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# Laser Acupuncture Effects on Speech and Social Interaction in Patients with Autism Spectrum Disorder

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## ABSTRACT

**Objective:** Disorders of speech ability and social interaction are the most-common symptoms in children with autism spectrum disorder (ASD). Acupuncture, as an adjunctive therapy, is known to help improve speech ability and social interaction in children with this condition. One of the acupuncture modalities with minimal side-effects, and that is safe for children, is laser acupuncture or *laserpuncture*. This study's aim was to determine laserpuncture's effects on speech ability and social interactions in patients with ASD.
**Materials and Methods:** This randomized, double-blinded clinical trial involved 46 patients in 2 groups. All respondents qualified, and none dropped out. The treatment group ($n=23$) received sensory–occupational integrative therapy and verum laserpuncture therapy and the control group ($n=23$) received sensory–occupational integrative therapy and placebo laserpuncture. The groups' speech ability and social interaction were evaluated with a WeeFIM® questionnaire; parental reports were collected, using sensory profiles before and after treatment.
**Results:** There were improvements in speech ability and social interaction in the verum laserpuncture group more than in the placebo group after treatment. Perception score was $P<0.001$; odds ratio (*OR*): 18.8; 95% confidence interval (CI): 4.09–87.17. Expression score was $P<0.001$; *OR:* 50.2; 95% CI: 5.61–450.2. Social interaction score was $P=0.005$; *OR:*7.2; 95% CI: 1.68–31.42. Parental report score was $P=0.765$.
**Conclusions:** Verum laserpuncture in this clinical trial improved speech ability and social interaction scores more effectively than placebo laserpuncture did in patients with ASD.

**Keywords:** speech ability, social interaction, autism spectrum disorder, laser acupuncture.

## INTRODUCTION

Autism spectrum disorder (ASD) is a series of complex neurodevelopmental disabilities that can affect social interaction and communication and overall individual behavior. Deficits in social interaction, communication, and behavioral patterns, as well as repetitive activities are indicators commonly found in many autistic children.[1] Disruption of social interaction and communication cause behavioral disorders related to the autism spectrum, including speech abnormalities, sensory sensitivity, and obsession.[2]

According to data and reports in Indonesia in 2015, specifically for pediatric outpatient visits at the RSUPN Dr. Cipto Mangunkusumo National General Hospital, in Central Jakarta, Indonesia, 626 patients visited the hospital's integrative outpatient unit. In 2016, there were 656 patients,

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and, in 2017, there were 778 patients. The age range of most of the pediatric patients from 2015 to 2017 was between 2 and 8.[3] According to the data, the number of visits of patients with ASD was relatively large; hence, more attention is needed for diagnosis and therapy for such patients.

Autistic children have the same brain development as normal children. The brain develops quickly when a child is under age 5. The most-ideal age for early intervention is when a child is 2–3 years old, because, at this time, the child's brain undergoes the quickest development. Implementation of therapy is most effective before the child reaches age 5, because, after the child becomes 5–7 years' old, the child's brain development slows to 25%.[4,5]

The current standard of pharmacologic therapy involves using a single drug that only helps a small percentage of individuals with ASD. That drug is risperidone, one of the few drugs approved by the U.S. Food and Drug Administration (FDA) for treating autism. These drugs reduce irritability, hyperactivity, and repetitive and limited behavior, but most of these agents are ineffective for reducing impaired social interactions and language deficits in individuals with autism.[6] In fact, some drugs only reverse some symptoms of ASD.

Autism has an impact on children and also on their families. It can be in the form of poor school achievement, disruption of socialization, and increased risk of accidents. The impact on the family is the emergence of stress and depression in parents and caregivers, affecting family harmony. Because autism disorders are chronic, there is a need for higher energy and costs in efforts to overcome the disorders; even so, these efforts cannot offer better hope for treatment outcomes.[7,8]

Acupuncture is a nonpharmacologic therapy that uses fine needles inserted at specific points of the body (acupuncture points). One type of acupuncture is laser acupuncture, also called *laserpuncture*. Compared to manual acupuncture therapy, laserpuncture has several advantages, such as easy application, accurate ''dose'' measurements, painlessness, and noninvasiveness. Laserpuncture has been used in medicine for 30 years, and various studies have proven that laserpuncture is effective for relieving symptoms of ASD—especially difficulties with speech and social interaction as well as several other pediatric problems—and is safe for children.[9]

Therefore, this current study was expected to be able to determine the effect of verum laserpuncture on speech and social interaction in patients with ASD.

## MATERIALS AND METHODS

The current study was a double-blinded, randomized, controlled clinical trial, conducted from January to April 2019. The trial was conducted at the Anakku clinic, the Pondok Pinang Center, and the Buahati Mandiri Clinic, in Jakarta, Indonesia. This research was a collaborative study between the medical department of acupuncture's faculty of medicine and the pediatric neurology division of the department of pediatrics' faculty of medicine, at the University of Indonesia (FMUI)/Dr. Cipto Mangunkusumo Hospital.

The inclusion criteria of this study were subjects ages 2–6, female or male, who had been diagnosed with ASD by a pediatric neurologist consultant. The children's parents/guardians had to sign informed consents. The subjects also had to be able to take part in the study until it was finished, at a frequency of arrival 3 times per week for 18 therapy sessions, and to undergo or receive integrative sensory–occupational therapy. Exclusion criteria were subjects who were taking psychotropic drugs or using high-dose corticosteroids or drugs containing arsenic or nonsteroidal immunosupressants, subjects with contraindications to laserpuncture (such as malignancy, uncontrolled epilepsy, infections with body temperatures ≥38°C, wounds, or dermatitis in the acupuncture-point areas), medical emergencies,[23] increased photoallergic responses, cytostatic therapy, exacerbations of chronic skin disorders (such as acute dermatitis, systemic lupus erythematosus, or cutaneous tuberculosis), and patients who were uncooperative.

