Scalp acupuncture for Autism spectrum disorder: a systematic review

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Abstract. Objective: To systematically review the clinical efficacy of scalp acupuncture for autism spectrum disorders, and to update the evidence of clinical effectiveness of scalp acupuncture. Methods: Cochrane Library, PubMed, CNKI, CBM, Wan Fang Data, VIP database were electronically searched to collect randomized controlled trials (RCT) or case-controlled trials (CCT), published during the period of December 2018 about "Scalp acupuncture for autism spectrum disorder" essays according to the Cochrane Handbook 5.1.0 standards in the research methodology for quality evaluation and bias risk assessment and using Revman 5.3 software for statistical analysis. Results: A total of 11 studies involving 859 cases were included. The results of meta-analysis showed that scalp acupuncture could reduce the scores of CARS (MD= -1.56, 95% CI -2.40 to -0.72, \(P=0.0003\)), ABC (MD= -3.07, 95% CI -5.18 to -0.97, \(P=0.004\)), and improve the treatment efficiency of autism (RR = 1.31, 95% CI 1.16 to 1.49, \(P<0.0001\)). Conclusion: The clinical evidence indicates that scalp acupuncture is effective for autism and can reduce the scores of diagnostic scales such as CARS and ABC; Safety could not be evaluated because adverse reactions were not described in all the included literatures.

1. Introduction
Autism Spectrum Disorder (ASD) is a pervasive developmental disorders characterized by impaired social interaction, narrow interest, repetitive and stereotyped behaviours, including Autism Disorder (AD), Asperger Syndrome (AS) and Pervasive Developmental Disorder-not Otherwise Specified (PDD-NOS) [1-2]. The prevalence rate is high and cure rate is extremely low among ASD, which has become a public health issue of global concern [3-4]. There is currently a trend of diversified development in terms of intervention and treatment of ASD that drug treatment has adverse reactions, comprehensive rehabilitation treatment is relatively complex, while acupuncture treatment is simple and no adverse reactions have been found yet [5]. As an emerging acupuncture therapy in recent years, scalp acupuncture can significantly improve the clinical efficacy of neurological disorders by stimulating the motor area, sensory area, dance tremor control area, vasomotor area, halo area, speech area 2, speech area 3 and other areas of the head [6]. Based on this, this study systematically evaluates the clinical efficacy of scalp acupuncture in the treatment of autism spectrum disorders, aiming to
update and improve the evidence of the clinical efficacy of scalp acupuncture, with a view to providing some reference for the clinical treatment of ASD.

2. Methods

2.1. Types of studies
We searched six major electronic databases including Cochrane Library, Pubmed, China National Knowledge Infrastructure (CNKI), Chinese BioMedical Literature Database (CBM), Wanfang Database (Wanfang) and Chinese Scientific Journal Database (VIP). The retrieval date is from the establishment of the database to December 31, 2018. The searching terms used in Chinese databases included "zhen jiu" (Acupuncture), "zhen ci" (Acupuncture), "zi bi zheng" (Autism spectrum disorder), "gu du zheng" (Autism spectrum disorder), "tou xue zhen ci" (Scalp acupuncture), "tou zhen" (Acupuncture in head acupuncture point), "tou xue liu zhen" (Acupuncture in head acupuncture point). The English searching terms were Autism spectrum disorder, Autism, Acupuncture, Needle. Take PubMed database as an example and review the references of included literatures.

Box 1. PubMed search strategy

2.2. Inclusion and exclusion criteria
All inclusion criteria: (1) RCT or CCT related to scalp acupuncture for ASD; (2) The research objects have clear criteria for diagnosis and efficacy evaluation; (3) Acupuncture techniques and acupoint selection for scalp acupuncture were not considered; (4) After statistical comparison, the baseline data of the groups divided by subjects showed good inter-group equilibrium.

Exclusion criteria: (1) Repeated studies, with convincing statistical data; (2) Review, case report, expert experience report, conference notice, literature irrelevant to research purpose; (3) Animal experiments.

2.3. Literature screened
The two researchers searched the literature in a double-blind form, and used NoteExpress 3.2 to automatically eliminate the repeated Chinese literature. The literature that clearly met the inclusion criteria was screened out by reading the title and abstract of the article. After further independent reading and initial screening of the full text, the literatures that meet the exclusion criteria are deleted, and then the included literatures are cross-checked to ensure the accuracy of the literatures and reduce errors as much as possible. If there are differences, the third researcher will evaluate.

