•Systematic review and meta-analysis•

Electroconvulsive therapy for agitation in schizophrenia: meta-analysis of randomized controlled trials

Xiaojing GU[1#], Wei ZHENG[2#], Tong GUO[3], Gabor S. UNGVARI[4,5], Helen F.K. CHIU[6], Xiaolan CAO[6, 7], Carl D'ARCY[8], Xiangfei MENG[9], Yuping NING[1]*, Yutao XIANG[10]*

Background: Agitation poses a significant challenge in the treatment of schizophrenia. Electroconvulsive therapy (ECT) is a fast, effective and safe treatment for a variety of psychiatric disorders, but no meta-analysis of ECT treatment for agitation in schizophrenia has yet been reported.

Aims: To systematically evaluate the efficacy and safety of ECT alone or ECT-antipsychotics (APs) combination for agitation in schizophrenia.

Methods: Systematic literature search of randomized controlled trials (RCTs) was performed. Two independent evaluators selected studies, extracted data about outcomes and safety with available data, conducted quality assessment and data synthesis. The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) was used to judge the level of the overall evidence of main outcomes.

Results: Seven RCTs from China, including ECT alone (4 RCTs with 5 treatment arms, n=240) and ECT-APs combination (3 RCTs, n=240), were identified. Participants in the studies were on average 34.3(4.5) years of age and lasted an average of 4.3(3.1) weeks of treatment duration. All 7 RCTs were non-blinded, and were rated as low quality based on Jadad scale. Meta-analysis of the pooled sample found no significant difference in the improvement of the agitation sub-score of the Positive and Negative Syndrome Scale (PANSS) when ECT alone (weighted mean difference=-0.90, (95% confidence interval (CI): -2.91, 1.11), p=0.38) or ECT-APs combination (WMD=-1.34, (95%CI: -4.07, 1.39), p=0.33) compared with APs monotherapy. However, ECT alone was superior to APs monotherapy regarding PANSS total score (WMD=-7.13, I^2=0%, p=0.004) and its excitement sub-score (WMD=-1.97, p<0.0001) as well as the PANSS total score at 14 days (WMD=-7.13, I^2=0%, p=0.004) and its excitement sub-score at 7 and 14 days (WMD=-1.97 to -1.92, p=0.002 to 0.0001) after ECT. The ECT-APs combination was superior to APs monotherapy with respect to the PANSS total score at treatment endpoint (WMD=-10.40, p=0.03) and 7 days (WMD=-5.01, p=0.02). Headache (number-needed-to-harm (NNH)=3, 95%CI=2-4) was more frequent in the ECT alone group compared to AP monotherapy. According to the GRADE approach, the evidence levels of main outcomes were rated as ''very low'' (37.5%) and "low" (50%).

Conclusion: Pooling of the data based on 7 RCTs from China found no advantage of ECT alone or ECT-APs combination in the treatment of agitation related outcomes in schizophrenia patients. However, ECT alone or ECT-APs combination were associated with significant reduction in the PANSS total score. High-quality RCTs are needed to confirm the current interpretations.

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Key words: Electroconvulsive therapy; agitation; schizophrenia; headache, meta-analysis

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[1]The Second Affiliated Hospital of Xinxiang Medical University, Henan Mental Hospital, Henan, China;
[2]Guangzhou Brain Hospital (Guangzhou Huiai Hospital), Affiliated Hospital of Guangzhou Medical University, Guangzhou China;
[3]The National Clinical Research Center for Mental Disorders & Beijing Anding Hospital, Capital Medical University, China;
[4]School of Psychiatry & Clinical Neurosciences, University of Western Australia, Perth, Australia;
[5]The University of Notre Dame Australia / Marian Centre, Perth, Australia;
[6]Department of Psychiatry, Chinese University of Hong Kong, Hong Kong SAR, China;
[7]Shenzhen Key Laboratory for Psychological Healthcare & Shenzhen Institute of Mental Health, Shenzhen Kangning Hospital & Shenzhen Mental Health Center, Shenzhen, China;
[8]Department of Psychiatry & School of Public Health, University of Saskatchewan, Saskatoon, Canada;
[9]Department of Psychiatry, McGill University and the Douglas Mental Health University Institute, Montreal, Canada;
[10]Unit of Psychiatry, Faculty of Health Sciences, University of Macau, Macao SAR, China;
[#]These authors equally contributed to the work.
*correspondence: Dr. Yu-Tao Xiang. Mailing address: 3/F, Building E12, Faculty of Health Sciences, University of Macau, Avenida da Universidade, Taipa, Macau SAR, China. E-mail: xyutly@gmail.com; Dr. Yu-Ping Ning. Mailing address: the Affiliated Brain Hospital of Guangzhou Medical University (Guangzhou Huiai Hospital), Guangzhou, China. E-mail: ningjeny@126.com

1. Introduction

Agitation, excessive motor and/or verbal activity, characterized by excitement, restlessness, and psychic and motor tension, is common in patients with schizophrenia. Agitation can escalate into aggressive behavior leading to high risk of injury for patients, relatives or staff.[1-3] Furthermore, agitation increases the frequency of patient emergency department visits with further negative consequences.[4]

In order to minimize the risk posed to self or others, agitated patients should be managed, first and preferably by non-pharmacological interventions such as environmental and behavioral modification, and secondly by pharmacological agents.[3-5] However, in most cases the management of agitation largely depends on pharmacological agents,[6] mainly benzodiazepines and antipsychotics (APs) with their well-known adverse effects particularly if they are administered repeatedly.[1,3]

Electroconvulsive therapy (ECT) is a fast, effective and safe treatment for a variety of psychiatric disorders.[7] Use of ECT for acute or even prolonged agitation has received scant attention in contemporary literature and it appears that ECT is hardly ever used for this purpose in developed countries. However, ECT remains an option for agitation or aggression in China and developing countries.[8] There have been a number of studies published in China, including randomized controlled trials (RCTs)[9-15] to compare the efficacy of ECT alone or the ECT-AP combinations to AP monotherapy with conflicting results.

To the best of our knowledge, no systematic review or meta-analysis of ECT treatment for agitation in schizophrenia has been published. This was the impetus for this meta-analysis concerning the efficacy and safety of ECT treatment for agitation in schizophrenia.

2. Methods

2.1 Selection of studies

According to PICOS acronym, the inclusion criteria were: Participants (P): adult schizophrenia patients (≥18 years) with agitation. Intervention (I): ECT alone and ECT-AP combination. Comparison (C): AP monotherapy. Outcomes (O): primary outcomes were the improvement of agitation related outcomes at last-observation-carried-forward (LOCF) study endpoint measured by the Positive and Negative Syndrome Scale (PANSS),[16] Brief Psychiatric Rating Scale (BPRS),[17] and any other scales or sub-scales or item for agitation: 1) total psychopathology scores, 2) the excitement sub-scores, and 3) the agitation sub-scores. Key secondary outcomes included early symptomatic improvement (at 1, 3, 7, and 14 days), rate of all-cause discontinuation and patient-reported adverse events. Study design (S): RCT with available data. The exclusion criteria were case series, non-randomized studies, and non-original research (reviews and meta-analyses).

2.2 Search strategy

English databases (PubMed, PsycINFO, and Cochrane Library) and Chinese databases (WanFang Database, