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ISSN 0883-0738

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Original Article

Pilot Study of Positron Emission Tomography (PET) Brain Glucose Metabolism to Assess the Efficacy of Tongue and Body Acupuncture in Cerebral Palsy

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ABSTRACT

We aimed to assess the efficacy of tongue and body acupuncture with clinical function and brain glucose metabolism in children with a severe type of cerebral palsy. Four children were recruited. The motor function belonged to grade 5 of the Gross Motor Function Measure (ie, completely nonambulatory). Daily tongue and body acupuncture was applied for 5 days a week for 8 weeks. The Functional Independence Scale for Children (WeeFIM), Clinical Global Impression Scale (CGIS), and positron emission tomography of the brain with [¹⁸F]fluorodeoxyglucose (FDG) were performed at baseline and after acupuncture. None of the children had any significant change in the Functional Independence Scale for Children score, despite the fact that all mothers scored 3 on the Clinical Global Impression Scale (ie, 25% improvement) in overall function. The brain glucose metabolism, however, showed a > 10% increase in the frontal, parietal, temporal, and occipital cortices and cerebellum. Thus, a short course of tongue and body acupuncture was shown to increase brain glucose metabolism, despite lacking any clinical functional improvement seen within the 8-week course, possibly owing to the severity of the motor dysfunction and the short duration of treatment. The objective increase in brain glucose metabolism might serve as a surrogate marker for assessing the subclinical efficacy of an alternative treatment before any objective clinical improvement is evident. A larger-scale study for different degrees of severity of cerebral palsy and an impairment model should be undertaken to correlate clinical with neurometabolic change. (*J Child Neurol* 2006;21:455-462; DOI 10.2310/7010.2006.00101).

There is a tendency for parents of children with chronic disabilities such as cerebral palsy to seek alternative medicine. Most claims of success of alternative medicine for cerebral palsy lack scientific evidence.¹⁻⁴ A few double-blind, randomized, controlled trials have been conducted for the use of traditional Chinese medicine, such as acupuncture, in cerebral palsy. We demonstrated within a randomized controlled trial that traditional Chinese acupuncture was effective in improving the functioning of patients with cerebral palsy.⁵

In traditional Chinese medicine, nearly 400 acupoints on the body surface are interrelated to various functions. The surface acupoints are linked through 14 meridians to various organs or viscera of the human body. The approach in traditional Chinese medicine, in sharp contrast to that of Western medicine, is "holistic," with a more philosophical background of balancing the "yin and yang." The main objective of traditional Chinese medicine is to improve the health of the body and the mind.⁶

The pathophysiologic basis of traditional Chinese medicine aims to improve "energy" or "body flow" (*de-qui* in Chinese). Even a normal human subject will respond to acupuncture owing to the flow of energy. The effect of acupuncture was hypothesized and proven in animal and human studies to be due to direct neural stimulation, changes in neurotransmitters such as endorphins, immunologic markers, and endocrinologic signals. Thus, acupuncture is effective in chronic disorders, especially in neurologic disorders.⁶

We demonstrated the clinical efficacy of tongue and body acupuncture in improving various functional modalities of patients with chronic neurologic disorders, such as cerebral palsy and drooling.^{5,7-28} We used a different approach in looking at cerebral palsy to assess the efficacy of traditional Chinese medicine in improving the functional status of these children.

The objective was to study the efficacy of a short course of tongue and body acupuncture in improving the overall functional status of cerebral palsy. We hope to study as the first pilot project the integration of traditional Chinese medicine with Western medicine to see whether traditional Chinese medicine is useful in affecting brain metabolism in children with cerebral palsy.

METHODOLOGY

We started a research program of integration of traditional Chinese medicine with Western medicine in the comprehensive management of children with various neurologic disabilities in 1999 at The University of Hong Kong.

Four children were recruited from the Cerebral Palsy Research Clinic. The inclusion criteria included a diagnosis of cerebral palsy using standard criteria. The motor function belonged to grade 5 of the Gross Motor Function Measure (ie, completely nonambulatory).²⁹ Each patient had baseline neurologic, developmental, and functional evaluations before and after treatment.

Received November 1, 2004. Received revised February 6, 2005, April 4, 2005, and June 1, 2005. Accepted for publication July 13, 2005.

