

# Randomized Controlled Trial of Electro-Acupuncture for Autism Spectrum Disorder

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## Abstract

**OBJECTIVE:** To study the efficacy, safety, and compliance of short-term electro-acupuncture for children with autism spectrum disorder (ASD). **DESIGN:** Randomized, double-blind, sham-controlled, clinical trial. **SUBJECTS AND METHODS:** Children with ASD were randomly assigned to an electro-acupuncture (EA) group (n=30) or a sham electro-acupuncture (SEA) group (n=25) matched by age and severity of autism. The EA group received electro-acupuncture for selected acupoints while the SEA group received sham electro-acupuncture to sham acupoints. A total of 12 EA and SEA sessions over four weeks were given. Primary outcome measures included Functional Independence Measure for Children (WeeFIM®), Pediatric Evaluation of Disability Inventory (PEDI), Leiter International Performance Scale-Revised (Leiter-R), and Clinical Global Impression-Improvement (CGI-I) scale. Secondary outcome measures consisted of Aberrant Behavior Checklist (ABC), Ritvo-Freeman Real Life Scale (RFRLS), Reynell Developmental Language Scale (RDLS), and a standardized parental report. Data were analyzed by the Mann-Whitney test. **RESULTS:** There were significant improvements in the language comprehension domain of WeeFIM (p=0.02), self-care caregiver assistant domain of PEDI (p=0.028), and CGI-I (p=0.003) in the EA group compared to the SEA group. As for the parental report, the EA group also showed significantly better social initiation (p=0.01), receptive language (p=0.006), motor skills (p=0.034), coordination (p=0.07), and attention span (p=0.003). More than 70 percent of children with ASD adapted to acupuncture easily, while eight percent had poor acupuncture compliance. Mild side effects of minor superficial bleeding or irritability during acupuncture were observed. **CONCLUSION:** A short, four-week (12 sessions) course of electro-acupuncture is useful to improve specific functions in children with ASD, especially for language comprehension and self-care ability.

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## Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by the triad of impairment of social interaction, communication, and stereotypic behavior.<sup>1</sup> There is lack of evidence and consensus about the best treatment for the core features of ASD.<sup>2</sup>

Complementary and alternative medicine (CAM) as defined by Cochrane Collaboration<sup>3</sup> is: "...a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period. CAM includes all such practices and ideas self-defined by their users as preventing or treating illness or promoting health and well being. Boundaries within CAM and between the CAM domain and that of the dominant system are not always sharp or fixed." About 40 percent of ASD children have used CAM, with acupuncture being the most common modality.<sup>4</sup> Acupuncture has been widely practiced in China and is being increasingly practiced in many Western countries.<sup>5</sup>

## Objective

To date, no randomized, controlled trial has studied the efficacy and safety of electro-acupuncture in ASD. This is the first double-blind, randomized, controlled trial (RCT) of electro-acupuncture for children with ASD and is based on the selected acupoints from a previous pilot study.<sup>6</sup> This trial was registered at ClinicalTrials.gov (2006 July 13; identifier: NCT00346736).

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**Key words:** autism spectrum disorder, ASD, traditional Chinese medicine, TCM, acupuncture, autistic, electro-acupuncture,

## Study Design

A double-blind, randomized, controlled trial was conducted from May 2005 to June 2006 at the Hong Kong West Cluster (Queen Mary Hospital, Duchess of Kent Children's Hospital, and Tung Wah Group of Hospitals [TWGH]).

The research protocol was approved by the Institutional Review Board of the Faculty of Medicine of the University of Hong Kong and Hospital Authority (Hong Kong West Cluster). Written informed consents were obtained.

## Subjects and Methods

### Patients

Children with ASD receiving treatment at Duchess of Kent Children's Hospital were invited to participate. In addition, letters were mailed to special child care centers and special schools under Tung Wah Group to invite parents of children with ASD to participate. Clinical history and comprehensive examination were performed during the respondents' initial interview.

Inclusion criteria included those satisfying the diagnostic criteria of ASD based on:

- ◆ Diagnostic and Statistical Manual (4th Edition) (DSM-IV)<sup>7</sup>
- ◆ Autism Diagnostic Interview-Revised (ADI-R)<sup>8</sup>
- ◆ Autism Diagnostic Observation Scale (ADOS)<sup>9</sup>
- ◆ Ages 3-18 years

Exclusion criteria included children who had been on anti-epileptic drugs or who had received acupuncture in the preceding six months. Eligibility of included children was confirmed by the principal investigator (VC Wong). The wash-out period for eligible children was two weeks to provide a psychological preparation period for parents and prevent potential confounding factors.

