Corrections and Retraction

CORRECTIONS

MEDICAL SCIENCES. For the article "*Ex vivo* cell labeling with ^{64}Cu–pyruvaldehyde-bis(N^4-methylthiosemicarbazone) for imaging cell trafficking in mice with positron-emission tomography," by Nora Adonai, Khoi N. Nguyen, Joseph Walsh, M. Iyer, Tatsushi Toyokuni, Michael E. Phelps, Timothy McCarthy, Deborah W. McCarthy, and Sanjiv Sam Gambhir, which appeared in issue 5, March 5, 2002, of *Proc. Natl. Acad. Sci. USA* (**99,** 3030–3035; first published February 26, 2002; 10.1073/pnas.052709599), the author name Nora Adonai should have appeared as Nona Adonai. The corrected author line appears below. The online version has been corrected.

Nona Adonai, Khoi N. Nguyen, Joseph Walsh, M. Iyer, Tatsushi Toyokuni, Michael E. Phelps, Timothy McCarthy, Deborah W. McCarthy, and Sanjiv Sam Gambhir

www.pnas.org/cgi/doi/10.1073/pnas.0604177103

MEDICAL SCIENCES. For the article "Familial hypercatabolic hypoproteinemia caused by deficiency of the neonatal Fc receptor, FcRn, due to a mutant β_2-microglobulin gene," by Manzoor A. Wani, Lynn D. Haynes, Jonghan Kim, C. L. Bronson, Chaity Chaudhury, Sudhasri Mohanty, Thomas A. Waldmann, John M. Robinson, and Clark L. Anderson, which appeared in issue 13, March 28, 2006, of *Proc. Natl. Acad. Sci. USA* (**103,** 5084–5089; first published March 20, 2006; 10.1073/pnas.0600548103), the authors note that on page 5087, the first full sentence in the left column appears incorrectly, due to a printer's error. "Most of these mutations have been cytoplasmic tail (CT) deletions in the leader sequence that result in reading frame shifts and downstream nonsense mutations" should read: "Most of these mutations have been CT deletions in the leader sequence that result in reading frame shifts and downstream nonsense mutations." This error does not affect the conclusions of the article.

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APPLIED BIOLOGICAL SCIENCES. For the article "Human vitamin B_{12} absorption measurement by accelerator mass spectrometry using specifically labeled ^{14}C-cobalamin," by Colleen Carkeet, Stephen R. Dueker, Jozsef Lango, Bruce A. Buchholz, Joshua W. Miller, Ralph Green, Bruce D. Hammock, John R. Roth, and Peter J. Anderson, which appeared in issue 15, April 11, 2006, of *Proc. Natl. Acad. Sci. USA* (**103,** 5694–5699; first published April 3, 2006; 10.1073/pnas.0601251103), the authors note an ambiguity in the units of Fig. 5, which contradicted one of the axes. The figure and its corrected legend appear below.

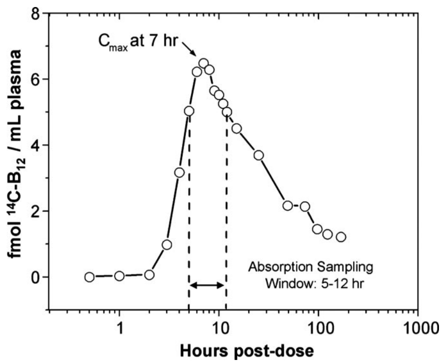

Fig. 5. AMS detection of ^{14}C in human plasma. Measurements were performed on 30 μl of plasma; the entire sample set consumed <1 ml of whole blood.

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ENVIRONMENTAL SCIENCES. For the article "Consistent simulations of multiple proxy responses to an abrupt climate change event," by A. N. LeGrande, G. A. Schmidt, D. T. Shindell, C. V. Field, R. L. Miller, D. M. Koch, G. Faluvegi, and G. Hoffmann, which appeared in issue 4, January 24, 2006, of *Proc. Natl. Acad. Sci. USA* (**103,** 837–842; first published January 13, 2006; 10.1073/pnas.0510095103), the authors note that the color bar label for Fig. 2*a* is inverted. The corrected figure and its legend appear below. This error does not affect the conclusions of the article.

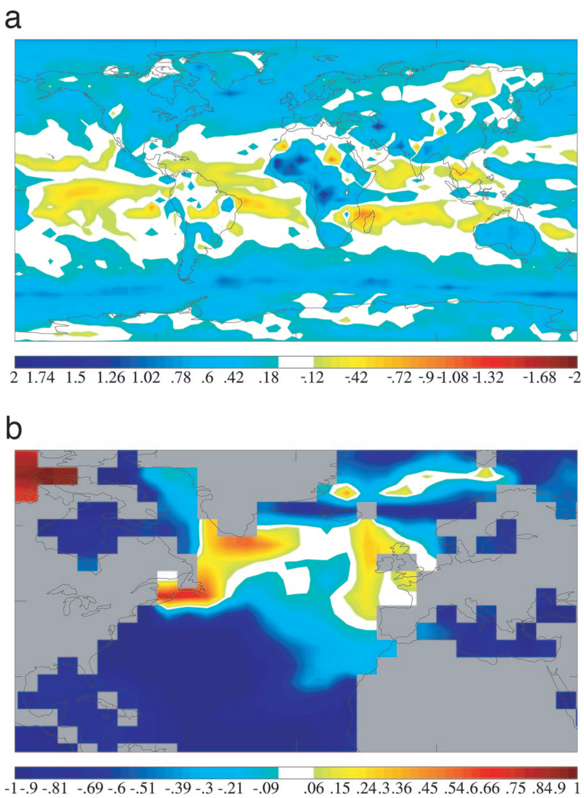

Fig. 2. Proxy validation for model simulations indicates the relationship between $\delta^{18}O$ and temperature in the atmosphere and ocean. (*a*) The temporal gradient in SAT vs. $\delta^{18}O_{precip}$ (‰/°C), the relationship crucial for interpreting many atmospheric paleoclimate records, is steepest and most highly correlated at high latitudes and is very shallow or reversed with lower correlation in the subtropics and tropics. (*b*) The correlation of SST vs. $\delta^{18}O_{calcite}$, the relationship crucial for interpreting many sediment core paleoclimate records, breaks down in most of the northern North Atlantic, with the exception of areas along the northern Greenland, Iceland, and Norwegian (GIN) Seas.

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RETRACTION

PHYSIOLOGY. For the article "New findings of the correlation between acupoints and corresponding brain cortices using functional MRI," by Z. H. Cho, S. C. Chung, J. P. Jones, J. B. Park, H. J. Park, H. J. Lee, E. K. Wong, and B. I. Min, which appeared in issue 5, March 3, 1998, of *Proc. Natl. Acad. Sci. USA* (**95,** 2670–2673), the authors reported a specific cortical correlation with a given acupoint and suggested that there could be correlation between acupoint stimulation and cortical activation, for example via increased blood flow in the visual cortex. Accumulating evidence suggests that the central nervous system is essential for processing these effects, via its modulation of the autonomic nervous system, neuro-immune system, and hormonal regulation. We, therefore, carried out a series of studies questioning whether there really is point specificity in acupuncture, especially vis-à-vis pain and acupuncture analgesic effects as we originally reported in our PNAS article, that had not yet been confirmed by other studies. We have reported some of these results as preliminary observations (1, 2). Having concluded that there is no point specificity, at least for pain and analgesic effects, and that we no longer agree with the results in our PNAS article, the undersigned authors are retracting the article. J. P. Jones, J. B. Park, and H. J. Park have not approved this retraction.

