TECHNICAL COMMENTARY

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Acupuncture

Introduction

Acupuncture is practiced as an accepted health care model in China, Korea and Japan. Traditionally, it involves the stimulation of specific points (acupoints) by inserting needles into the skin. Electro-acupuncture is similar in that the same points are stimulated during treatment with needles inserted on specific points along the body. Electro-acupuncture uses two needles at time with the needles attached to an electrical device that generates continuous electric pulses that pass from one needle to the other with varying frequency and intensity dictated by the condition. Administration is usually for no more than 30 minutes at a time. Laser acupuncture is essentially the same except that a laser is used instead of needles[1]. Moxibustion is a technique by which either heat from burning a specific herb (*artemisia vulgaris)* or an electric source is used to stimulate specific points or areas of the body. One of the challenges in performing efficacy trials of acupuncture is that it is difficult to provide a control condition. Sham methods that have been used include needling the wrong points or with very superficial technique, or using a simluation of laser acupuncture without full stimulation.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[2]. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[3]. The resulting table represents an objective summary of the available evidence, although the conclusions

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found two systematic reviews that met our inclusion criteria[1, 4].

- Moderate to low quality evidence suggests there may be some general improvement with needle or electro-acupuncture (with or without antipsychotics) when compared to antipsychotic medications alone.
- Low quality evidence is uncertain as to the effects of laser acupuncture.

Acupuncture

Lee, MS, Shin, BC, Ronan, P, Ernst, E

Acupuncture for schizophrenia: a systematic review and meta-analysis

The international journal of clinical practice 2009; 63(11): 1622-1633

View review abstract online

Comparison 1	**Needle or electro-acupuncture vs. antipsychotic medication.**
Summary of evidence	**Moderate to low quality evidence (consistent, precise, direct, medium-sized sample, low study quality) suggests there may be a benefit of needle or electro-acupuncture alone over antipsychotic medication alone for general improvement.**
Response rate measured by recovery and improvement **Assessed by clinician**	
Small effect favouring acupuncture at end of treatment; 4 RCT, N = 360, RR = 1.18, 95%CI 1.03 to 1.34, p = 0.01, I^2 = 0%, p = 0.39 Authors report studies are of very low quality	
Risks	Not reported
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Needle or electro-acupuncture with concurrent antipsychotic medication vs. antipsychotic medication alone.**
Summary of evidence	**Moderate to low quality evidence (consistent, precise, direct, medium to large-sized samples, low study quality) suggests there may be a benefit for needle or electro-acupuncture with concurrent antipsychotic medication over antipsychotic medication alone for general improvement and improvement of negative symptoms.**
Response rate measured by recovery and improvement **Assessed by clinician**	

Small effect favouring acupuncture at end of treatment; 7 RCT, N = 457, RR = 1.15, 95%CI 1.04 to 1.28, *p* = 0.008, I^2 = 9%, *p* = 0.36 Authors report studies are of very low quality	
Scale for the Assessment of Negative Symptoms **Measured by the SANS**	
Large effect favouring acupuncture at end of treatment; 3 RCT, N = 192, WMD = 10.95, 95%CI 8.22 to 13.69, *p* = 0.00001, I^2 = 0%, *p* = 0.87 *d* = 0.90, 95%CI -0.03 to 1.82, *p* = 0.06, I^2 = 88%, *p* = 0.0003	
Risks	Not reported
Consistency in results	Consistent for response rate, inconsistent for SANS (Cohen's *d* results).
Precision in results	Precise for response rate, imprecise for SANS.
Directness of results	Direct
Comparison 3	**Electro-acupuncture with concurrent antipsychotic medication vs. antipsychotic medication alone.**
Summary of evidence	**Moderate to low quality evidence (consistent, precise, direct, small to medium-sized samples, low study quality) suggests there may be a benefit for electro-acupuncture with concurrent antipsychotic medication over antipsychotic medication alone for general improvement and improvement of symptoms.**
Response rate measured by recovery and improvement **Assessed by clinician**	
Small effect favouring acupuncture at end of treatment; 5 RCT, N = 365, RR = 1.19, 95%CI 1.00 to 1.43, *p* = 0.05, I^2 = 35%, *p* = 0.19	
Mental state **Measured by BPRS**	
Medium-sized effect favouring acupuncture at end of treatment; 2 RCT, N = 140, WMD = 6.02, 95%CI 2.53 to 9.51, *p* = 0.0007, I^2 = 17%, *p* = 0.27 *d* = 0.64, 95%CI 0.30 to 0.99, *p* = 0.0003, I^2 = 0%, *p* = 0.40	
Risks	Not reported

Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct
Comparison 4	**Laser acupuncture with or without concurrent antipsychotic medication vs. sham laser acupuncture with or without concurrent antipsychotic medication.**
Summary of evidence	**Low quality evidence (low study quality, small samples) is uncertain as to the effects of laser acupuncture for general improvement and symptom improvement.**
Response rate measured by recovery and improvement **Assessed by clinician**	
Significant effect of laser acupuncture; 1 RCT (N = 31) no statistics reported	
Global improvement **Measured by CGI**	
Significant effect of laser acupuncture; 1 RCT (N = 31) no statistics reported	
Mental state **Measured by BPRS**	
Significant effect of laser acupuncture; 1 RCT (N = 31) no statistics reported	
Hallucinations	
No treatment effect; 1 RCT (N = 60) no statistics reported	
Risks	Not reported
Consistency in results	N/A – 1 RCT only
Precision in results	CIs not reported
Directness of results	Direct