After considering the possibility of a 10% dropout rate, the sample sizes for the verum and placebo laserpuncture groups needed to be 46 people in each group. The study subjects were allocated randomly, using a computer-based random-number table, and were divided into 2 groups: group 1 (treatment) received verum laserpuncture and group 2 (control) received placebo laserpuncture.

Both groups had a total of 18 sessions, 3 times per week for 6 weeks. Before starting the first session, each subject underwent an initial assessment of speech and social interaction with a WeeFIM questionnaire administered by a pediatric neurologist. In addition, a parental-report sensory-profile questionnaire was completed by the parents, who were accompanied by a researcher. Then, the patient was given either verum or placebo laserpuncture therapy. At the initiation of therapy, the patient was placed in a comfortable position, lying or sitting on a lap, and was given laser goggles to wear. The researcher performed asepsis and antisepsis at the sites where the laserpuncture was to be administered, which were GV 20 *Baihui*, HT 7 *Shenmen*, LI 4 *Hegu*, SP 6 *Sanyinjiao*, ST 36 *Zusanli*, GB 34 *Yanglingquan*, and LR 3 *Taichong* points, as well as scalp acupuncture of the speech area.

The tools used were an RJ-Laser Laserpen Praxis, type 130 (Waldkirch, Germany), with a maximum power of 50 m*W* and a wavelength of 785 nm (infrared). In the treatment group, verum laserpuncture was then activated at each acupuncture point with a Nogier G 18688-Hz frequency modulation wave, at 1 Joule dose/acupuncture point, at 40 m*W* power, and at 785 nm (infrared) wavelength. In the placebo group, laser acupuncture was attached to each acupuncture point with the device not activated.

The dose used was 1 Joule. The treatment time for laser therapy for continuous waves was calculated by the formula:

$$\begin{aligned} \textit{Treatment time } (TT) &= [\text{Dose (Joule [J])} \\ &\quad \times 1000] : \text{Power } (\text{m}W) \\ &= [1\ \text{J} \times 1000] : 40\ \text{m}W \\ &= 25\ \text{seconds} \end{aligned} \qquad <\text{unnumbered eq}>$$

The *TT* is doubled if the acupuncture point is stimulated using a modulation wave, so that:

$$\begin{aligned} TT &= TT \times 2 \\ &= 25\ \text{seconds} \times 2 \\ &= 50\ \text{seconds} \end{aligned} \qquad <\text{unnumbered eq}>$$

After the last therapy session, a final assessment of speech and social interaction was made on each subject. The collected research data was put into the parent table and processed with a statistical test, using SPSS 20.0. This study was approved by the Ethics Committee of the Faculty of Medicine of University Indonesia (FMUI), Central Jakarta, DKI Jakarta (1369/UN2.F1/ETIK/2018). See Figure 1.

## RESULTS

This study was conducted on 46 patients with ASD who met the selection criteria. All patients were randomly allocated into 2 groups: (1) a verum laserpuncture therapy group (the treatment group) and a placebo laserpuncture group (the placebo group). Each group consisted of 23 research subjects.

Before starting the research, each subject's parents received an explanation of the research procedure and signed an informed consent form. The group to which the subject was allocated was unknown by the examiner and parents. The evaluator made an initial assessment of the child's speech and social interaction, using the WeeFIM