### Randomization and Concealment Allocation

Stratified randomized assignment procedure was performed; allocation was conducted by the second author. A computer program generated randomization numbers, matched by chronological age and severity of autism, using the Childhood Autism Rating Scale (CARS).<sup>10</sup> CARS is a diagnostic tool designed to assess children with suspected autism and to determine severity.<sup>10</sup> Each child was randomly assigned by drawing an envelope containing a randomization number.

The parents and assessor were blinded to allocation of groupings. They were informed by the second author that children would be allocated into either A or B groups. The third author

(acupuncturist) was not blinded to the actual electro-acupuncture (EA) or sham electro-acupuncture (SEA) group allocations. The code was broken upon completion of the trial. To ensure the integrity of blinding, the acupuncturist was not allowed to discuss the acupuncture procedure with parents.

### Intervention

Children received three sessions of electro-acupuncture weekly on alternate days for four weeks. Sterile disposable 0.3 x 4 cm acupuncture needles (made in China-HWA-TO) were used. No sedation was used, and parents or caretakers were encouraged to stay with the child throughout the acupuncture course.

### Electro-acupuncture (EA) Group

Eight acupoints were selected:

Sishencong (EX-HN1), Yintang (EX-NH3), Neiguan (PC6), Shenmen (HT7), TaiChong (LR3), Ear naodian (AT3), Ear shenmen (TF4), and Sanyinjiao (SP6).

The treatment took place with the child in either a supine or sitting position. Needle sites were disinfected, and disposable needles were inserted into the acupoints selected.

A portable electro-acupuncture machine (Model HWATO SDZ-II, Electronic Acupuncture Treatment Instrument, Suzhou Medical Appliance Factory, China) was connected to the handles of the acupuncture needles to provide electrical stimulation for 30 minutes. Spacing-density wave stimulation was applied.

In both groups the conventional interventional or educational program for ASD was continued. Two cases from the EA group were maintained on neuroleptic drugs at the same dose during the study.

### Sham Electro-acupuncture (SEA) Group

Points 3-5 mm from the selected acupoints for the EA group were disinfected. Disposable needles were inserted into and maintained at a superficial level. The same electro-stimulation model as the EA group was used (i.e., the same electro-acupuncture machine was connected to the handles of acupuncture needles to provide electrical stimulation for 30 minutes with spacing-density wave stimulation).

### Outcome Measures

The primary outcome measures included Functional Independence Measure for Children

(WeeFIM®),<sup>11</sup> Pediatric Evaluation Disability Inventory (PEDI),<sup>12</sup> Leiter International Performance Scale-Revised (Leiter-R),<sup>13</sup> and Clinical Global Impression-Improvement (CGI-I)<sup>14</sup> scale. Secondary outcome measures included Aberrant Behavioral Checklist (ABC),<sup>15</sup> Ritvo-Freeman Real Life Scale (RFRLS),<sup>16</sup> Reynell Developmental Language Scale (RDLS),<sup>17</sup> and parental report.

### **Blinded Parental Assessment**

The following outcome measures were provided by parents:

**ABC:** A behavior rating scale for the assessment of treatment effects, consisting of five subscales (irritability, lethargy, stereotypy, hyperactivity, inappropriate speech), used at baseline and post-treatment.

**RFRLS:** A scale for rating symptoms of patients with autism in real life settings, consisting of five subscales (sensory motor, social relationships to people, affectual response, sensory response, language), used at baseline and post-treatment.

**PEDI:** A measure of functional ability in children, taking into account the use of special equipment and amount of caregiver assistance. It consists of 197 functional skill items, 20 caregiver assistance activities, and 20 environmental modifications, used at baseline and post-treatment.

**CGI-I:** The Clinical Global Impression-Improvement scale is a seven-point scale that requires the assessor to evaluate how much the subject's illness has improved or worsened with regard to a baseline state (beginning of the intervention). Children were rated on a Likert scale of 1-7, with 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse, and 7=very much worse. The CGI-I was assessed by the parent at post-treatment and verified by the clinician (Chen WX).