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

Rathbone J, Xia J

Acupuncture for schizophrenia

Cochrane Database of Systematic Reviews 2005; (4): CD005475

View review abstract online

Comparison 1	**3 weeks of electro-acupuncture - points used; Yi feng (SJ17), Ting Gong (SI19), Tou Nie (non meridinal), Cheng Ling (GB18), Lin Qi (GB41), Bai Hu (GV20) Ding Shen (non meridinal). Needles: stainless steel, gauge 28, length 33 mm vs antipsychotic treatment (chlorpromazine).** **Or 5 weeks of laser acupuncture with moxibustion. Points used; Da zhui (GV14), shen ting (GV24) + shuang tai yang on alternate days. Laser fibre output >2 milliwatts vs chlorpromazine.**
Summary of evidence	**Moderate to low quality evidence (consistent, direct, imprecise, low study quality) suggests no benefit of electro or laser acupuncture alone compared to chlorpromazine antipsychotic medication alone for global improvement by 3 months. Low quality evidence is uncertain of the risks (1 small RCT).**
Global improvement	
No significant treatment effect by 3 months; 2 RCT, N = 109, RR = 1.05, 95%CI 0.68 to 1.64, p = 0.82, I^2 = 0%, p = 0.59 Authors report studies are of very low quality	
Risks	*Less extrapyramidal symptoms in the laser acupuncture group;* 1 RCT, N = 21, RR = 0.05, 95%CI 0.00 to 0.83, p = 0.036
Consistency in results‡	Consistent for global improvement, N/A for extrapyramidal symptoms (1 RCT).
Precision in results§	Imprecise
Directness of results‖	Direct
Comparison 2	**6 to 8 weeks of electro-acupuncture frequency 180 cycles per second, pulse width 500 microseconds and current up to 60mA plus antipsychotic treatment. Points used: 6 weeks of Yin tang + Bai Hu (GV20) or 6 weeks of Yin tang tou xinqu, Daling (PC7), Neiguan (PC6) and Taiyang (Ex-HN5). 8 weeks of Yin tang and Bai hui (Gv 20) + shen ting (GV 24) and ya men (GV 15) on alternate**

	days. Needles: stainless steel filiform, gauge #30, length 40mm vs. antipsychotic treatment (chlorpromazine). **Or 5 weeks of laser acupuncture with moxibustion. Points used; Da zhui (GV14), shen ting (GV24) + shuang tai yang on alternate days. Laser fibre output >2 milliwatts vs. chlorpromazine.**
Summary of evidence	**Moderate to low quality evidence (consistent, precise, direct, small samples, low study quality) shows some benefit of electro-acupuncture with concurrent antipsychotic medication compared to chlorpromazine antipsychotic medication alone for mental state as measured by the BPRS by 3 months.** **Low quality evidence (imprecise) is uncertain as to the effects for global improvement or risks of treatment.**
Mental state **Measured by BPRS**	
Medium-sized effect favouring acupuncture + antipsychotics by 3 months; 2 RCT, N = 109, WMD = -4.31, 95%CI -7.04 to -1.58, p = 0.002, I^2 = 0%, p = 0.93 d = -0.61, 95%CI -1.01 to -0.22, p = 0.002, I^2 = 0%, p = 0.97 Authors report studies are of very low quality	
Mental state **Measured by HAMD**	
Large effect favouring acupuncture + antipsychotics by 3 months; 1 RCT, N = 42, WMD = -10.41, 95%CI -12.81 to -8.01, p = 0.00001 d = -2.58, 95%CI -3.42 to -1.74, p = 0.00001	
Mental state **Measured by ZDS (higher score = worse symptoms)**	
Large effect favouring acupuncture + antipsychotics by 3 months; 1 RCT, N = 42, WMD = -24.25, 95%CI -28.01 to -20.49, p = 0.00001 d = -3.82, 95%CI -4.87 to -2.77, p = 0.00001	
Global improvement	
No significant treatment effect by 3 months; 1 RCT, N = 20, RR = 0.80, 95%CI 0.30 to 2.13, p = 0.66	

Acupuncture

Global improvement Measured by CGI - severity of illness	
No significant treatment effect by 3 months; 1 RCT, N = 40, WMD = -0.40, 95%CI -1.08 to 0.28, *p* = 0.25 *d* = -0.38, 95%CI -1.02 to -0.27, *p* = 0.25	
Risks	*Large effect favouring 6 electro-acupuncture + antipsychotics for global impact of treatment by 3 months;* 1 RCT, N = 40, WMD = -0.50, 95%CI -0.86 to -0.14, *p* = 0.0067 *d* = -0.91, 95%CI -1.58 to -0.24, *p* = 0.008
	No differences in extrapyramidal symptoms by 3 months; 1 RCT, N = 20, RR = 0.88, 95%CI 0.53 to 1.46, *p* = 0.61
Consistency in results	Consistent for mental state (BPRS), N/A for other outcomes (1 RCT).
Precision in results	Precise for leaving study early and mental state (BPRS).
Directness of results	Direct

Explanation of acronyms

BPRS = Brief Psychiatric Rating Scale, CI = Confidence Interval, CGI = Clinical Global Impression Scale, *d* = Cohen's *d* and *g* = Hedges' *g* = standardized mean differences (see below for interpretation of effect sizes), HAMD = Hamilton Rating Scale for Depression, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - see ‡ below for interpretation, N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q = Q statistic (chi-square) for the test of heterogeneity in results across studies, RCT = randomized controlled trial/s, RR = relative risk, vs = versus, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms, TESS/F = Treatment Emergent Symptom Scale/Form, WMD = weighted mean difference, ZDS = Zung Depression Scale

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small.

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† Different effect measures are reported by different reviews.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large treatment effect[5].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[6]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified - 100% sensitivity = predict all people who are at high risk as developing psychosis and specificity is the proportion of negatives that are correctly identified - 100% specificity = not predicting anyone as being at high risk if they are truly not.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of treatment effect across trials (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed[7].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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