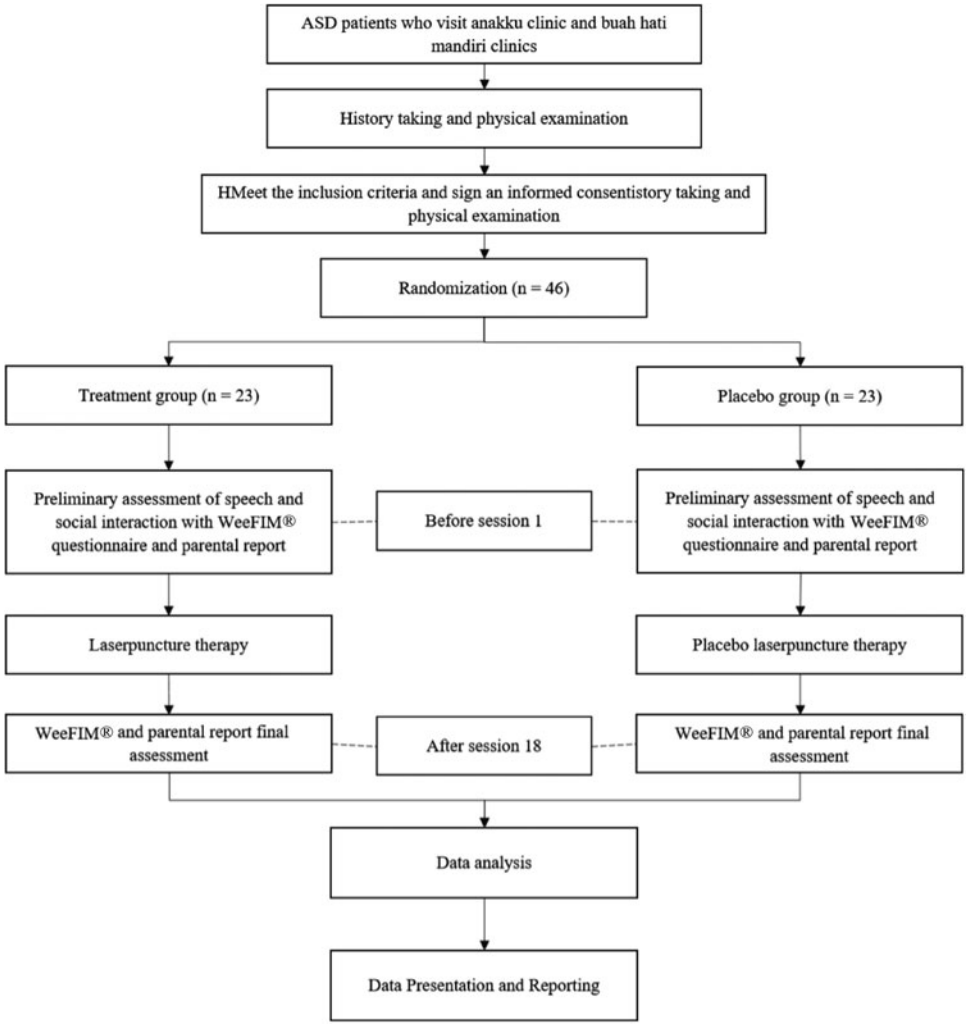


**FIG. 1.** Research flow. ASD, autism spectrum disorder.

Table 1. Characteristics of Research Subjects

| *Variable* | *Treatment group* | *Placebo group* | P |
|---|---|---|---|
| Gender | | | |
| Male | 22 (95.7%) | 18 (78.3%) | 0.187* |
| Female | 1 (4.3%) | 5 (21.7%) | |
| Age (year) | 3.00 (2–5) | 3.00 (2–6) | 0.964** |
| Speech ability | | | |
| Comprehension | 2.00 (1–3) | 2.00 (1–3) | 0.363** |
| Expression | 2.00 (1–3) | 1.00 (1–2) | 0.507** |
| Social interaction | 2.00 (1–3) | 2.00 (1–3) | 0.414*** |
| Parental report | 70 (51–91) | 65 (51–86) | 0.163** |

*Fisher's exact test; **Mann–Whitney-*U* test; ***unpaired t-test.

questionnaire, and the parents completed the sensory-profile questionnaire. Assessments of speech and social interaction and the parental reports were carried out twice, before laserpuncture or placebo laserpuncture and after 18 treatments (Table 1).

The characteristics of the study subjects based on gender showed no significant difference ($P = 0.187$) between male and female according to the Fisher's exact test. Mean age, comprehension, expression, social interaction, and parental report scores in the placebo group were 3.00, 2, 1, 2, and 65, respectively. Mean age, comprehension, expression, social interaction, and parental report scores on the treatment groups were 3.00, 2, 2, 2, and 70, respectively. Based on statistical tests, there were no significant differences between the treatment group and the placebo group according to age ($P = 0.964$), comprehension score ($P = 0.363$), expression score ($P = 0.507$), social interaction score ($P = 0.414$), and parental report score ($P = 0.163$). See Tables 2 and 3 for more details and see the section below for an analysis of these results.

## DISCUSSION

The term *autism* was first introduced by Leo Kanner, MD (1894–1981 AD), in 1943. Dr. Kanner described this condition as the inability to interact with other people, delayed mastery of language, reversal of sentences, repetitive and stereotypic play activities, and an obsessive desire to maintain order in the environment.[10]

Table 2. Mean Differences in WeeFIM® Scores for Comprehension, Expression, and Social Interaction After Treatment in Verum or Placebo Laserpuncture Group

| *Δ before and after* | *Mean ± SD verum laserpuncture* | *Mean ± SD placebo laserpuncture* | P |
|---|---|---|---|
| Variable | | | |
| Comprehension | 2.86 ± 0,86 | 0.95 ± 0,63 | |
| Expression | 1.73 ± 0,81 | 0.69 ± 0,55 | **<0.001*** |
| Social interaction | 2.86 ± 1,09 | 1.39 ± 0,78 | |
| Parental report | 9.30 ± 9,39 | 7.74 ± 7,62 | **0.367*** |

*Mann–Whitney-*U* test.
Δ, change; SD, standard deviation.

According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,*[11] autism is a developmental disorder that involves a variety of problematic behaviors, including communication problems, perception problems, motor problems, and social development problems.[12]

The disorder can be divided into 2 types: (1) dysfunction in the neural structure of brain tissue and (2) biochemical abnormalities of brain tissue. In relation to brain structure, postmortem examinations of the brains of some patients with autism showed two regions that were less developed in the limbic system, the amygdala and hippocampus. These two regions are responsible for emotions, aggression, sensory input, and learning.[13] The researchers also found Purkinje-cell deficiencies in the cerebellum. Using magnetic resonance imaging (MRI), two areas have been found in the cerebellum—the VI and VII lobules—that, in autistic individuals, were significantly smaller than those areas in found in nonautistic people. One of these two regions is understood to be the center that is responsible for attention.[14] Supported by neuropharmacologic and neurochemical empirical studies on autism, much attention has been focused on neurotransmitters and neuromodulators—first the mesolimbic dopamine system, then the endogenous opioid system and oxytocin, and then serotonin—because connections between autism and abnormalities in this system were found.

The etiology of ASD is not yet known. Oxidative stress plays a pathologic role. A 2012 study by Al Ayadhi reported that serum levels of the Sonic hedgehog (SHH) protein and brain-derived neurotrophic factor (BDNF) could be linked to oxidative stress in ASD.[15] By using blood plasma or polymorphonuclear leukocytes, that study showed that autistic children produce significantly higher oxygen free radicals. The study also found a high level of serum SHH protein and decreased BDNF serum in autism.[15]

Mitochondria are the main producers of free reactive oxygen species (ROS). At the same time, mitochondria are also targets of damage mediated by ROS. Disruption of the function of the mitochondrial electron-transport chain can lead to the production of ROS and excessive oxidative stress, which can then affect mitochondrial function and increase ROS production even more; thus a vicious circle can emerge. It has also been shown that some of the environmental risk factors of ASDs can, at the same time, cause mitochondrial dysfunction, especially in cases when the mitochondria are indeed susceptible to them (Fig. 2).[12,16,17]

Laserpuncture is a combination of acupuncture therapy with modern technology in the form of light therapy. Laserpuncture is one of the modalities of acupuncture therapy that uses lasers to stimulate acupuncture points. Laserpuncture,

