinese Medicine in Early Communist China 1945–63. New York, NY: Routledge Curzon, 2005
8. World Health Organization. Acupuncture: Review and Analysis of Reports on Controlled Clinical Trial. WHO Library Cataloguing-in-Publication Data. Geneva: World Health Organization, 2003
9. Lundström M. “Students’ beliefs in pseudoscience.” Paper presented at: ESERA conference, Malmö, Sweden, 2007
10. Jarvis WT. Quackery: a national scandal. *Clin Chem* 1992;38:1574–86
11. Barrett SJ, Jarvis WT, eds. The Health Robbers: A Close Look at Quackery in America. New York, NY: Prometheus, 1993
12. Colquhoun D. Secret remedies: 100 years on. *BMJ* 2009;339:b5432
13. Taub A. Thumbs down on acupuncture [letter]. *Science* 1998; 279:159
14. Wahlberg A. A quackery with a difference-new medical pluralism and the problem of ‘dangerous practitioners’ in the United Kingdom. *Soc Sci Med* 2007;65:2307–16
15. Kapur PA. The big “Little Problem” [editorial]. *Anesth Analg* 1991;73:243–5
16. White PF. Are nonpharmacologic techniques useful alternatives to antiemetic drugs for the prevention of nausea and vomiting? [editorial]. *Anesth Analg* 1997;84:712–4
17. Gan TJ. Postoperative nausea and vomiting—can it be eliminated? *JAMA* 2002;287:1233–6
18. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Post-operative pain experience: results from a national survey suggest post-operative pain continues to be undermanaged. *Anesth Analg* 2003;97:534–40

19. McGrath B, Elgendy H, Chung F, Kamming D, Curti B, King S. Thirty percent of patients have moderate to severe pain 24 hr after ambulatory surgery: a survey of 5,703 patients. *Can J Anaesth* 2004;51:886–91
20. Robinson RL, Birnbaum HG, Morley M A, Sisitsky T, Greenberg PE, Claxton AJ. Economic cost and epidemiological characteristics of patients with fibromyalgia claims. *Journal of Rheumatology* 2003;30:1318–25
21. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002. *Spine* 2006;31:2724–7
22. Lee A, Done ML. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting. *Anesth Analg* 1999;88:1362–9
23. Lee A, Done ML. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. *Cochrane Database Syst Rev* 2004;3:CD003281
24. Lee A, Fan LTY. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. *Cochrane Database Syst Rev* 2009;3: CD003281
25. Wang SM, Kain ZN. P6 acupoint injections are as effective as droperidol in controlling early postoperative nausea and vomiting in children. *Anesthesiology* 2002;97:359–66
26. Gan TJ, Jiao KR, Zenn M, Georgiade G. A randomized controlled comparison of electro-acupoint stimulation or ondansetron versus placebo for the prevention of postoperative nausea and vomiting. *Anesth Analg* 2004;99:1070–5
27. Butkovic D, Toljan S, Matolic M, Kralik S, Radesić L. Comparison of laser acupuncture and metoclopramide in PONV prevention in children. *Paediatr Anaesth* 2005;15:37–40
28. Henzi I, Sonderegger J, Tramèr MR. Efficacy, dose-response, and adverse effects of droperidol for prevention of postoperative nausea and vomiting. *Can J Anaesth* 2000;47:537–51
29. Wallenborn J, Gelbrich G, Bulst D, Behrends K, Wallenborn H, Rohrbach A, Krause U, Kühnast T, Wiegel M, Olthoff D. Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial. *BMJ* 2006;333:324
30. Misra MN, Pullani AJ, Mohamed ZU. Prevention of PONV by acustimulation with capsicum plaster is comparable to ondansetron after middle ear surgery. *Can J Anaesth* 2005;52:485–9
31. Sun Y, Gan TJ, Dubose W, Habib AS. Acupuncture and related techniques for postoperative pain: a systematic review of randomized controlled trials. *BJA* 2008; 101:151–60
32. Sun Y, Gan TJ. Acupuncture for the management of chronic headache: a systematic review. *Anesth Analg* 2008;107:2038–47
33. Vickers AJ, Cronin AM, Maschino AC, Lewith G, Macpherson H, Foster NE, Sherman KJ, Witt CM, Linde K. Acupuncture for chronic pain: Individual patient data meta-analysis. *Arch Intern Med* 2012;172:1444–53