**Parental report:** A standardized, self-devised parental report was used for parents to record daily changes, consisting of open questions for parents to answer in a written format. Researchers can follow up with personal interviews. This parental report has been used for other acupuncture research in our center.<sup>18-20</sup>

During baseline assessment the parents were instructed on how to properly apply the above assessment tools.

### **Blinded Assessor Assessment**

The following outcome measures were performed at baseline and post-treatment in both groups by a "blinded" assessor:

**Leiter-R:** A measure of nonverbal intelligence in fluid reasoning, visualization, visuo-spatial memory, and attention.

**WeeFIM:** A concise, comprehensive assessment that compares a child's consistent and usual performance to criterion standards of essential self-care activities, bowel and bladder management, locomotion, transfers, communication, and social cognition. WeeFIM consists of 18 questions concerning three domains (mobility, self care, and cognition) that assess the functional independence of children. Scores range from 1 to 7, with 7 indicating complete independence. (The use of the WeeFIM instrument to collect data for this clinical trial study was authorized and conducted in accordance with the terms of a special purpose license granted to licensee by Uniform Data System for Medical Rehabilitation [a division of UB Foundation Activities, Inc., "UDSMR"]. Disclaimer: The patient data collected during the course of this clinical trial was not submitted to or processed by UDSMR. No implication is intended that such data has been subjected to UDSMR's standard data processing procedures or that it is otherwise comparable to data processed by UDSMR.)

**RDLS:** A measure of a child's receptive and expressive language abilities.

The following measures were adopted to monitor the safety of electro-acupuncture:<sup>6</sup>

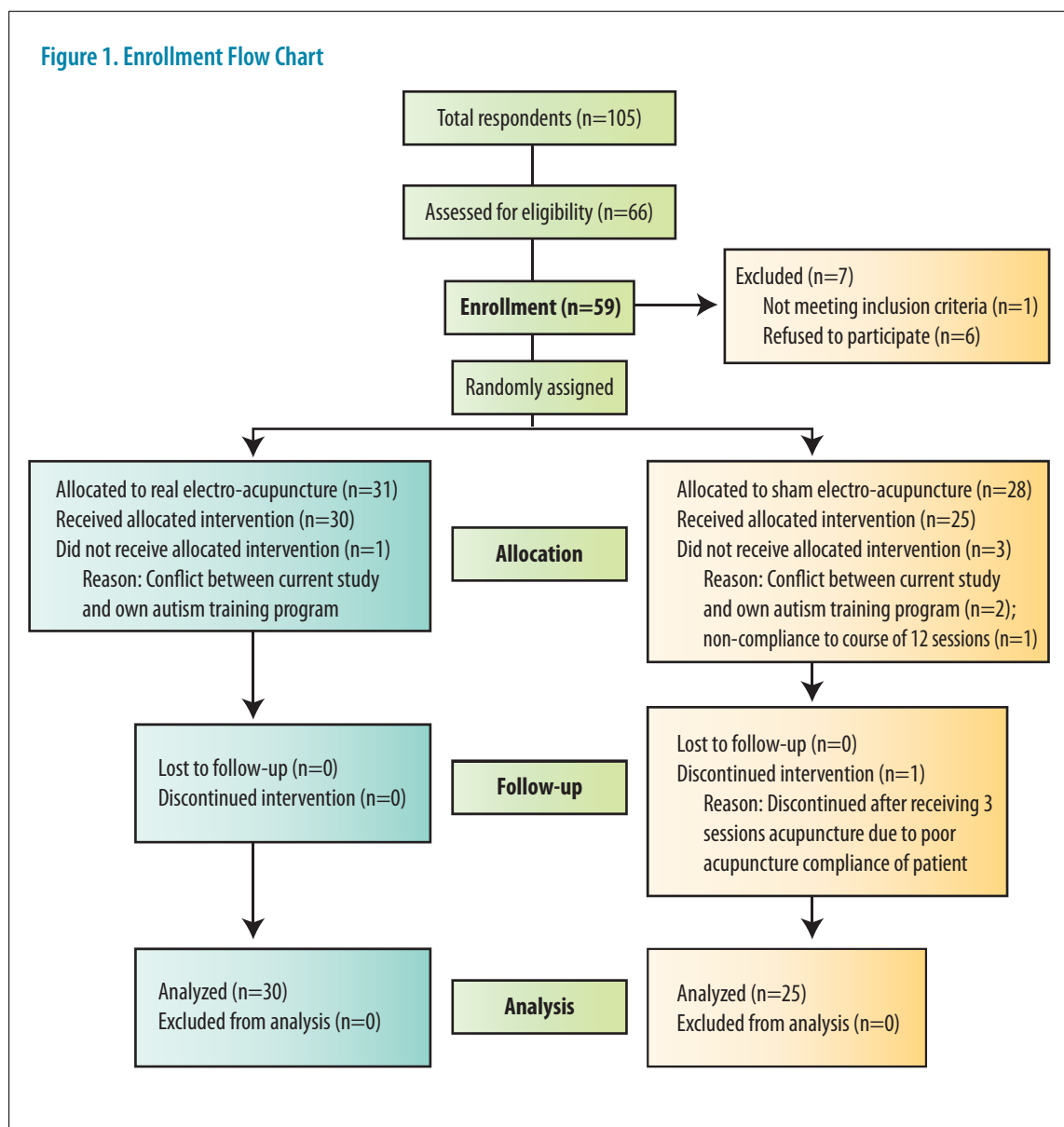
- ◆ Parents were advised to directly report possible adverse events to the research team or via the parental report.
- ◆ Researchers (including acupuncturist and clinicians) directly observed for adverse events during the acupuncture session.
- ◆ Researchers (clinicians) directly monitored treatment compliance for each case.