Table 3. Number of Subjects Who Experienced Improvement After Treatment in the Verum or Placebo Laserpuncture Group

| | *Groups* | | | | |
|---|---|---|---|---|---|
| *Variables* | *Verum laserpuncture* | *Placebo laserpuncture* | OR | *95% CI* | P |
| Comprehension | | | | | |
| Improvement | 20 | 6 | 18.88 | 4.09–87.17 | <0.001* |
| No improvement | 3 | 17 | | | |
| Expression | | | | | |
| Improvement | 16 | 1 | 50.28 | 5.61–450.2 | <0.001* |
| No improvement | 7 | 22 | | | |
| Social Interaction | | | | | |
| Improvement | 20 | 11 | 7.273 | 1.68–31.42 | 0.005* |
| No improvement | 3 | 12 | | | |
| Parental report | | | | | |
| Improvement | 10 | 9 | 1.197 | 0.36–3.87 | 0.765* |
| No improvement | 13 | 14 | | | |

*$\chi^2$ test.
*OR;* odds ratio; CI; confidence interval.

with a power of 35–40 m*W*, can create effects so similar to the needles used in manual acupuncture that stimulation of acupuncture points by needles or lasers produce the same therapeutic effects. Needle puncture can release chemical substances, such as histamine, bradykinin, and adenosine triphosphate, which cause depolarization of acupuncture points. Therefore, the action potential occurs and is transmitted through afferent fibers to the brain, so that it activates the hypothalamus and limbic system,[18] and the effects of neuroprotection and regeneration occur.

The photobiomodulation effect of laserpuncture increases vascular dilatation, which increases blood flow to the brain. This circulation improvement helps reduce tissue damage, reduce neuroinflammation, and decrease the number of proinflammatory cytokines, such as tumor necrosis factor–α (TNF-α), interleukin (IL)–6, C-reactive protein (cRP), and nitric-oxide synthase (NOS), thus preventing further cell death and activating tissue neuroprotection. Verum laserpuncture modulates activity in several areas of the brain related to motor function and affects changes in the activity of sensorimotor and cerebellar areas.

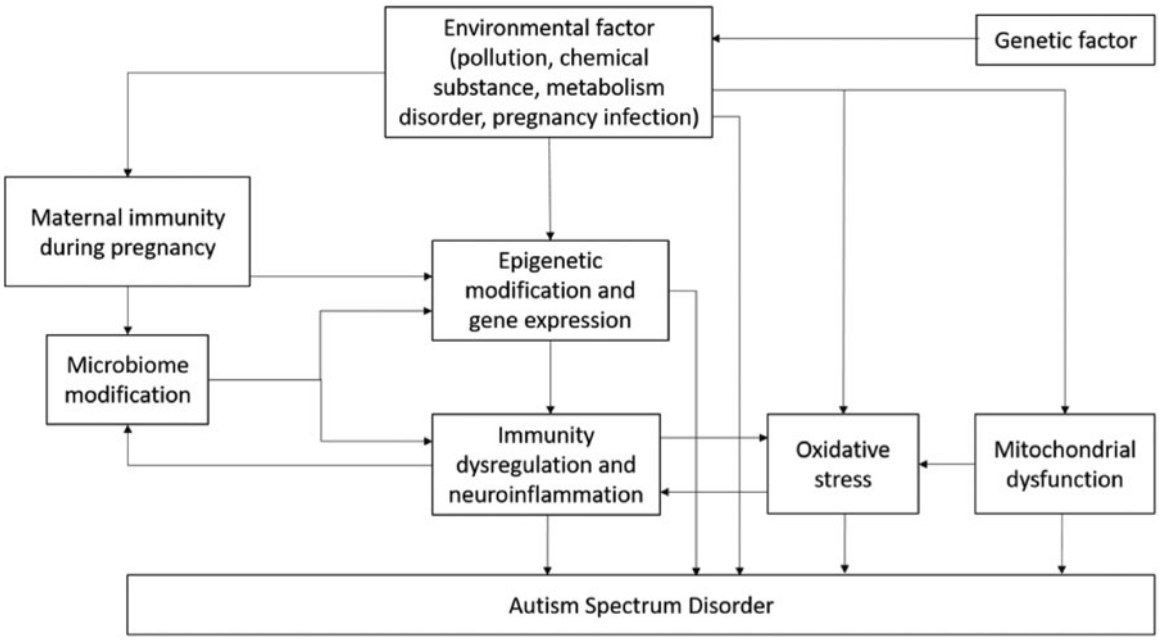


**FIG. 2.** Factors that trigger autism spectrum disorder.

There was a preliminary study by Sujudi et al., in 2004,[21] on the effects of laserpuncture on autistic children. A total of 46 children were divided equally into a treatment group and a control group. Both groups received behavioral therapy 3 times per week for a total of 12 sessions. In the treatment group, additional therapy was given in the form of laserpuncture at GV 20 *Baihui*, Ex-HN 1 *Sishencong*, GV 15 *Yamen*, HT 7 *Shenmen*, BL 20 *Pishu*, BL 23 *Shenshu,* KI 3 *Taixi*, and LR 3 *Taichong* points, and the ear acupuncture point for *Shen Men*, 3 times per week for a total of 10 sessions. The laser device used was a helium neon laser, with a 632.8-nm output power of 5 m*W*. The doses used for each point were: for children ages 2–5, 0.2 Joules for 40 seconds, and, for children > age 5, 0.3 Joules for 60 seconds. There were significant differences in the decreases in Childhood Autism Rating Scale$^{tm}$ scores (7 variables) or in autistic symptoms between the treatment and control groups ($P < 0.05$).[21]