Z. H. Cho
S. C. Chung
H. J. Lee
E. K. Wong
B. I. Min

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2. Cho, Z. H., Hwang, S. C., Wong, E. K., Son, Y. D., Kang, C. K., Park, T. S., Bai, S. J., Kim, Y. B., Lee, Y. B., Sung, K. K., *et al.* (2006) *Acta Neurol. Scand.* **113,** 370–377.

www.pnas.org/cgi/doi/10.1073/pnas.0602520103

Proc. Natl. Acad. Sci. USA
Vol. 95, pp. 2670–2673, March 1998
Physiology

New findings of the correlation between acupoints and corresponding brain cortices using functional MRI

(acupuncture/fMRI/correlation between visual and acupuncture stimulation)

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Communicated by Lawrence A. Shepp, AT&T Laboratories, Piscataway, NJ, November 13, 1997 (received for review August 25, 1997)

ABSTRACT **A preliminary study of the correlation between acupuncture points (acupoints) for the treatment of eye disorders suggested by ancient Oriental literature and the corresponding brain localization for vision described by Western medicine was performed by using functional MRI (fMRI). The vision-related acupoint (VA1) is located in the lateral aspect of the foot, and when acupuncture stimulation is performed there, activation of occipital lobes is seen by fMRI. Stimulation of the eye by directly using light results in similar activation in the occipital lobes by fMRI. The experiment was conducted by using conventional checkerboard 8-Hz light-flash stimulation of the eye and observation of the time-course data. This was followed by stimulation of the VA1 by using the same time-course paradigm as visual light stimulation. Results obtained with 12 volunteers yielded very clean data and very close correlations between visual and acupuncture stimulation. We have also stimulated nonacupoints 2 to 5 cm away from the vision-related acupoints on the foot as a control, and activation in the occipital lobes was not observed. The results obtained demonstrate the correlation between activation of specific areas of brain cortices and corresponding acupoint stimulation predicted by ancient acupuncture literature.**

Oriental medicine in general and acupuncture in particular have been used for thousands of years in China, Korea, and Japan. In the West, oriental medicine, especially that of acupuncture, has been known only recently (1–3); however, its acceptance has increased rapidly. The development of oriental medicine is relatively slow and still relies on ancient literature, which is largely descriptive rather than quantitative or even factual. In oriental medicine there has been little effort to show the connection between the brain and various disorders or diseases. An example is the relationship between vision and the visual cortex, which is unknown and not mentioned in the literature of oriental medicine. The lack of such information may be due to the complexity of the brain, which has made this information too complex for ancient observers to comprehend. With the recent development of positron emission tomography (PET) (4, 5) and MRI, many secrets of brain function are being revealed but still remain qualitative rather then quantitative. Since the development of functional MRI (fMRI) in 1992, secrets of brain function have begun to be revealed and mysteries such as visual stimulation and activation of corresponding brain cortices have begun to provide "brain" and "organ" relationships hitherto unknown (6–13). How acupuncture really works is largely a mystery and has been neither scientifically proven nor experimentally verified. Acupuncture is largely dependent on the classical literature of oriental medicine, such as the Eastern Medical Handbook (1), which is derived largely from experience without scientific correlation. In oriental medicine, acupuncture treatment was believed to treat directly the diseased organs or related disorders without intermediary control mechanisms. For example, the visual-related acupoint (VA1) (known as urinary bladder channel of BL67) is believed to be an effective acupoint that directly treats eye-related disorders (2, 3); that is, various acupoints are related to corresponding specific organs rather than via the central nervous system (CNS). In Western medicine, however, it is known that many disorders are either controlled or affected by the brain, i.e., specific corresponding brain functional areas. Some basic relationships between the various organs and corresponding brain cortical areas have been demonstrated by the newly developed fMRI (6–13). Human brain and various organ functions of the brain, such as visual, motor, auditory, sensory, as well as cognitive, have already been studied by fMRI (12, 13). These recent developments (14–17) in fMRI can be used for the quantitative study of the correlation between various acupoints and specific functional areas of the brain with the hope of establishing a clear correlation between acupoints and organ disorders or diseases. If these correlations are found to exist, then the treatment of some disorders or diseases by acupuncture may be due to the mediation of the CNS, not the direct interaction between acupoints and involved organs. Eventually, fMRI may also facilitate more accurate treatment of disorders and diseases developed from empirical data and experiences. Recently, some acupuncture effects have been reported when using fMRI (18, 19), but no direct brain–acupoint correlation study has been reported.

Fig. 1 is a diagram showing the conceptual relationship between the brain, organs, and acupoints. Because a large amount of experimental data has already been obtained by fMRI to demonstrate the relationship between the brain and various organs, this diagram may provide a reference point for the establishment of new relationships to be obtained between acupuncture stimulation and functional areas of brain cortex.