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Method of Tongue and Body Acupuncture

Based on our clinical experience of tongue and body acupuncture in more than 100 children with cerebral palsy, three acupoints of the tongue were used: (1) two acupoints on the lateral surface of the tongue (tongue acupoint 1 = *Xian Zuo* [midline between the tip and root of the left lateral surface of the tongue] and tongue acupoint 2 = *Xian You* [midline between the tip and root of the right lateral surface of the tongue]) and (2) one acupoint at the tongue base (tongue acupoint 3 = *Di Men* [midline of the tongue base]) were punctured. Both tongue acupoint 1 and 2 were punctured obliquely at 45 degrees at a depth of 0.3 to 0.5 cm. Tongue acupoint 3 was punctured perpendicularly 0.3 to 0.5 cm in depth. The same body acupoints were also used for the same child to improve the holistic function according to the traditional Chinese medicine concept.

Daily tongue and body acupuncture was applied for 5 days a week for 8 weeks. The acupuncture lasted for less than 15 seconds. No sedation was required. The child was allowed to sit on the mother's lap with the head tilted 45 degrees upward, and sterile gauze was used to pick up and station the tongue with the acupuncturist's left hand. The child was encouraged to open his or her mouth. Quick and accurate insertion into acupoints was performed with the right hand. We used a 30-gauge (0.3 mm) sterile disposable acupuncture needle, 4 cm in length (made in China HWA TO).

Assessment and Treatment

All children continued their conventional cerebral palsy program. They were assessed before (week 0) and after (week 8) acupuncture. The following assessment tools were used:

Functional Independence in Children

The Functional Independence in Children (WeeFIM) is a concise, comprehensive, standardized assessment for functional outcome. It assesses a child's consistent and usual performance to criterion standards of 18 items in 3 domains: (1) self-care, (2) mobility, and (3) cognitive. The rating is based on a seven-level ordinal scale, ranging from complete independence (score of 7) to total assistance (score of 1). This will subsequently be converted to a functional quotient, based on age-based norms.³¹

Clinical Global Impression Scale (CGIS) (Parental Report)

The Clinical Global Impression Scale (CGIS) score was obtained after a course of acupuncture.³¹ All parents were asked to send back a standardized form rating their impression on any improvement as shown by a seven-level ordinal scale. The Clinical Global Impression Scale is a measure on a Likert scale of 0 to 7. Zero means not assessed, 1 means very much improved (75%), 2 means much improved (50%), 3 means minimally improved (25%), 4 means no change, 5 means minimally worse (-25%), 6 means much worse (-50%), and 7 means very much worse (-75%). They also rated any adverse effects on a four-level ordinal scale: none, present but not significantly interfering with patient's functioning, significantly interfering with functioning, or outweighing the therapeutic effect.

Cerebral [¹⁸F]Fluorodeoxyglucose Metabolism by Positron Emission Tomography

[¹⁸F]fluorodeoxyglucose (FDG) per 1.73 m² body surface area with dose correction for blood glucose normalized to 5 mmol/L was injected. Such an approach tends to minimize the variability caused by glucose level and body size.³⁰ If necessary, sedation with a lytic cocktail was given 25 minutes later, approximately 20 minutes prior to the positron emission tomographic (PET) scan. A three-dimensional brain PET scan was obtained using Siemens' ECAT Exact Scanner (Long Island PET Imaging, New York, NY),

Table 1. Demographic Data of Four Cerebral Palsy Cases

| Case | Sex | Age (yr; mo) | Cause | Gestational Age (wk) | Birthweight (g) | Types of Cerebral Palsy | Gross Motor Functional Scale | Associated Diseases | | |
|------|-----|--------------|------------------------------------|----------------------|-----------------|-------------------------|------------------------------|-----------------------------|----------|--------------------|
| | | | | | | | | Mental Retardation (Yes/No) | Epilepsy | Cortical Blindness |
| 6 | F | 7; 9 | Prematurity and perinatal asphyxia | 24 | 680 | Spastic tetraplegia | 5 | Yes (severe) | No | Yes |
| 8 | M | 5; 9 | Perinatal asphyxia | 34 | 2500 | Spastic tetraplegia | 5 | No | No | No |
| 12 | M | 1; 11 | Perinatal asphyxia | 42 | 3460 | Spastic tetraplegia | 5 | Yes (severe) | Yes | Yes |
| 13 | F | 3; 10 | Perinatal asphyxia | 28 | 900 | Spastic tetraplegia | 5 | Yes (moderate) | Yes | No |

acquiring 120 million counts for emission and 50 million/5-minute counts for transmission. The PET scan was reconstructed using order subset estimation for maximum likelihood in 1 iteration and 30 subsets. The zoom factor was 2.5. Quality control was obtained for reproducibility of baseline and a second scan in terms of blood glucose, mCi dose of FDG injected, the time of performing the FDG PET scan, and the time of sedation to minimize variation in the same patient.

Altogether, 22 regions of interests for each side of the brain were drawn on the FDG PET scan with the assistance of a template by expert interaction on the transverse slice images of the brain at different levels. The region of interest includes the superior, middle, and inferior frontal gyri, precentral and postcentral gyri, superior and inferior parietal lobules, anterior and posterior cingulate gyri, Broca's area, angular gyri, auditory temporal cortex, associative auditory temporal cortex, precuneus, cuneus, lingual gyri, hippocampus, cerebellum, pons, caudate head, lentiform nucleus, and thalamus.

Standardized uptake value maximum and standardized uptake value average of each region were obtained. An increase of 10% between the baseline and post-treatment standardized uptake value maximum or standardized uptake value average in one or both occipital lobes was considered a significant response.

With our previous experience of using PET glucose metabolism as a surrogate marker for improvement in brain function, we arbitrarily defined 10% as the most suitable value for demonstrating improvement in glucose metabolism in a PET scan.

Outcome data for items 1, 2, and 3 were performed after completion of 40 sessions (ie, 8 weeks) of acupuncture.

Ethical Approval

This study was approved by the Ethics Committee of the Faculty of Medicine of The University of Hong Kong. The parents were informed about the methodology, and written consent was obtained.

RESULTS

Altogether, four cases (two boys, two girls), aged 23 months to 7 years, were recruited (Table 1). The cause of cerebral palsy was

severe perinatal hypoxic-ischemic encephalopathy in all four. Two children were born prematurely.

Clinical Outcome

Functional Independence in Children

None of the children had any improvement in the Functional Independence in Children score after the 8-week course of acupuncture.

Clinical Global Impression Scale (Parental Report)

The mothers of all four cases noted 25% improvement as measured by the Clinical Global Impression Scale (Table 2). None of the parents reported any adverse events.

PET Glucose Metabolism

Using the criteria of a $\geq 10\%$ increase in cortical mean standardized uptake value maximum and cortical mean standardized uptake value average as a significant change in PET glucose metabolism between the baseline and postintervention PET scan, there was a positive response in at least one region in all cases.

FDG PET Brain Scan

The PET scans of the four cases are illustrated in Figures 1 and 2 and Table 3.

PET Scan Report of Four Cerebral Palsy Cases

Case 6: Female, 7 Years Old

The overall cerebral cortical metabolism showed no significant interval change. However, there was a significant improvement in the occipital lobe metabolism, which correlated with the clinical finding of visual improvement. There was also an improvement in the basal ganglia, cerebellum, vermis, and pons metabolism correlating with the motor improvement noted by the mother. There was some mild down-regulation of the superior frontal lobe metabolism.

Table 2. Outcome Using the Clinical Global Impression Scale

| Case | Clinical Global Impression Scale Score* | Parental Report After 8 wk |
|------|---|---|
| 6 | 3 | Improvement in vision; could read characters better |
| 8 | 3 | Improvement in motor function, with more active movement seen |
| 12 | 3 | Improved hearing, smiled more, could clap hands while smiling, increased vocalization |
| 13 | 3 | Improvement in squinting, reaching out for objects with her upper limbs, increased vocalization |

*1 = +75%; 2 = +50%; 3 = +25%; 4 = no change; 5 = -25%; 6 = -50%; 7 = -75%.