Anwar et al. conducted a randomized controlled trial in 2012 on laserpuncture for ASD.[22] The aim of that study was to assess the efficacy, safety, and effectiveness of laserpuncture in pediatric patients with ASD. The children were divided into 2 groups: (1) a treatment (verum laserpuncture) group of 60 patients and (2) a sham laserpuncture control group of 56 patients. The treatment group received verum laserpuncture at the EX-HN 1 *Sishencong*, EX-HN 3 *Yintang*, GV 16 *Fengfu*, CV 24 *Chengjian*, *Naodian* at 3 ear points, TF 4 *Shen Men*, PC 6 *Neiguan*, HT 5 *Tongli*, LR 3 *Taichong*, ST 36 *Zusanli*, and SP 6 *Sanyinjiao* points 24 times over 12 weeks. The primary assessment used several questionnaires, including the WeeFIM,® the Pediatric Evaluation of Disability Inventory (PEDI), the Leiter-R, and the Clinical Global Impression (CGI)–I (Improvement) scale. A secondary assessment used the Activities-specific Balance Confidence (ABC) questionnaire, the Ritvo Freeman Real Life Scale (RFRLS), the Reynell Developmental Language Scale (RDLS), and a standardized parental report.[22]

There were significant changes in the WeeFIM's comprehensive speech score ($P = 0.02$), in self-care ability on the PEDI ($P = 0.028$), and in the CGI-I ($P = 0.003$) in the verum laserpuncture group, compared to the sham laserpuncture group. There were significant improvements in the standardized parental report on social interactions ($P = 0.01$), receptive speech ($P = 0.006$), motor skills ($P = 0.034$), coordination ($P = 0.07$), and attention ($P = 0.003$).[22]

The study of the effect of laserpuncture was carried out on 46 children with ASD by assessing speech and social interactions using the WeeFIM questionnaire as a primary assessment and parental report using the sensory-profile questionnaire as a secondary assessment. All study subjects were randomly divided into 2 groups, the treatment group whom received verum laserpuncture and the control group whom received placebo laserpuncture. Masking or randomizations were performed with computer-based randomization allocation programs. Subjects did not know which group allocations they received and remained in the study to the end. To increase compliance of the subjects, the researcher gave telephone and Whatsapp numbers to facilitate communication if the parents/guardians of the subjects had complaints or questions about the ongoing study. These methods of communication were also used to remind the parents of the therapy schedules. All subjects received either verum of placebo laserpuncture therapy 18 times with a frequency of 3 times a week. There were no dropouts. No subjects complained about any side-effects, such as local infections or vision problems, during the study.

This study was the latest acupuncture research conducted in the Faculty of Medicine of the University of Indonesia/Dr. Cipto Mangunkusumo Hospital—and also in Indonesia—that assessed the effects of specific speech and social interaction ASD symptoms when using laserpuncture techniques. The reason for using laserpuncture, compared to other acupuncture modalities, was is that laserpuncture is easy to apply, dosage can be measured precisely, and this modality is painless and noninvasive. Laserpuncture is also a fast therapy, and the risk of infection is low. In addition, laserpuncture does not induce a stabbing sensation, so application is easy for double-blinded, randomized, controlled clinical trials.[9]

Primary assessment of speech and social interactions with the WeeFIM questionnaire was performed twice, before the subjects were given treatment and after the 18 treatments. Speech skills included comprehension, expression, and social interaction. It was considered an improvement if there was a change in score of more than 2 or more than the initial score, whereas it was considered no improvement if there was a change in score of 1 or if it remained the same. These parameters were compared between the 2 groups and analyzed statistically.

The equality tests conducted on the 2 groups—for gender, age, comprehension score, expression, social interaction, and parental report before treatment—resulted in a *P*-value >0.05. This ensured that the 2 groups were equivalent at the start of the study; thus, they were comparable. Secondary assessment was made through the parental reports, using the sensory-profile questionnaire.

After treatment, there were statistically significant differences between the verum and placebo laserpuncture groups, with respect to the mean difference in the scores for comprehension, expression, and social interaction, as elicited by the WeeFIM questionnaire. For the comprehension score, the mean difference was 2.86 in the verum laserpuncture group and 0.95 in the placebo laserpuncture group. This difference was statistically significant ($P < 0.001$). For the expression score, the mean difference was 1.73 in the verum laserpuncture group and 0.69 in the placebo laserpuncture group. This difference was statistically significant ($P < 0.001$). For the social interaction score, the average difference was 2.86 in the laserpuncture group and 1.39 in the

placebo laserpuncture group. This difference was statistically significant ($P < 0.001$).

With respect to the comprehension score, in the verum laserpuncture group, 20 subjects experienced improvement and 3 subjects did not experience improvement. In the placebo laserpuncture group, 6 subjects experienced improvement and 17 subjects did not experience improvement. Of the total number of subjects in both groups, 26 subjects experienced improvement and 20 subjects did not experience improvement. These data were analyzed by a $\chi^2$ test with *P*-values <0.001 and an *OR:* 18.8; 95% CI: 4.09–87.17, so it can be concluded that verum laserpuncture increased the WeeFIM comprehension score 18.8 times greater than placebo laserpuncture.

With respect to the expression score, 16 subjects experienced improvement and 7 subjects did not experience improvement in the verum laserpuncture group. In the placebo laserpuncture group, 1 subject experienced improvement and 22 subjects did not experience improvement. Of the total number of subjects in both groups, 17 subjects experienced improvement and 29 subjects did not experience improvement. These data were analyzed by a $\chi^2$ test with *P*-values <0.001 and an *OR:* 50.2; 95% CI: 5.61–450.2, so it can be concluded that verum laserpuncture increased the WeeFIM expression score by 50.2 times greater than placebo laserpuncture.

With respect to the social interaction score, 20 subjects experienced improvement and 3 subjects did not experience improvement in the verum laserpuncture group. In the placebo laserpuncture group, 11 subjects experienced improvement and 12 subjects did not experience improvement. Of the total number of subjects in both groups, 31 subjects experienced improvement and 15 subjects did not experience improvement. These data were analyzed by the $\chi^2$ test with $P = 0.005$ and an OR: 7.2, 95% CI: 1.68–31.42 so it can be concluded that verum laserpuncture increased the WeeFIM social interaction score 7.2 times greater than placebo laserpuncture.