METHODS AND RESULTS

Experiments were carried out by using the conventional gradient echo (CGE) sequence with the 2.0 T whole-body MRI system. Healthy human volunteers (12 volunteers, ages 21–30 years) were studied for both acupuncture and visual light stimulation. Each volunteer was positioned and secured in the standard head coil to avoid misregistration artifacts. Initially for each fMRI experiment, an inversion-recovery T1-weighted image was obtained for the reference anatomical image of the

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Abbreviations: fMRI, functional MRI; VA1, vision-related acupoint; CNS, central nervous system.

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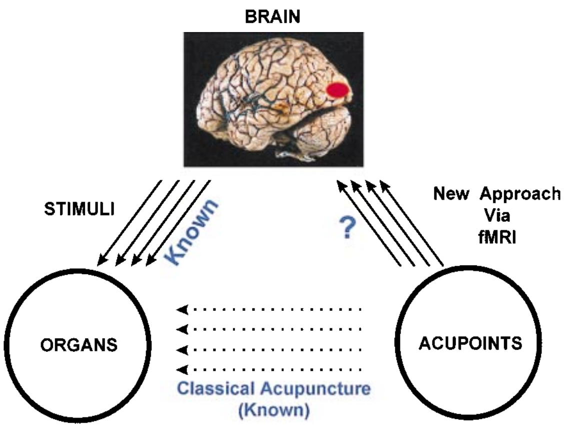

FIG. 1. New approach to old acupuncture. Conceptual relationship of therapeutic acupuncture, functional MRI, and the role of the brain.

visual cortex. For the experimental study, a repetition time of 60 msec, an echo time of 27 msec, a flip angle of 40°, a field of view (FOV) of 220 mm, a slice thickness of 10 mm, and a total acquisition time per image of 10 sec were used.

The first attempt was to study the relationship between an acupoint and the corresponding eye disorder by stimulation of the vision-related acupoints VA1–VA8 (BL67 to BL60) shown in Fig. 2, which are known to treat eye disorders. The results are compared with the visual light stimulation study normally used in fMRI of the visual cortex. The visual acupoint VA1 (BL67) shown in Fig. 2*b* was tried first, and the results obtained for the volunteers were then compared with the results of fMRI visual light stimulation (see Fig. 3*a* and *b*). There is a clear correlation between the visual light stimulation experiment and acupoint stimulation. An experimental control was then obtained by stimulating a nonacupoint location 2–5 cm away from VA1, resulting in no fMRI response (see Fig. 3*c*).

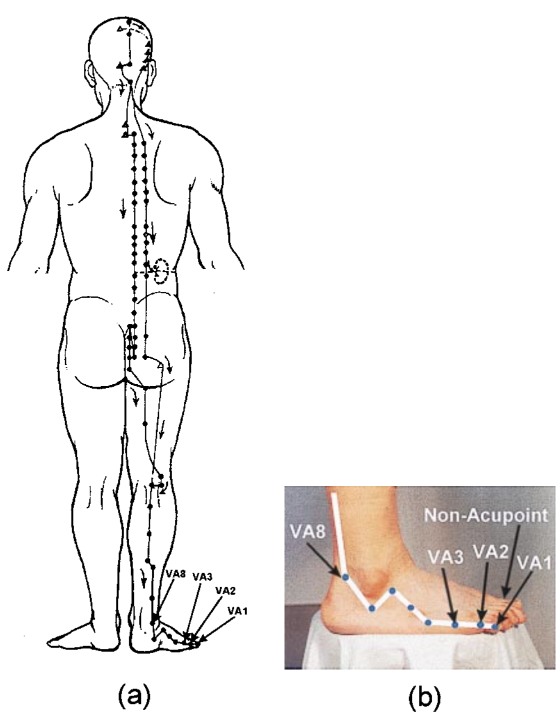

FIG. 2. The vision-related acupoints VA1, VA2, VA3, and VA8. These acupoints are known in the oriental acupuncture literature as BL67 (VA1), BL66 (VA2), BL65 (VA3), and BL60 (VA8), respectively.