34. Wonderling D, Vicker AJ, Grieve R, McCaryney R. Cost effectiveness analysis of a randomized trial of acupuncture for chronic headache in primary care. *BMJ* 2004;328:747
35. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998;279:1200–5
36. U.S. Food and Drug Administration. Reports received and reports entered into AERS by year. Available at: <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070434.htm>
37. Yamashita H, Tsukayama H, White AR, Tanno Y, Sugishita C, Ernst E. Systematic review of adverse events following acupuncture: the Japanese literature. *Complement Ther Med* 2001;9:98–104
38. Lao L, Hamilton GR, Fu J, Berman BM. Is acupuncture safe? A systematic review of case reports. *Altern Ther Health Med* 2003;9:72–83
39. White A. A cumulative review of the range and incidence of significant adverse events associated with acupuncture. *Acupunct Med* 2004;22:122–33
40. Witt CM, Jena S, Selim D, Brinkhaus B, Reinhold T, Wruck K, Liecker B, Linde K, Wegscheider K, Willich SN. Pragmatic randomized trial evaluating the clinical and economic effectiveness of acupuncture for chronic low back pain. *Am J Epidemiol* 2006;164:487–96
41. Witt CM, Reinhold T, Brinkhaus B, Roll S, Jena S, Willich SN. Acupuncture in patients with dysmenorrhea: a randomized study on clinical effectiveness and cost-effectiveness in usual care. *Am J Obstet Gynecol* 2008;198:166.e1–8
42. Willich SN, Reinhold T, Selim D, Jena S, Brinkhaus B, Witt CM. Cost-effectiveness of acupuncture treatment in patients with chronic neck pain. *Pain* 2006;125:107–13
43. Reinhold T, Witt CM, Jena S, Brinkhaus B, Willich SN. Quality of life and cost-effectiveness of acupuncture in patients with osteoarthritis pain. *Eur J Health Econ* 2008;9:209–19
44. Yoo SS, Teh EK, Blinder RA, Jolesz FA. Modulation of cerebellar activities by acupuncture stimulation: evidence from fMRI study. *Neuroimage* 2004;22:932–40
45. Bai L, Yan H, Li L, Qin W, Chen P, Liu P, Gong Q, Liu Y, Tian J. Neural specificity of acupuncture stimulation at pericardium 6: evidence from an fMRI study. *J Magn Reson Imaging* 2010;31:71–7
46. Napadow V, Kettner N, Liu J, Li M, Kwong KK, Hui KKS, Audette J. somatosensory cortical plasticity in carpal tunnel syndrome treated by acupuncture. *Hum Brain Mapp* 2007; 28:159–71
47. Napadow V, Kettner N, Liu J, Li M, Kwong KK, Vangel M, Makris N, Audette J, Hui KK. Hypothalamus and amygdala response to acupuncture stimuli in Carpal Tunnel Syndrome. *Pain* 2007;130:254–66
48. Dhond RP, Kettner N, Napadow V. Do the neural correlates of acupuncture and placebo effects differ? *Pain* 2007;128:8–12
49. Pariente J, White P, Frackowiak RS, Lewith G. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *Neuroimage* 2005;25:1161–7
50. Kong J, Kapituk TJ, Polich G, Kirsch I, Vangel M, Zyloney C, Rosen B, Gollub RL. An fMRI study on the interaction and dissociation between expectation of pain relief and acupuncture treatment. *Neuroimage* 2009;47:1066–76
51. Harris RE, Zubietka JK, Scott DJ, Napadow V, Gracely RH, Clauw DJ. Traditional Chinese acupuncture and placebo (sham) acupuncture are differentiated by their effects on mu-opioid receptors (MORs). *Neuroimage* 2009;47:1077–85
52. Bell IR, Caspi O, Schwartz GE, Grant KL, Gaudet TW, Rychener D, Maizes V, Weil A. Integrative medicine and systemic outcomes research: issues in the emergence of a new model for primary health care. *Arch Intern Med* 2002;162:133–40
53. Barrett B, Marchand L, Scheder J, Plane MB, Maberry R, Appelbaum D, Rakel D, Rabago D. Themes of holism, empowerment, access, and legitimacy define complementary, alternative, and integrative medicine in relation to conventional biomedicine. *J Altern Complement Med* 2003;9:937–47
54. Kligler B, Maizes V, Schachter S, Park CM, Gaudet T, Benn R, Lee R, Remen RN. Core competencies in integrative medicine for medical school curricula: a proposal. *Acad Med*. 2004;79: 521–31
55. Owen D, Lewith GT. Teaching integrated care: CAM familiarisation courses. *Med J Aust* 2004;181:276–8