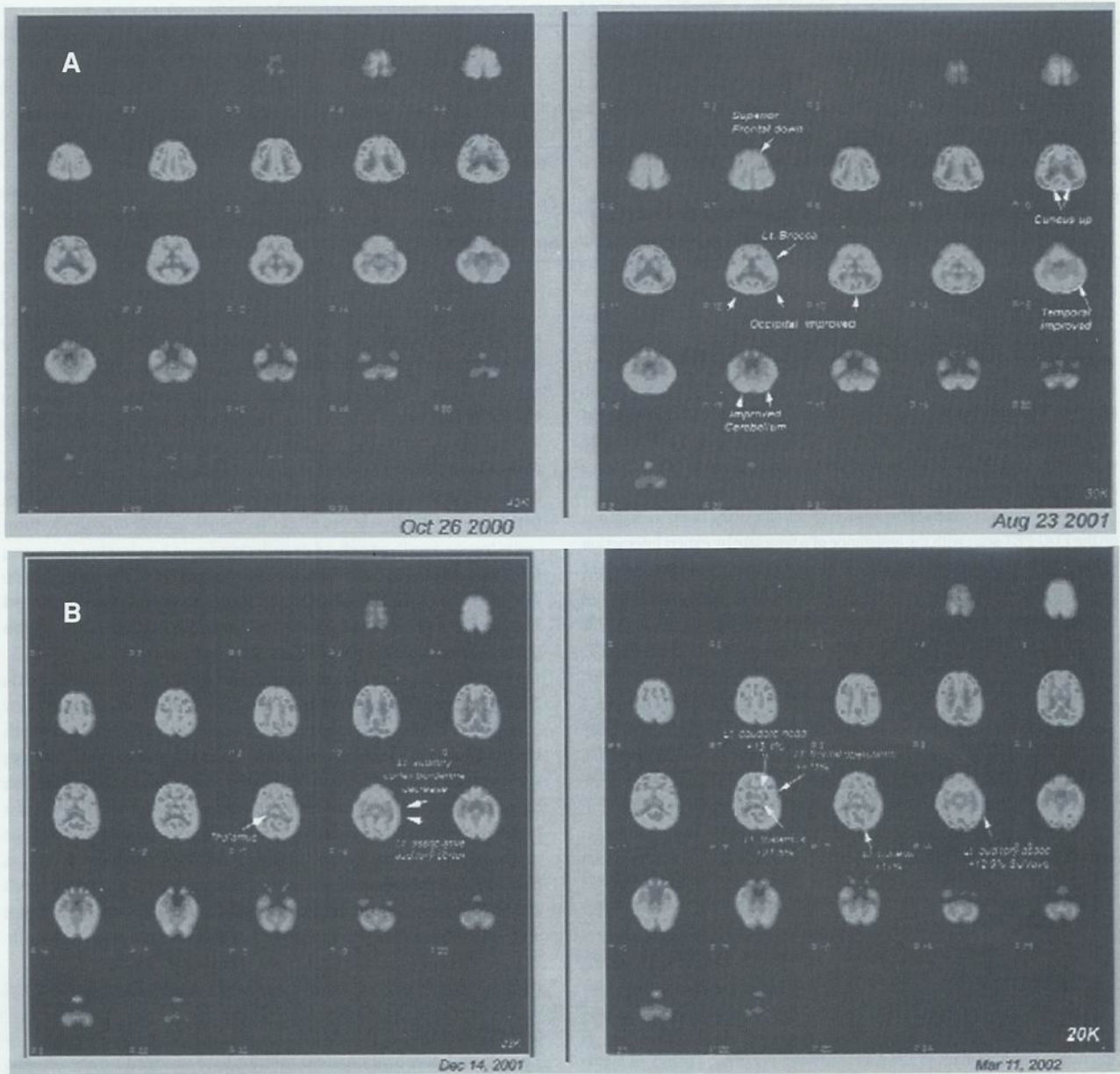


Figure 1. Positron emission tomography (PET) brain scan for four cerebral palsy cases. A, Case 6, female, 7 years. B, Case 8, male, 6 years.