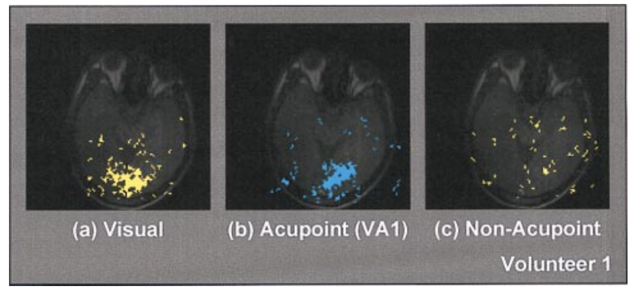

FIG. 3. Nonacupoint stimulation (control) in comparison with visual and acupoint stimulation. The activation maps of the visual cortex resulting from visual stimulation of the eye and acupuncture stimulation at VA1, and nonacupoint stimulation, respectively (volunteer 1).

For the time-course study, the stimulation was delivered to VA1 by continuously twisting the acupuncture needle for stimulation and resting for nonstimulation, respectively. Sets of complementary experiments were also performed with the same paradigm on other acupoints such as VA2, VA3, and VA8 (see the results shown in Fig. 4).

For the corresponding visual stimulation experiments, an 8-Hz checkerboard was used. Images of numbers 1–5 were obtained at the resting state (off), whereas images of numbers 6–10 were obtained with the stimulation (on). This type of stimulation was then repeated for both acupuncture and visual experiments. Time-course signal processing was carried out by using the correlation coefficient (cc) method for each pixel (16). The box-car waveform was used as the reference waveform (16). The value of cc varied between −1 and +1. A

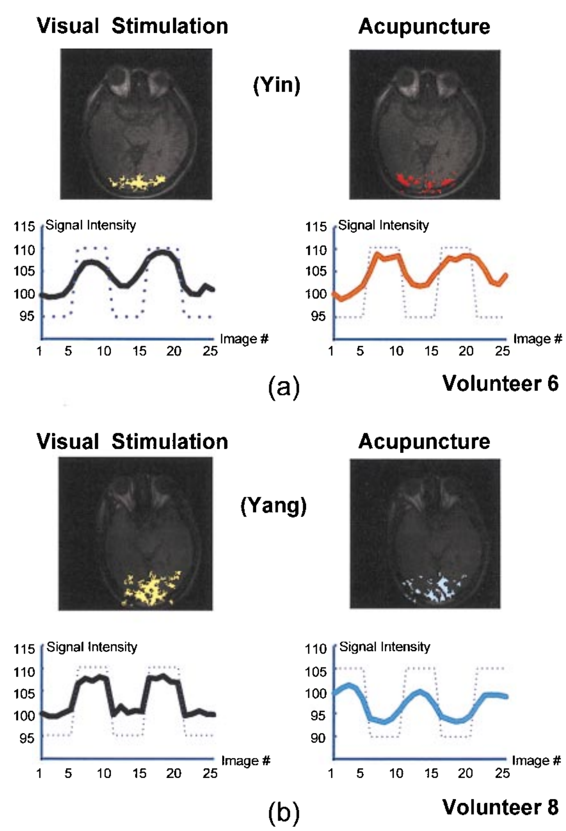

FIG. 4. Visual and acupuncture stimulation. The activation maps and time-course data of visual and acupuncture stimulation at VA1 (volunteers 6 and 8). (*a*) The results of visual and acupuncture stimulation of a volunteer of "yin" character. (*b*) Same as *a* for "yang" character.