2.4. Statistical analysis
The two researchers used data extraction tables to extract data independently, including the author of the year of publication, disease type, diagnostic criteria, sample content, patient age, research type and research results. Quality evaluation and risk assessment of bias of the included research methodologies were conducted in accordance with Cochrane Handbook 5.1.0, and statistical analysis was performed using Revman 5.3 software. Risk ratio (RR) and 95% confidence interval (CI) were used as effect analysis statistics. Data of continuous variables (For example: autism diagnostic scale score) used mean difference (MD) and 95% CI as effect analysis statistics. Statistical heterogeneity was assessed by $\chi^2$ test and referred to $I^2$. If there was no statistical heterogeneity ($P>0.10, I^2<50\%$), fixed-effect model analysis was adopted. If there was statistical heterogeneity ($P<0.10, I^2>50\%$), random effect
model analysis was used and sensitivity analysis was performed. Subgroup analysis was performed on clinical factors that might lead to heterogeneity.

Figure 1. Literature selection process and results

* The searched databases and the number of detected literatures are as follows: Cochrane Library (n=50), PubMed (n=42), CNKI (n=146), CBM (n=78), Wan Fang Data (n=230), VIP (n=122)

2.5. Outcome indicators
Childhood Autism Rating Scale (CARS), Autism Behavior Checklist (ABC), Psycho-educational Profile (PEP), effectiveness.
3. Results

3.1. Inclusion of the literature
A total of 11 articles [7-17] were retrieved and adopted, and 859 cases were included. The basic information of the literature is shown in Table 1. Among them, Tang Qiang and others divided the study into three groups. In this study, cluster needling of scalp acupuncture and rehabilitation group, the conventional acupuncture and rehabilitation group were set as Tang Qiang and Tang Qiang 2 respectively, and the study treatment is divided into 12 weeks and 24 weeks. Considering the statistical difference of the literature results, the course of treatment was selected for 24 weeks. Zheng Fangli et al. were divided into 3 months and 6 months, and only 6 months of treatment were compared. Please refer to the Table 1 of appendix one for details.

Table 1. Basic information of included literatures

| Researcher       | Random method        | Baseline Disease | Diagnostic criteria | Sample size (E/C) | Age | Therapy group                                                                 | Control group                  | Course of treatment | Outcome indicator | Adverse reactions |
|------------------|----------------------|------------------|---------------------|-------------------|-----|--------------------------------------------------------------------------------|--------------------------------|--------------------|-------------------|------------------|
| Tang Qiang 1-2013 | Random number table  | Comparable AD    | DSM-IV, CARS        | 20/18             | 2-7 | Scalp Acupuncture + Rehabilitation Training                                    | Rehabilitation Training        | 24 weeks           | CARS, Effective Rate | Not mentioned     |
| Tang Qiang 2-2013 | Random number table  | Comparable AD    | DSM-IV, CARS        | 18/18             | 2-7 | Routine scalp acupuncture + rehabilitation training                              | Rehabilitation Training        | 24 weeks           | CARS, Effective Rate | Not mentioned     |
| Yuan Qing 2013   | Computer random      | Comparable AD    | DSM-IV, CARS, PEP   | 30/30             | 2-8 | Needle retention at scalp points + Conventional acupuncture                     | Conventional Acupuncture      | 3 months           | CARS, PEP, Effective Rate | Not mentioned     |
| Xiong Yuhang 2014| Only mention random  | Comparable AD    | CCMD-3, CARS        | 32/32             | 2-14| Scalp Acupuncture + Rehabilitation Training                                      | Rehabilitation Training        | 6 months           | CARS              | Not mentioned     |
| Zhou Qingrui 2015| Stratified stochastic| Comparable AD    | DSM-IV, CARS, ABC, SM, DQ | 56/60 | 2-6 | Scalp Acupuncture + Comprehensive Rehabilitation                                | Comprehensive Rehabilitation    | 6 months           | CARS, ABC         | Not mentioned     |
| Zheng Fangli 2016 | Stratified stochastic| Comparable AD    | DSM-IV, CARS, ABC, SM, DQ | 68/68 | 2-7 | Scalp Acupuncture + Rehabilitation Training                                      | Rehabilitation Training        | 6 months           | PEP               | Not mentioned     |
| Zeng Rui 2017    | Random number table  | Comparable AD    | DSM-IV, CARS, ABC   | 27/27             | 3-8 | Scalp Acupuncture + Rehabilitation Training                                      | Rehabilitation Training        | 4 months           | CARS, ABC, Effective Rate | Not mentioned     |
| Jiang Xiuflang 2017| Not mentioned        | Comparable AD    | CARS, PEP           | 35/35             | 4-12| Scalp Acupuncture + Rehabilitation Training                                      | Rehabilitation Training        | Not mentioned      | CARS, Effective Rate | Not mentioned     |
| Qiu Li 2017      | Random number table  | Comparable AD    | DSM-IV, CARS, PEP   | 25/25             | 1-7 | Scalp Acupuncture + Language Training                                            | Language Training              | 3 months           | PEP, Effective Rate | Not mentioned     |
| Liu Lianjun 2017 | Random number table  | Comparable AD    | DSM-IV, CARS, ABC   | 43/40             | 1-5 | Scalp Acupuncture + Music Education                                              | Music Education                | 3 months           | CARS, ABC, Gecell | Not mentioned     |
| Zhou Hongtao 2018| Random number table  | Comparable AD    | ICD-10, CCMD-3, CARS, ABC, ATEC | 45/45 | 1-11 | Scalp Acupuncture + Behavioral Therapy                                           | Behavioral Therapy             | 6 weeks            | CARS, ABC, ATEC, PEP | Not mentioned     |
| Cao Maozheng 2018| Not mentioned        | Comparable AD    | PEP                 | 31/31             | 3-9 | Scalp Acupuncture + Comprehensive Rehabilitation                                | Comprehensive Rehabilitation    | 10 months          | PEP, Effective Rate | Not mentioned     |