### **Statistical Analysis**

Baseline characteristics and differences between EA and SEA groups with different outcomes measures (RFRLS, ABC, PEDI, WeeFIM, RDLS, Leiter-R, CGI-I), parental report, and acupuncture compliance were analyzed using the Mann-Whitney test.

The intention-to-treat approach was used and  $p < 0.05$  indicated statistical significance.

Figure 1. Enrollment Flow Chart



## Results

### Baseline Characteristics

The flow chart of enrollment is shown in Figure 1. Of a total of 105 questionnaires received, 59 children were recruited and randomly assigned to electro-acupuncture (31 cases) or sham electro-acupuncture (28 cases). Four cases defaulted after randomization, leaving 55 subjects who began treatments – 30 cases receiving EA and 25 receiving SEA. Fifty-four subjects (30, EA group; 24, SEA group) were available for post-treatment assessment because one SEA subject dropped out after three sessions.

The baseline characteristics of both groups are shown in Table 1, including age, gender, severity of

autism, CGI scale, social status, parent education status, family history, whether acupuncture had been received prior to six months preceding the start of the study, and use of neuroleptic drugs. There were no significant differences between groups.

### Outcome Measures

Table 2 shows significant improvement after treatment in language comprehension ( $p=0.02$ ) of cognition domain of WeeFIM, self-care assistant domain ( $p=0.028$ ) of PEDI, and CGI-I ( $p=0.003$ ) in the EA group compared to the SEA group.

**Table 1. Baseline Characteristics**

	Electro-acupuncture group			Sham electro-acupuncture group			P value
	N	Mean	SD	N	Mean	SD	
Chronological age (year)	30	9.17	4.12	25	9.56	4.22	0.697
Gender (male/female)	25/5			22/3			0.628
Severity of autism (CARS)	30	37.23	3.32	25	36.54	3.05	0.525
<b>Clinical global impression-severity (CGI-S) scale</b>							
Mildly ill	6			5			0.563
Moderately ill	8			8			
Markedly ill	2			3			
Severely ill	13			9			
Most extremely ill	1			0			
<b>Social status (parents)</b>							
Professional	5			1			0.958
Managerial & technical	4			7			
Clerical and minor supervisory and skilled manual	8			7			
Semi-skilled manual	4			3			
Unskilled manual	9			7			
<b>Parent education status (paternal/maternal education status)</b>							
University or above	13 (8/5)			6 (4/2)			0.094 (0.131/0.436)
Middle school	39 (19/20)			33 (15/18)			
Primary school	8 (4/4)			9 (4/5)			
Illiterate	0 (0/0)			2 (2/0)			
<b>Family history</b>							
Negative for ASD	15			17			0.357
Positive for ASD	1			0			
Positive for SLD	9			3			
Positive for sibling ASD	2			2			
Positive for mental handicap	3			3			
<b>Received acupuncture prior to six months preceding enrollment</b>							
No	23			20			0.768
Yes	7			5			
<b>Use of neuroleptic drug</b>							
No	28			25			0.193
Yes	2			0			