With respect to the parental report score, 10 subjects experienced improvement and 13 subjects did not experience improvement in the verum laserpuncture group. In the placebo laserpuncture group, 9 subjects experienced improvement and 14 subjects did not experience improvement. Of the total number of subjects in both groups, 19 subjects experienced improvement and 27 subjects did not experience improvement. These data were analyzed by the $\chi^2$ test with a *P*-value = 0.765 ($P > 0.05$). There was no significant difference from the parents' assessment with an *OR:* 1.1; 95% CI: 0.36–3.87, so that it can be concluded that verum laserpuncture increased the parental report score 1.1 times greater than placebo laserpuncture.

Statistically significant results were also seen in patients who received placebo laserpuncture treatment. In this case, that result could be due to the influence of integrative sensory–occupational therapy given to the patients with ASD in both groups.

A study based on questionnaires or family reports showed improvements in 53.2% children with ASD who received integrative sensory therapy; 29.4% of the subjects experienced dramatic improvement, 43.9% experienced significant changes, and only 4.3% experienced deterioration.[24] Based on these results, integrative sensory–occupational therapy is a therapeutic modality that is quite popular and requested by parents of children with ASD.[25,26]

The current study can be considered better, because: (1) the acupuncture points were coupled with the scalp acupuncture, especially to the speech area; (2) there were 18 therapy sessions over 6 weeks; subjects in both groups received integrative sensory therapy; and special assessments were performed for speech and social interaction, as well as for comprehension and expression ($P < 0.001$) and social interaction ($P < 0.001$).

Verum laserpuncture on the HT 7 *Shenmen* point stimulates the dopaminergic system, free radicals, and the cholinergic system through acetylcholinesterase and monoamine oxidase-B to induce an increase in acetylcholine and dopamine. Free radicals and antioxidants cause glutathione peroxidase (GSH-Px) to increase and 3,4-methylenedioxyamphetamine to decrease so that oxidative stress decreases and neurodegeneration in brain tissue structure is hampered, resulting in improved memory, and emotional or mood functioning, and reduced aggressiveness.[27]

Verum laserpuncture on HT 7 *Shenmen*, together with GB 34 *Yanglingquan*, has modulated neuroprotection and activated BDNF.[28] This stimulation has been shown to be neuroprotective through regulation of *Creb*, *BDNF*, *Bcl-2,* and *Bax* gene expression.[29] This stimulation also reduces oxidative stress, and promotes expression of IL-6, and γ-aminobutyric acid (GABA)–T activity, but increases expression of glutamic acid decarboxylase 65 along with Purkinje-cell density in the cerebellum.[30] Therefore, by influencing the biochemical balance of brain tissue and BDNF activation in the hippocampus, the amygdala (with its cognitive and emotional function) and cerebellum (the center of attention and the speech area of temporal lobe that affects the local microcirculation) can influence speech and social interactivity in patients with ASD.

Verum acupuncture at ST 36 *Zusanli* and GV 20 *Baihui* has been proven to increase neuroblast plasticity through activation of pCREB and BDNF in the hippocampal dentate gyre[31]; improve hippocampal function by modulating the cAMP/PKA/CREB-signaling pathway[32]; activate the bilateral limbic system (piriformis cortex), bilateral temporal lobes, amygdala, and hippocampus[33]; and increase superoxide dismutase (SOD) and GSH-Px in the hippocampus by converting superoxidase radicals to $H_2O_2$.

Verum acupuncture at the SP 6 *Sanyinjiao* point can regulate and reduce the number of proinflammatory cytokines—such as IL-1ß, TNF-α, cRP, and NOS—thus preventing further cell death and activating tissue neuroprotection.

Verum acupuncture at the LR 3 *Taichong* point has been shown to affect neuronal activity in the frontalis area associated with motor disorders, with the presence of decreased functional MRI (fMRI) signals in the frontal lobes (Brodmann areas 10, 4, 8 and 46). This acupuncture decreased fMRI signals in the contralateral temporal lobe (Brodmann area 21) and the parahippocampus gyrus, both of which affect the auditory and visual pathways.[34]

Verum acupuncture at the LI 4 *Hegu* point was proven by fMRI examination to activate brain areas such, as the insula and putamen, which play an important role in motor activity; the superior parietal lobe; the medium temporal gyrus; and the post central gyrus. Along with LR3 *Taichong*, L1 4 *Hegu* has activated the bilateral temporal gyri.[35] This combination of points has been shown to increase blood perfusion through vasodilators such as P and calcitonin gene-related peptide substances, increase nitrite oxide, and reduce the activity of the sympathetic nervous system.[36]

During the current study, changes reported by parents/guardians of several of the children, as well as observations from researchers, included:

- There were changes in reactions and facial expressions, such as children being more responsive when called by their names by moving their eyes or turning toward the sounds.
- Eye contacts were made with persons these children were are talking to, from those who had avoided contact; now the children maintain that contact longer. According to the parents, the children began to look in their parents' eyes when called and also looked longer at the parents.
- There were reductions in behavior that was often repetitive (stereotypes), such as jumping from a bed, turning on the tap, and going up on a table.
- Subjects looked calmer while undergoing a laserpuncture therapy session. In the experience of the researcher, the patients appeared calmer during the eighth and subsequent therapy sessions.
- Some subjects babbled more or made more noise than before, for example, voicing vowels in words such as mama; papa; and numbers one, two, and so on.
- Subjects made changes in their social interactions with the surrounding environment, for example, when playing with friends of the same age or interacting with animals.