3.2. Methodological quality evaluation
The quality of the literature included 11 documents in Figure 2: (1) Random sequence: 8 articles [7,8,9,11,12,14,15,16] describe how random sequences are generated, 3 articles [10,12,17] did not mention random allocation; (2) None of the included literatures stated that the allocation was hidden,
no blind method was used, and no blind method of result evaluation was mentioned; (3) The integrity of the result data: Two papers mentioned the number of cases of shedding [8,11] (not intentional analysis), and the results of the included literature are complete before and after the data; (4) Selective report: the included literature was pre-set with relevant indicators, without selective reporting in the included literature; (5) Other biases: None of the included literature mentions safety, follow-up, etc.

Figure 2. Overview of document quality evaluation

3.3. Clinical efficacy

Childhood Autism Rating Scale (CARS), Autism Behavior Checklist (ABC), Psycho-educational Profile (PEP), effectiveness.

3.3.1. Autism Spectrum Disorder Diagnostic Scale. A total of 9 studies analysed the CARS score after scalp acupuncture treatment, as shown in Figure 3. The results of the random effects model showed that the MD value was -3.54 (95% CI -5.32, -1.77 \( P < 0.0001 \)). The study of better quality and similar needle-handling techniques was again analysed, as shown in Figure 4. The results of the fixed-effects model showed that the MD value was -1.56 (95% CI -2.40, -0.72 \( P = 0.0003 \)), which was statistically significant. It is suggested that the treatment of scalp acupuncture can help the reduction of CARS score compared with the control group.

Four studies listed ABC results statistics, as shown in Figure 5. The random effects model showed that the MD value was -4.63 (95% CI -6.83, -2.44 \( P < 0.0001 \)); as above, screen analysis of more convincing data, as shown in Figure 6. The results of the fixed effect model showed that the MD value was -3.07 (95% CI -5.18, -0.97 \( P = 0.004 \)), suggesting statistical significance compared with the control group. The treatment of scalp acupuncture was helpful to reduce the CARS score.

![Figure 3. Meta-analysis of CARS in ASD diagnosis scale for acupuncture treatment](image-url)
Figure 4. Meta-analysis of CARS with ASD diagnosis scale similar to acupuncture site

Figure 5. Meta-analysis of ABC diagnosis of ASD diagnosis of scalp acupuncture

Figure 6. Meta-analysis of ABC diagnosis of ASD diagnosis scale similar to acupuncture site

A total of 5 [8,11,14,16,17] studies listed the PEP results statistics, but because the results of the literature comparison are inconsistent, for example Zheng Fangli and others only compared the communication synthesis part of PEP-3, and their sample size was less, so do not analysis.