CARS: Childhood autism rate scale; CGI-S: Clinical global impression scale; ASD: Autistic spectrum disorder; SLD: Specific language delay



Table 2. Comparison of Differences in Outcome Measures

	Electro-acupuncture group			Sham electro-acupuncture group			P value
	N	Mean	SD	N	Mean	SD	
<b>Ritvo-freeman real life scale (RFRLS)</b>							
Sensory motor	30	-0.06	0.36	25	-0.11	0.32	0.851
Social	30	-0.11	0.33	25	-0.02	0.38	0.450
Affectual	30	-0.13	0.54	25	-0.05	0.39	0.313
Sensory response	30	-0.04	0.39	25	0.00	0.39	0.879
Language	30	-0.13	0.32	25	-0.03	0.35	0.448
Total score	30	-0.10	0.27	25	-0.05	0.26	0.361
<b>Aberrant behavior checklist (ABC)</b>							
Irritability	30	-2.00	7.19	25	-1.00	4.67	0.297
Lethargy	30	-2.03	5.50	25	-1.40	7.09	0.819
Stereotypy	30	-0.40	3.20	25	0.24	3.87	0.629
Hyperactivity	30	-3.10	6.82	25	-2.00	5.86	0.582
Inappropriate speech	30	-0.33	1.77	25	-0.28	2.15	0.849
<b>Pediatric evaluation of disability inventory (PEDI)</b>							
Self-care	30	1.40	2.40	25	-0.36	6.31	0.520
Mobility	30	0.63	1.52	25	0.00	1.00	0.215
Social function	30	1.83	4.78	25	0.16	7.70	0.959
Self-care caregiver assistant	30	1.77	2.89	25	-0.20	4.23	0.028
Mobility caregiver assistant	30	0.23	0.63	25	-0.24	1.42	0.797
Social caregiver assistant	30	1.83	2.64	25	-2.08	3.63	0.545
<b>WeeFIM®</b>							
Self-care	30	0.30	3.29	25	-0.36	3.93	0.597
Mobility	30	-0.17	0.75	25	0.40	2.36	0.812
Cognition	30	1.07	1.29	25	0.56	1.92	0.269
Comprehension	30	0.53	0.57	25	0.16	0.85	0.020
Expression	30	0.30	0.84	25	0.16	0.75	0.779
Social interaction	30	0.07	0.52	25	0.20	0.58	0.354
Problem solving	30	-0.13	0.35	25	0.00	0.71	0.290
Memory	30	0.03	0.49	25	-0.04	0.54	0.595
Total score	30	1.03	3.85	25	-0.08	6.70	0.599
<b>Reynell developmental language scale (RDLS)</b>							
Comprehension age (year)	30	0.12	0.40	25	0.03	0.51	0.556
Expression age (year)	30	0.09	0.70	25	0.05	1.09	0.581
<b>Leiter international performance scale-revised (Leiter-R)</b>							
Visualization & reasoning (VR) battery (Full IQ)	30	4.60	10.47	25	3.24	10.46	0.892
Attention & memory (AM) battery (Composite score)	30	0.97	6.17	25	1.28	9.78	0.603
VR battery (Growth composite score)	30	5.97	10.39	25	0.24	22.90	0.515
AM battery (Growth composite score)	30	2.23	15.88	25	2.44	17.07	0.493
<b>Clinical global impression-improvement (CGI-I) scale</b>							
Much improvement (50% improvement)	7			1			0.003
Minimal improvement (25% improvement)	20			14			
No Change (0% improvement)	3			10			

## Parental Report

Table 3 illustrates the results of the parental report, which included social relatedness (social response, social initiation, eye contact, sharing, curiosity, and patience); non-verbal and verbal communication (expressive language, receptive language, pointing, and imitation), stereotypy interest and behavior (temper, compulsive behavior, and adaptation to change), cognition (memory and learning ability), motor abnormalities (motor skill, coordination, and drooling), and other parent-reported changes (attention span, appetite, sleeping pattern, and craftiness).