Case 8: Male, 6 Years Old

There was a slight decrease in superior cerebral frontal metabolism, but the difference was not significant. The premotor cortex of both sides had better metabolism. A mild decrease in the left primary auditory cortex and associative auditory cortex was no longer seen and was within normal standard deviation in comparison with the right side. In comparison with the last PET scan, there was no significant change in the cortical mean. In comparison with the last PET scan, there was a mild increase in the metabolism of the left caudate nucleus and left thalamus. The left cuneus also showed mild improvement in metabolism. There was also borderline improvement in the left auditory associative cortex and right frontal operculum metabolism. The findings correlated

with the maternal report of clinical improvement in muscle tone control of the right leg and visually and auditorily more receptive and better spontaneous speech.

Case 12: Male, 2 Years Old

There was 19.6% improvement in the cerebral cortical standardized uptake value maximum and a significant percentage of improvement in frontal and parietal lobe metabolism; the actual functionality of the cerebral hemisphere in the frontal lobe, parietal lobe, and occipital lobe is still markedly impaired. The right inferior temporal lobe still had good metabolism, with probably the only area of significant function remaining in the cerebrum. There was some improvement in the mesotemporal lobe on the right side, which was

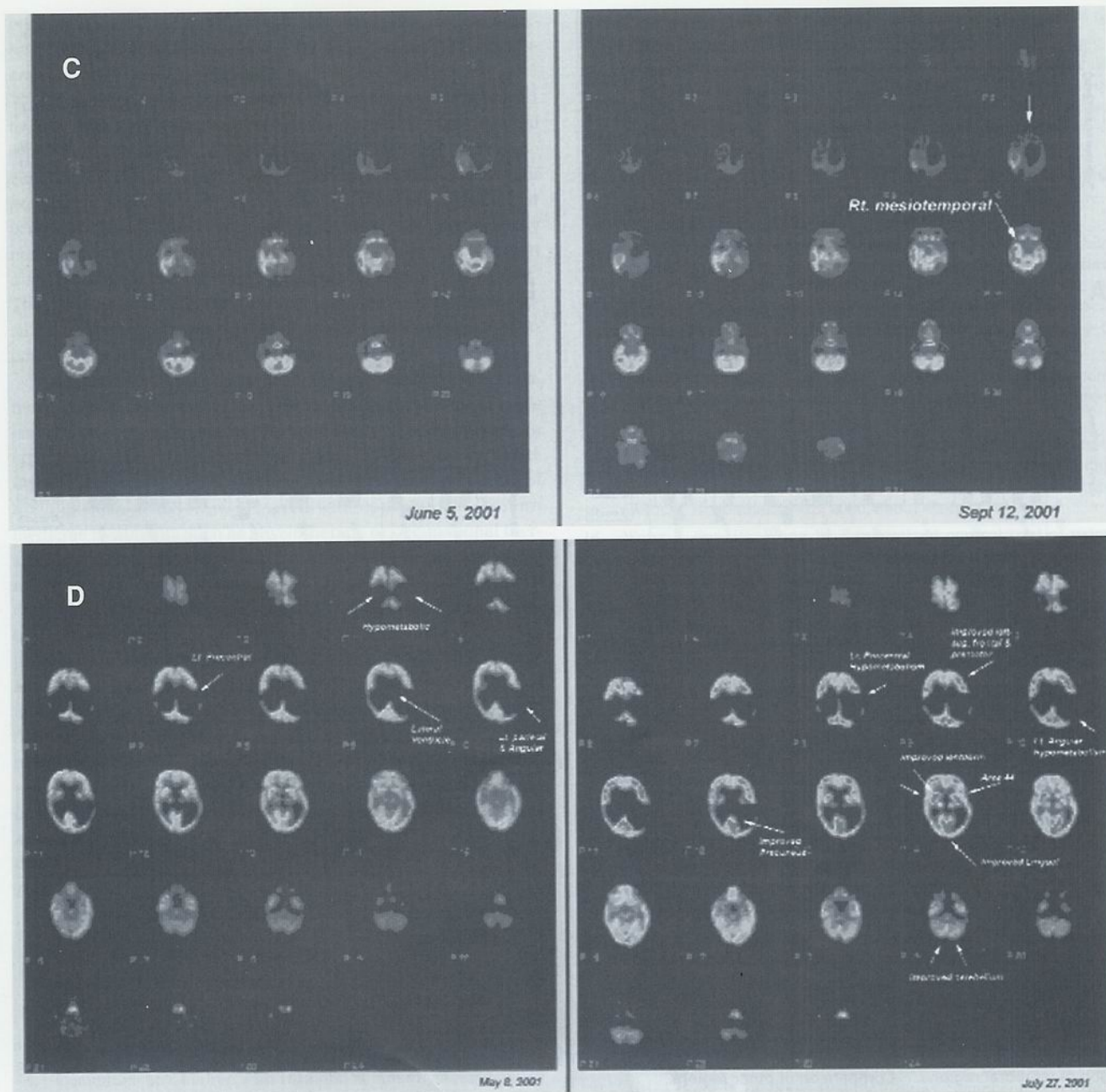


Figure 1. *continued* Positron emission tomography (PET) brain scan for four cerebral palsy cases. C, Case 12, male, 2 years. D, Case 13, female, 4 years.

compared before. The cerebellum was now down-regulated, and the hypermetabolic activity seen in the vermis had now returned to normal. There was no significant interval improvement seen in basal ganglia, thalamus, and pontine function.

Case 13: Female, 4 Years Old

There was a general 24.4% improvement in cerebral metabolism. The improvement in function appeared to be more noticeable on the left, which was the worse side previously. Improvement was seen in the superior frontal, premotor, area 44 (frontal operculum [Broca]), precuneus, occipital, visual, and primary auditory cortices.

There was also improvement seen in the metabolic function of the lentiform nucleus and cerebellum.

DISCUSSION

We demonstrated an objective increase in brain glucose metabolism in four cerebral palsy cases using a short course of daily tongue and body acupuncture (40 sessions in total applied for 5 days a week for 8 weeks), although the Functional Independence Measure for Children was not sensitive enough to show any change within 8 weeks. Although this scale is useful in monitoring the suc-