3.3.2. The efficiency of scalp acupuncture treatment of ASD. A total of 6 studies analysed the effectiveness of acupuncture at the scalp acupuncture. Among them, Tang Qiang's research on conventional scalp acupuncture +rehabilitation training and simple rehabilitation training. The difference was not statistically significant,so only the Tang Qiang group was retained. Significant and effective in the literature are classified as "effective", as shown in Figure 7. The heterogeneity test showed: $\chi^2 = 1.21, P=0.94, I^2=0\%$, suggesting that each study is homogeneous, so the fixed effect mode is used, and the RR value is 1.31 (95% CI 1.16, 1.49 $P<0.0001$), with statistically significant, suggesting that scalp acupuncture can improve autism better than the control group.

Figure 7. Meta-analysis of the effectiveness of acupuncture treatment of ASD
4. Discussions

TCM believes that ASD patients whose pathological location is in the brain, and the causes are congenital deficiency of kidney essence, mental disorder and liver disorder [18]. The head is the meeting of the yang and the center of meridians and collaterals. It regulates brain function through meridians and collaterals, and is related to viscera and limbs. Therefore, scalp acupuncture is based on meridians and acupoints to treat ASD [19-20]. Moreover, scalp acupuncture has the characteristics of short treatment time, simple operation, economical benefit and less side effects, etc. It has been included in the scope of medical insurance. Aiming at the weaker visceral functions of ASD patients, compared with the effects of long-term drug use on physical development and health status, and the large amount of material resources to be spent on rehabilitation training. Treatment is more advantageous for the treatment of ASD [21].

At present, the clinical research on acupuncture treatment of ASD is mainly focused on exploring the influence of acupuncture methods on diseases. Therefore, objective evaluation of the efficacy and safety of scalp acupuncture can provide reference for standardized treatment of clinical autism. In 2011, Daniel KL Cheuk et al. [22] conducted a systematic review of “acupuncture treatment of autism”. The included literatures have not been evaluated by CARS, ABC and other evaluation tools as the criterion of therapeutical effect; in 2012, Ming X et al.[23] made a literature evaluation on the subject without meta-analysis; in 2015, Zhang Ying qian meng [24] conducted a meta-analysis, but the amount of literatures included were small and the quality were low. In 2016, Yuan Zhaohong et al. [25] systematically evaluated the subject, but did not mention the concept of ASD including AD, and included mixed cases, including electro-acupuncture, tongue-acupuncture, body-acupuncture, scalp-acupuncture, etc. This study chooses "scalp acupuncture" as the research object, which is more detailed and comprehensive than the former.

In this study, 11 literatures were included, a total of nine literatures analyzed the CARS score, four literatures analyzed the ABC score and six literatures studied the efficiency. The meta-analysis results suggest that: Direct at the original literatures, the improvement of CARS and ABC scale score by scalp acupuncture plus other treatment groups in the treatment of ASD was heterogeneous with other treatment groups, which may be related to the site, manipulation and time of acupuncture. Selection of high-quality and similar sites of acupuncture research, it can be found that the acupuncture plus other treatment group can improve the CARS and ABC scale scores in the treatment of ASD compared with other treatment groups, and the difference is statistically significant; in terms of efficiency, the clinical effect of scalp acupuncture is better; In terms of safety, since no adverse reactions were described in the incorporated literatures, safety could not be evaluated.

There are still some deficiencies in the included literatures: none of the blind methods of distribution concealment, no blind method, no mention of result evaluation, no follow-up and safety analysis, etc. Because of the low quality of the literatures, it is easy to cause false negative clinical efficacy of scalp acupuncture, and the sample size is too small, the argument is not convincing; some of the randomized control methods are not standardized or show that they are not strictly in accordance with RCT requirements. In addition, this study also has some shortcomings: it is easy to omit other high-quality argumentation when searching only in Chinese and English literature; the subjective factors of screening literatures have a greater impact [26].

To sum up, considering the safety of the included literatures, the low quality of RCT and the small sample size, the evidence-based grade of the clinical efficacy of scalp acupuncture has been reduced. The existing evidence is not enough to promote scalp acupuncture in treating ASD. In the future, clinical researchers should strengthen the rigor of the research design of ASD, and carry out the research with the criteria of multi-center, large sample and randomized control, expecting the research and demonstration of higher quality RCT.

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