There were significant improvements in social initiation ( $p=0.01$ ), receptive language ( $p=0.006$ ), motor skills ( $p=0.034$ ), coordination ( $p=0.07$ ), and attention span ( $p=0.003$ ) in the EA group compared to the SEA group.

## Discussion of Results

### Social Relatedness, Communication, and Stereotypic Behavior

Significant improvement in social initiation as reported in the parental report (Table 3;  $p=0.01$ ) was seen in the EA group compared to the SEA group, although no significant differences in outcomes of the social domain of RFRLS were observed (Table 2). Non-significant improvement in the domain of eye contact was also detected in the parental report.

Similarly, significant improvement ( $p=0.006$ ) in receptive language was seen in the EA group compared to the SEA group, based on the parental report. This coincided with the outcome of WeeFIM, in which the ability of language comprehension was significantly improved in the EA group (Table 2;  $p=0.02$ ), although the RDLS did not detect significant improvement in comprehension (Table 2). A recent RCT<sup>21</sup> reported that scalp acupuncture is a safe complementary modality when combined with language therapy and has a significantly positive effect on language development in children with autism.

Significant improvement in attention span was found in subjects treated with acupuncture, as reported by parents (Table 3;  $p=0.003$ ), although Leiter-R did not find significant differences in this domain (Table 2). A non-significant improvement of expressive language ability, such as more frequency, more words, or being more articulate, was also noted in the parental report.

There were no significant effects of acupuncture in improvement of the sub-domains on the

Aberrant Behavioral Checklist (Table 2), although non-significant improvement in temper tantrums was noted in the parental report.

### Functional Status

The significant improvement in language comprehension contributes to the significant improvement (Table 2;  $p=0.028$ ) in self-care in the caregiver assistant domain of the PEDI.

Improvements in language comprehension, self-care, and other domains may contribute to the significant improvement of clinical global impression on CGI-I (Table 2;  $p=0.003$ ) in the EA group.

### Cognition

The presence of mental deficiencies in ASD may be the most important factor for long-term prognosis.<sup>22</sup> It is reported that up to 40 percent of ASD individuals are nonverbal, although nearly 50 percent (27 nonverbal; 28 verbal) of ASD children in this study were nonverbal.

The Leiter-R was adopted as a cognitive assessment tool in the current study, although it might be somewhat biased toward verbal subjects, especially for high functioning verbal ASD individuals.<sup>23</sup>

According to the parental report, a few parents from both groups reported improvement of memory, learning ability, or "craftiness." No significant between-group differences were found when comparing the Leiter-R reasoning and visualization battery or memory and attention battery.

### Motor Abnormalities

Most ASD subjects lack imitation abilities. In those with praxic deficits, imitation quality as well as quantity is impaired, with movements being awkward and inaccurate. Significantly greater improvements in motor skills (Table 3;  $p=0.034$ ) and coordination (Table 3;  $p=0.07$ ) were found in the EA group, although no significant improvement in drooling was found.

Improvements in writing ability – writing words within aligned lines and squares, instead of outside – were reported by some parents, which was also compatible with the outcomes of the pilot study.<sup>6</sup> One case of improvement in swimming ability and in paper cutting was reported in the EA group. Other motor skill improvements reported in patients in the EA group included less clumsiness and improvement in walking posture, speed of walking, or ability to go up and down stairs.