According to Helianthi, et al., in 2016,[37] the effect of laserpuncture was persistent after intervention for osteoarthritis in geriatric patients. On a visual analogue scale (VAS) and a Lequesne Index, there was a statistically significant difference in VAS scores 2 weeks post-treatment in a verum laserpuncture group ($P < 0.01$), compared to a group who received placebo laserpuncture.[36]

Al Rashoud et al. conducted a double-blinded, randomized clinical trial, comparing an active laserpuncture group and a group who received placebo laserpuncture. That study assessed the VAS and a Saudi Knee Function Score (SKFS) score to determine the effectiveness of the therapy. The result was significant VAS improvement at 6 weeks and 6 months post intervention in the active laserpuncture group, compared to the group who received placebo laserpuncture.[38] Thus, based on that study's results, the effectiveness of laserpuncture can still last for a time period of 2 weeks to 6 months after therapy. Based on the age of the majority of subjects, ages 2–4, who experienced improvement after verum laserpuncture, intervention for ASD is very appropriate if it is initiated as early as possible during the period of the child's major brain development.

Various evidence directly or indirectly shows the involvement of autism with BDNF, which plays an important role in the development of brain plasticity. Stimulation of acupuncture on HT 7 *Shenmen* regulates BDNF expression significantly, compared to other acupuncture points on different meridians in models of spatial-memory disorders or behavioral changes that resemble depression. Based on the consensus regarding growth of BDNF involvement in the pathophysiology of ASD, and the broadly demonstrated BDNF effect on modulation of synaptic plasticity and its improvement, this strong regulation of neurotropin can be an epigenetic factor in ameliorating autism. An acupuncture stimulus that increases brain BDNF levels seems to modulate molecular mechanisms so that synaptic plasticity can be restored. Therefore, acupuncture can potentially be used in the treatment of ASD through expression modulation and activation of BDNF.[19,20]

The evidence connecting BDNF with autism shows that BDNF also plays an important role in the development of brain plasticity. Recent research has shown the neuroprotective effect of acupuncture-induced BDNF activation in subjects with various neurologic disorders. BDNF is found in many brain structures, including the cerebral cortex, hypothalamus, hippocampus, amygdala, and cerebellum. BDNF functions include memory, emotion/mood control, synaptic plasticity, and differentiation of neuron cells. Acupuncture involving BDNF can affect the balance of the neuro–endocrine–immune system and affect the release of neurotransmitters (glutamate, acetylcholine, GABA, and serotonin) and neuropeptides both in the central nervous system and in the peripheral nervous system. Several studies have shown that stimulation of certain acupuncture points increases BDNF production through neurotransmitters (glutamate and serotonin) and neuropeptides (norepinephrine and enkephalin).[38]

Some subjects had just started to receive integrative sensory occupational therapy, and had started it 1 month prior to the study. Thus, there was the possibility of integrative sensory occupational therapy plus placebo laserpuncture affecting the final assessments of the study subjects. The duration of the study was not too long, so

that the laserpuncture therapy given was limited and clinical monitoring could not be used to determine how long the effect of laserpuncture would persist in the study subjects.

Given that ASD with abnormal speech and social interactions is a disorder that lasts a lifetime, cannot be cured, and autistic children will later become autistic adults, it is necessary to performed long-term observations to clarify the clinical benefits obtained from verum laserpuncture. Further research is needed to determine the duration of the laserpuncture effect and the optimal duration of therapy with a longer period of time.

## CONCLUSIONS

Verum laserpuncture in this clinical trial was effective for improving speech ability and social interaction in patients with ASD, compared to placebo laserpuncture, especially improving comprehension, expression, and social interaction.

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No competing financial interests exist.