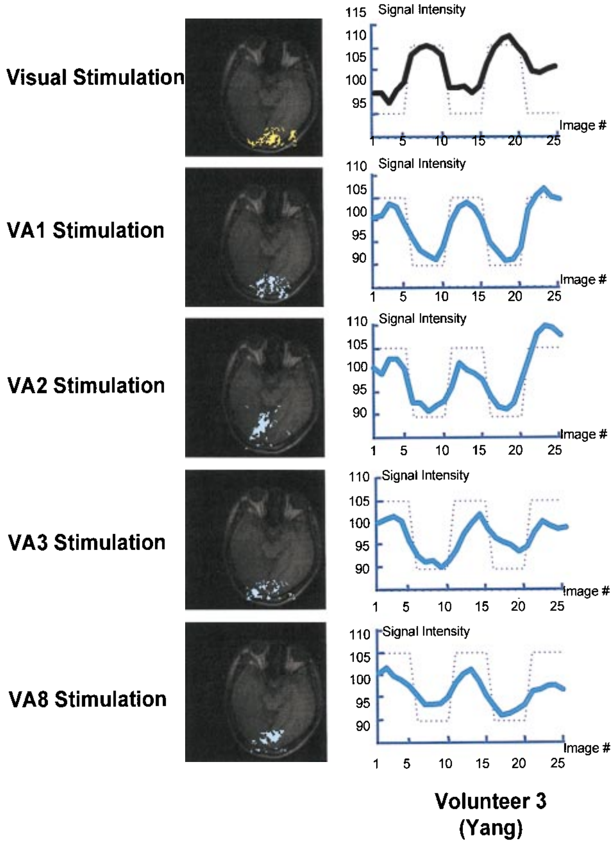

FIG. 5. Visual and acupunctural stimulation with different acupoints (VA1–VA8). The activation maps and time-course data of acupuncture stimulation of four different, vision-related acupoints, namely, VA1, VA2, VA3, and VA8. An activation of occipital lobes by visual stimulation is given for reference (volunteer 3).

threshold value "TH" was set between 0 and $|\pm 1|$, and each pixel was then selected and assumed activated if cc was equal or larger than TH, i.e., cc $\geq$ TH. These activated pixels were then superimposed on the anatomical images, and time-course data were derived by summing all the activated data on each image at a given image data acquisition time. For most of the study, the value TH was set at 0.4. Time-course studies of VA1 for two representative cases are shown in Fig. 4. In both Fig. 4 *a* and *b*, activation resulting from conventional visual stimulation and acupoint (VA1) stimulation was obtained and shown. The difference between *a* and *b* appears to be caused by the two types of reactions dependent on individual physical characteristics described in oriental medicine. These two types are known in oriental medicine as "yin" and "yang" characters. Distribution of yin and yang among the current volunteers was found to be relatively even (see Table 1). The acupuncture response of the yin character exhibits the same direction in signal intensity variation as the visual stimulation, i.e., it follows the same time-course pattern of the visual stimulation whereas the yang character shows an opposite behavior. Among 12 volunteers, 8 were "yang" and 4 were "yin." Functional MRI data were then tested by blind tests for identification of the yin and yang character of each individual and were found to be consistent except in one case.

The summary of the acupuncture study at the VA1 location and cortical activation of visual stimulation for the 12 volunteers is given in Table 1 and Fig. 6. As mentioned, the results of the acupuncture study are divided into two groups, i.e., one is termed "yin," which follows the same signal intensity variation as the visual cortex and the other is termed "yang," which is opposite of "yin." Fig. 5 shows the extended test results of the relative acupuncture effects of the four visual acupoints, namely, VA1, VA2, VA3, and VA8, for the study of relative effectiveness of the three other acupoints in relation to VA1. Acupoints VA1–VA8 are all known to be related to the treatment of eye disorders, although each acupoint plays a slightly different therapeutic role. The activated areas resulting from acupoint stimulations of VA1, VA3, and VA8 are all found to be in the primary visual cortex (V-1), except VA2, which did not activate the primary visual cortex as the others (see Fig. 5).