Table 3. Parental Report: Outcomes Comparisons

		EA group n	SEA group n	P value	Remarks
<b>Social relatedness</b>					
Social response	No change	26	20	0.510	Improvement of frequency in response to parents social interaction
	Better than before	4	5		
Social initiation	No change	23	25	0.01	Improvement of frequency in social initiation with parents
	Better than before	7	0		
Eye contact	No change	23	21	0.502	Improvement of eye contact with parents
	Better than before	7	4		
Share	No change	30	24	0.273	Improvement of frequency of share behavior with parents
	Better than before	0	1		
Curiosity	No change	30	24	0.361	Improvement of curiosity to environment
	Better than before	0	1		
Patience	No change	29	25	0.361	Improvement of patience when asked by parent
	Better than before	1	0		
<b>Non-verbal and verbal communication</b>					
Expressive language	No change	19	17	0.391	Improvement of frequency, words, or articulation
	Better than before	11	7		
Receptive language	No change	13	20	0.006	Improvement in understanding language given by parents
	Better than before	17	5		
Pointing	No change	29	25	0.361	Improvement of frequency in using pointing gestures
	Better than before	1	0		
Imitation	No change	29	25	0.361	Improvement in imitation ability
	Better than before	1	0		
<b>Stereotypy interest and behavior</b>					
Temper	No change	21	17	0.371	Better: Improvement in temper Worse: Worse in temper in the initial sessions
	Better than before	8	5		
	Worse than before	1	3		
Compulsive behavior	No change	27	23	0.684	Better: Improvement in compulsive behavior Worse: Worse in compulsive behavior in the initial sessions
	Better than before	1	1		
	Worse than before	2	1		
Adaption to change	No change	30	24	0.273	Improvement in adaption to change
	Better than before	0	1		
<b>Cognition</b>					
Memory	No change	29	23	0.452	Improvement in memory ability
	Better than before	1	2		
Learning ability	No change	28	23	0.851	Improvement in learning ability, e.g. reading comprehension, etc.
	Better than before	2	2		
<b>Motor abnormalities</b>					
Motor skill	No change	25	25	0.034	Improvement in walking posture, the speed of walking, or the ability of going up and down stairs, etc.
	Better than before	5	0		
Coordination	No change	22	23	0.07	Improvement in word writing, cutting paper, or swimming
	Better than before	8	2		
Drooling	No change	28	24	0.667	Improvement in drooling
	Better than before	2	1		
<b>Other parent reported changes</b>					
Appetite	No change	27	24	0.398	Improvement in appetite
	Better than before	3	1		
Attention span	No change	21	25	0.003	Improvement in attention span
	Better than before	9	0		
Sleeping pattern	No change	20	22	0.828	Better: Improvement in sleep pattern Worse: worse in sleep pattern in the initial sessions (Wake earlier or slept later)
	Better than before	7	3		
	Worse than before	3	0		
"Crafty"	No change	28	24	0.667	Improvement in problem solving ability
	Better than before	2	1		

EA: Electro-acupuncture, SEA: Sham electro-acupuncture



### Acupuncture Compliance and Side Effects

The definition of “acupuncture compliance” is that subjects were able to sit or lie on a couch to accept acupuncture, even if they cried or needed gentle hand or head holding. Good compliance was defined as being able to accomplish this within the first three sessions, while poor compliance meant they were unable to sit or lie on the couch for treatment for nine or more sessions. Table 4 summarizes the categories of acupuncture compliance. There were no significant differences between groups regarding acupuncture compliance, with more than 70 percent of subjects adapting with good compliance, while only eight percent demonstrated poor compliance.

**Table 4. Treatment Compliance**

Compliance	EA Group n	SEA Group n	Total	P value
< 3 sessions	20	20	40	0.382
< 6 sessions	5	1	6	
< 9 sessions	3	2	5	
≥ 9 sessions	2	1	3	
Discontinued intervention	0	1	1	

A systematic review of prospective studies of acupuncture safety found the most common adverse events were needle pain, tiredness, and bleeding. Feeling of faintness and syncope were uncommon, and pneumothorax was rare.<sup>24</sup> In this study, the mild side effects of minor superficial bleeding or crying and irritability during acupuncture were experienced by some.

### General Discussion

Clearly, existing epidemiological and genetic studies on autism spectrum disorder support a complex etiology.<sup>25</sup> Twin<sup>26,27</sup> and family aggregation studies<sup>28,29</sup> strongly support a heritable component to autism etiology. However, the model of inheritance is still not clear, and the identity and number of genes involved remain unknown.<sup>30</sup> In addition, epidemiological studies indicate that environmental factors such as toxic exposures, teratogens, perinatal insults, and prenatal infections such as rubella and cytomegalovirus account for a few

cases.<sup>30</sup> It is suggested that autism might result from an interaction between genetic, epigenetic, environmental, and immunological factors, with oxidative stress as a mechanism linking these risk factors.<sup>31</sup> Recently, research has focused on the role of synapse structure and function as central to the development of ASD, suggesting possible targets of intervention.<sup>32</sup>