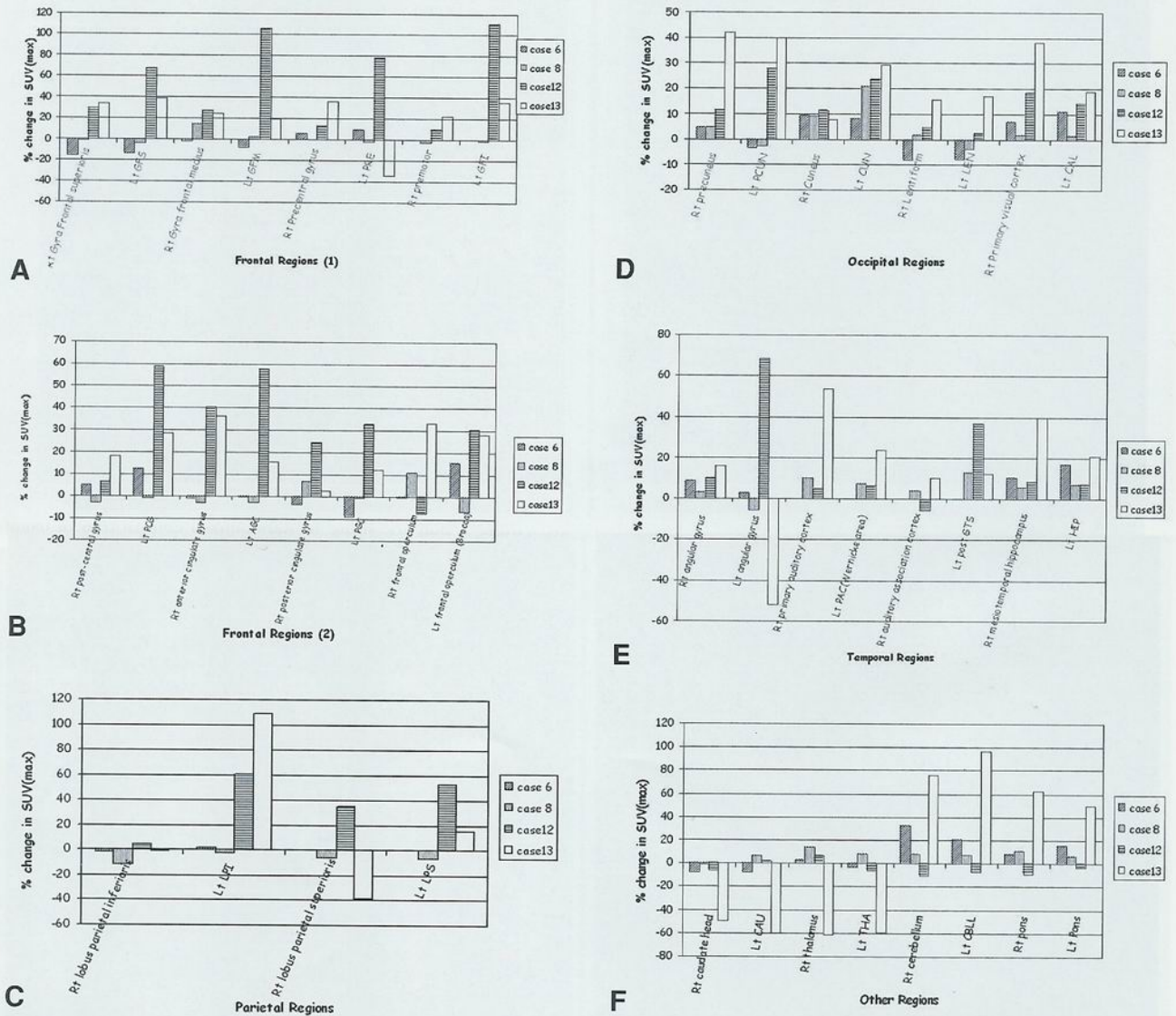


Figure 2. Comparison of percent change in standardized uptake value maximum (SUVmax) for the four cerebral palsy cases. A, Comparison of frontal regions (1). B, Comparison of frontal regions (2). C, Comparison of parietal regions. D, Comparison of occipital regions. E, Comparison of temporal regions. F, Comparison of other regions.

Table 3. Brain Positron Emission Tomography Glucose Metabolism in Cerebral Palsy Cases

| Case | Frontal | Parietal | Temporal | Occipital | Caudate | Thalamus | Cerebellum | Pons | PET +ve in Any One Region? |
|------|---------|----------|----------|-----------|---------|----------|------------|------|----------------------------|
| 6 | + | - | + | + | - | - | + | + | + |
| 8 | + | - | + | + | + | + | - | + | + |
| 12 | + | + | + | + | - | - | - | - | + |
| 13 | + | + | + | + | - | - | + | + | + |

PET = positron emission tomography; PET +ve = + 10%

+ = Increase in brain glucose metabolism by 10% was taken as an arbitrary definition for [¹⁸F]fluorodeoxyglucose as a surrogate marker for improvement in brain function.

cess of any rehabilitation program, the short period of acupuncture might not be best reflected by this scale because this is a Likert scale of 7.³²

However, all mothers did observe clinical improvement, at least to 25%. Thus, the anecdotal reports of efficacy based on parental report might be subjective and biased. Thus, one needs to combine qualitative outcome measures with semiquantitative ones and, if possible, quantitative ones, such as the PET scan, although the cost is much higher. Children with severe cerebral palsy, being totally nonambulatory, might not show major clinical improvement within a short 2-month course using the available outcome measures. Thus, the use of a PET scan of the brain might be a useful dimension to assess objectively the use or any claims of the use of alternative medicine for chronic disability.

Acupuncture has been practiced widely in Oriental centers and, more recently, in European countries for children with various types and severity of cerebral palsy. Our pilot study is the first to use an objective and yet more sensitive surrogate marker to demonstrate the efficacy of alternative medicine. Whether similar changes of brain glucose metabolism occurred with conventional Western medicine treatments such as physiotherapy or occupational therapy for children with cerebral palsy or the natural clinical course needs more refined case-control studies to answer these questions. For patients with chronic neurologic disorder such as cerebral palsy undergoing conventional or adjunctive treatment, we propose that a combination of clinical information with objective assessment should be available to document the scientific basis of neuroplasticity. The combination of these objective tools should deter overpromotion of various forms of "quack medicine" to vulnerable families. One should apply the World Health Organization model of the *International Classification of Impairments, Disabilities, and Handicaps* to reach a consensus on the treatment aimed at impairment, disability, or handicap.³³

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