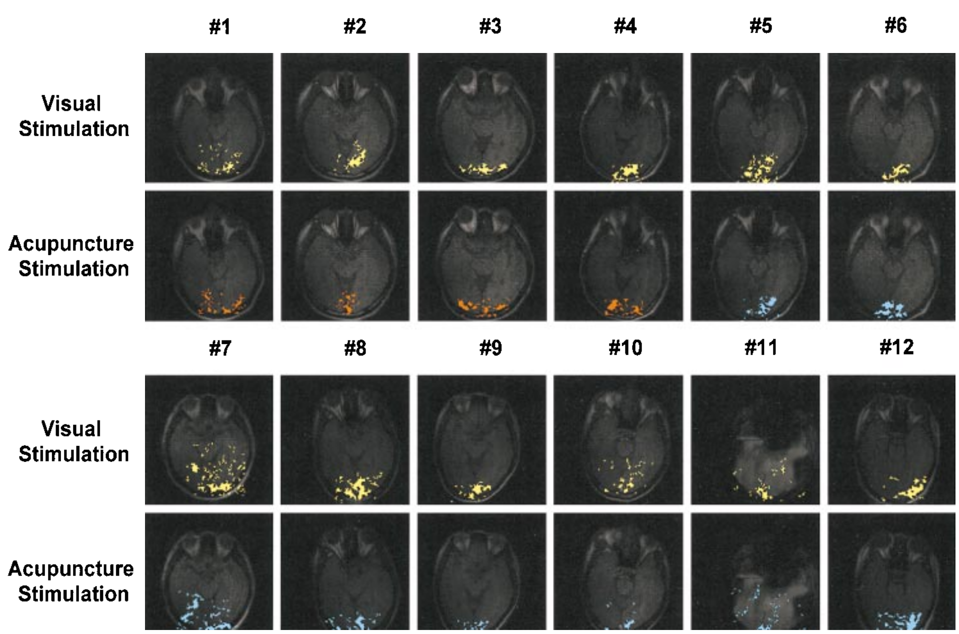

FIG. 6. Visual and acupuncture stimulation of VA1. Comparison of direct visual stimulation of the eye and acupuncture stimulation of vision-related acupoint VA1 for all 12 subjects. The fMRI activation responses, in color, are superimposed on MRI images. Yellow overlays correspond to responses from direct visual stimulation. Red overlays correspond to responses from acupuncture stimulation having a positive correlation with signal intensity, i.e., "yin" character. Blue overlays correspond to responses from acupuncture stimulation having a negative correlation with signal intensity, i.e., "yang" character. All subjects with "red" overlays were judged to have primarily "yin" characters whereas all subjects with "blue" overlays were judged to have primarily "yang" characters.

Table 1. Summary of the average changes of the correlated signal intensity during stimulation

Volunteer number (sex and age)	Signal change by visual stimulation, %	Signal change by acupuncture stimulation, %
#1 (female, 21) −	8.6	−9.4
#2 (male, 30) +	12.3	+14.5
#3 (male, 29) −	9.8	−8.8
#4 (male, 25) +	9.8	+6.0
#5 (female, 27) −	6.5	−4.7
#6 (male, 26) +	8.5	+8.2
#7 (male, 23) −	4.7	−7.1
#8 (female, 24) −	8.2	−7.3
#9 (male, 26) −	11.7	−9.5
#10 (male, 26) −	6.8	−6.9
#11 (male, 25) +	9.0	+8.0
#12 (male, 24) −	7.6	−6.8
Averaged results	9.9 ± 1.7: +(*Yin*) (*n* = 4)	9.2 ± 3.7: +(*Yin*) (*n* = 4)
	8.0 ± 2.1: −(*Yang*) (*n* = 8)	−7.6 ± 1.6: −(*Yang*) (*n* = 8)

"+" represents "yin" whose signal intensity of acupoint stimulation follows the same direction as visual stimulation, and "−" represents "yang" in which the signal intensity variation goes opposite to "yin."

DISCUSSION

The present study represents a major first step toward understanding oriental acupuncture in relationship to brain function, which has largely been ignored in classical oriental medicine. Shown in Fig. 1, the basic triangular relationship of the brain, target organs, and acupoints serves as a new paradigm to be studied and clarified by both modern Western medicine as well as oriental medicine. Based on our knowledge of Western medicine, it is difficult to believe that acupuncture treats disorders and diseases by direct control of organs or organ-related disorders and diseases. It is possible that acupuncture first stimulates or activates the corresponding brain cortex via the CNS, thereby controlling the chemical or hormone release (via the CNS) to the diseased or disordered organs for treatment. It is essential and also more plausible if corresponding brain cortices and disease-related acupoints are consistent and related in terms of known medical findings, especially those of fMRI data. These data demonstrate that both the static and dynamic activation of the visual cortex by acupoint VA1 stimulation are consistent with visual light stimulation previously observed by fMRI.

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