The effect of acupuncture has been demonstrated in animal and human studies to be due to direct neural stimulation and changes in neurotransmitters such as endorphins, immunological markers, or endocrinological signals.<sup>33</sup> These responses can occur locally or close to the site of application,<sup>34</sup> or at a distance, mediated mainly by sensory neurons to many structures within the central nervous system.<sup>35</sup> This can lead to activation of pathways affecting various physiological systems in the brain as well as in the periphery.<sup>36,37</sup> In traditional Chinese acupuncture, nearly 400 acupoints on the body surface are interrelated to various functions linked through 14 meridians to various organs or viscera of the human body.<sup>2</sup> By stimulating various meridian points, acupuncture may be able to correct the disharmony and dysregulation of organ systems, which might be involved in various dimensions of ASD, to relieve symptoms and restore the mind and body.<sup>2</sup> The scientific basis of how acupuncture could ameliorate different cognitive and behavioral dimensions of ASD has not been well studied, and the mechanisms of how acupuncture works are likely to be very complex, given the vast number of acupoints involved in the treatment of this complicated disease.<sup>2</sup>

Evidence-based clinical trials of acupuncture for ASD are lacking.<sup>2</sup> Despite a comprehensive search strategy used in our systematic Cochrane review,<sup>2</sup> there had been, prior to this study, no randomized, controlled trial of body-acupuncture for ASD identified in the international peer-reviewed journals, with the exception of three studies using tongue acupuncture (two accepted for publication in *J Altern Complement Med*) and one using scalp acupuncture.<sup>21</sup>

Since ASD is a heterogeneous disorder with co-morbidities, and there is a lack of a single standardized assessment tool, it is difficult to test the efficacy of a particular therapy. Therefore, this study adopted a comprehensive panel of assessment tools based on the researchers’ 25 years of experience with ASD interventions. In the current study, ABC and RFRLS were used to assess core

autistic features, PEDI and WeeFIM examined functional abilities, RDLS assessed language, Leiter-R was used to study cognition, and the CGI scale assessed global impression.

In addition, the parental report, based on the first author's experience in acupuncture studies in patients with various chronic neurological disorders,<sup>18-20</sup> was used as a complementary tool for parents to record daily observations. Although this tool may be too subjective for analysis in an RCT, parents were blinded to the actual group their child was in.

### Traditional Chinese Medicine and Autism Spectrum Disorder: Rationale for Treatment Protocol

Although no modern diagnosis like ASD was found in the history of traditional Chinese medicine, its origins might date back to ancient China because it might be categorized as one type of "childhood derangement,"<sup>6</sup> noted as a disease category.

According to TCM, the pathogenesis of ASD is the derangement and insufficiency of the brain and mind.<sup>6</sup> The pathological involvement is in the brain, relating to the Heart, Pericardium, Liver, Spleen, and Kidney. The etiology results from an innate lesion or insufficiency of the brain/mind and dysregulation of the Heart, Liver, Spleen, and Kidney after birth.<sup>6</sup>

Acupuncture involves complex theories of regulation of five elements (Fire, Earth, Metal, Water, and Wood), Yin and Yang, Qi, Blood, and body fluids. By stimulating various meridian points, disharmony and dysregulation of organ systems is corrected to relieve symptoms and restore natural internal homeostasis.<sup>38</sup>

The main objective is to "awake," to "assist," and to "calm" the mind, as well as enlighten the mentality and improve developmental profile. Consequently, the primary acupoints were selected from head acupoints: Sishencong (EX-HN1) and Yintang (EX-NH3); and ear acupoints: Ear Naodian (AT3) and Ear Shenmen (TF4).

To complement these primary points, other acupoints from the Heart (Shenmen, HT7), Pericardium (Neiguan, PC6), Liver (TaiChong, LR3), and Spleen (Sanyinjiao, SP6) meridians were selected. The intention was to make the heart "unobstructed," regulate the liver, correct derangements or imbalances, enforce the emotion, dredge stasis, invigorate the spleen and kidney, and facilitate the source of vital function.

Based on the acupoints selected, the primary outcome measures were involved in functional and cognitive domains, while secondary outcome measures concerned other related domains.

The pilot study<sup>6</sup> found that a short, intensive course of electro-acupuncture might improve some core features of children with ASD.

### Conclusion

A short, 12-session course of electro-acupuncture at selected acupoints was found to improve some functions in children with ASD, especially language comprehension and self-care ability. Thus, acupuncture might be a useful adjunctive therapy in early interventional programs for children with autism.

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