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## REFERENCES

1. Amjad A, Bakhtiar SM, Azevedo V. Autism spectrum disorders (ASD): From diagnosis to management. *J Mol Genetic Med*. 2015;9(1):1–3.
2. Kasran S. Autism: A developing concept [in Indonesian] *J Kedokter Trisakti.* 2003;22(1):24–30.
3. Ciptomangunkusumo General Hospital Outpatient Installation. *Report on the Number of Children's Polyclinic Patient Visits* [in Indonesian]. Jakarta: Offline Data; 2015.
4. Chugani DC, Muzik O, Behen M, et al. Developmental changes in brain serotonin synthesis capacity in autistic and nonautistic children. *Ann Neurol*. 1999;45(3):287–295.
5. Whitaker-Azmitia PM. Serotonin and brain development: Role in human developmental diseases. *Brain Res Bull.* 2001; 56(5):479–485.
6. Won H, Mah W, Kim E. Autism spectrum disorder causes, mechanisms, and treatments: Focus on neuronal synapses. *Front Mol Neurosci*. 2013;6:19.
7. Boat T, Wu J, eds. *Mental Disorders and Disabilities Among Low-Income Children.* Washington, DC: National Academies Press; 2015.
8. Autism Society of America. Living with Autism. Online document at: www.autism-society.org/living-with-autism/ Accessed April 17, 2020.
9. Yang C, Hao Z, Zhang LL, Guo Q. Efficacy and safety of acupuncture in children: An overview of systematic reviews. *Pediatr Res*. 2015;78(2):112–119.
10. Kanner L. Follow-up study of eleven autistic children originally reported in 1943. 1971. [in French]. *Psychiatr Enfant.* 1995;38(2):421–461.
11. American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders (DSM–5®), 5th ed.* Washington, DC: APA; 2013
12. Griffiths KK, Levy RJ. Evidence of mitochondrial dysfunction in autism: Biochemical links, genetic-based associations, and non-energy–related mechanisms. *Oxid Med Cell Longev*. 2017;2017:4314025.
13. Bauman M, Kemper T. *The Neurobiology of Autism*. Baltimore: Johns Hopkins University; 1994.
14. Courchesne E, Yeung-Courchesne R, Hesselink J, Jernigan T. Hypoplasia of cerebellar vermal lobules VI and VII in autism. *N Engl J Med*. 1988;318(21):1349–1354.
15. Al-Ayadhi LY. Relationship between Sonic hedgehog protein, brain-derived neurotrophic factor and oxidative stress in autism spectrum disorders. *Neurochemical Res.* 2012;37(2):394–400.
16. Rossignol DA, Frye RE. Evidence linking oxidative stress, mitochondrial dysfunction, and inflammation in the brain of individuals with autism. *Front Physiol.* 2014;5:150.
17. Guthrie W, Swineford LB, Nottke C, Wetherby AM. Early diagnosis of autism spectrum disorder: Stability and change in clinical diagnosis and symptom presentation. *J Child Psychol Psychiatry*. 2013;54(5):582–590.
18. Zhang D, Spielmann A, Wang L, et al. Mast-cell degranulation induced by physical stimuli involves the activation of transient-receptor–potential channel TRPV2. *Physiol Res*. 2012;61(1):113–124.
19. Allam H, Eldine N, Helmy G. Scalp acupuncture effect on language development in children with autism: A pilot study. *J Altern Complement Med.* 2008;14(2):109–114.
20. Zhen F, Jin Y. Clinical efficacy of scalp acupuncture therapy in rehabilitating the language barrier in children with autism. *J Pediatr Tradit Chin Med*. 2016;12(3):68–70.
21. Sujudi Y, Srilestari A, Siboe Y. *Effects of Laserpuncture on Children with Autism* [in Indonesian]. Jakarta: Universitas Indonesia; 2004.
22. Anwar S, Khan MMN, Qazi FM. Laser Acupuncture for Autism Spectrum Disorder: A Randomized Sham Controlled Trial. Online document at: www.academia.edu/19556382/ Laser_Acupuncture_for_Autism_Spectrum_Disorder_ASD_a_ Sham_Controlled_Randomized_Trial Accessed April 17, 2020.
23. Kreisel V, Weber M. *A Practical Handbook: Laser Acupuncture—Successful Treatment Concepts.* Starnberg, Germany: German Fuchtenbusch Verlag; 2012.
24. Goin-Kochel RP, Mackintosh VH, Myers BJ. Parental reports on the efficacy of treatments and therapies for their children with autism spectrum disorders. *Res Autism Spectrum Disord*. 2009;3(2):528–537.
25. Salomone E, Beranová Š, Bonnet-Brilhault F, et al. Use of early intervention for young children with autism spectrum disorder across Europe. *Autism*. 2016;20(2):233–249.

26. Carlon S, Stephenson J, Carter M. Parent reports of treatments and interventions used with children with autism spectrum disorders (ASD): A review of the literature. *Australasian J Special Ed.* 2014;38(1):63–90.
27. Wattanathorn J, Sutalangka C. Laser acupuncture at HT 7 acupoint improves cognitive deficit, neuronal loss, oxidative stress, and functions of cholinergic and dopaminergic systems in animal model of Parkinson's disease. *Evid Based Complement Alternat Med*. 2014;2014:937601.
28. Li LY, Jiang N, Zhao Y. Could acupuncture have a role in the treatment of autism spectrum disorder via modulation of BDNF expression and activation? *Acupunct Med*. 2014;32(6): 503–505.
29. Yun YC, Jang D, Yoon SB, et al. Laser acupuncture exerts neuroprotective effects via regulation of *Creb*, *Bdnf*, *Bcl-2*, and *Bax* gene expressions in the hippocampus. *Evid Based Complement Alternat Med*. 2017;2017:7181637.
30. Khongrum J, Wattanathorn J. Laser acupuncture at HT 7 improves the cerebellar disorders in valproic acid–rat model of autism. *J Acupunct Meridian Stud*. 2017;10(4):231–239.
31. Hwang IK, Chung JY, Yoo DY, et al. Effects of electroacupuncture at *Zusanli* and *Baihui* on brain-derived neurotrophic factor and cyclic AMP response element–binding protein in the hippocampal dentate gyrus. *J Vet Med Sci*. 2010;72(11):1431–1436.
32. Li QQ, Shi GX, Yang JW, et al. Hippocampal cAMP/PKA/CREB is required for neuroprotective effect of acupuncture. *Physiol Behav*. 2015;139:482–490.
33. Lu Y, Huang Y, Tang C, et al. Brain areas involved in the acupuncture treatment of AD model rats: A PET study. *BMC Complement Altern Med.* 2014;14:178.
34. Litscher G, Opitz G. Technical parameters for laser acupuncture to elicit peripheral and central effects: State-of-the-art and short guidelines based on results from the Medical University of Graz, the German Academy of Acupuncture, and the scientific literature. *Evid Based Complement Alternat Med*. 2012;2012:697096.
35. Shan Y, Wang ZQ, Zhao ZL, et al. An fMRI study of neuronal specificity in acupuncture: The multiacupoint *Siguan* and its sham point. *Evid Based Complement Alternat Med*. 2014;2014:103491.
36. Song YK, Seorim M, Hyangsook L, et al. Changes of local blood flow in response to acupuncture stimulation. *Evid Based Complement Alternat Med*. 2016;2016:9874207.
37. Helianthi DR, Simadibrata C, Srilestari A, Wahyudi ER, Hidayat R. Pain reduction after laser acupuncture treatment in geriatric patients with knee osteoarthritis: A randomized controlled trial. *Acta Med Indones*. 2016;48(2): 114–121.
38. Al Rashoud A, Abboud R, Wang W, Wigderowitz C. Efficacy of low-level laser therapy applied at acupuncture points in knee osteoarthritis: A randomised double-blind comparative trial. *Physiotherapy*. 2014;100(3):242–248.
39. Toma C, Hervas N, Balmana, et al. Neurotransmitter systems and neurotrophic factors in autism: Association study of 37 genes suggests involvement of *DDC*. *World J Biol Psychiatry.* 2013;14(7):516–527.

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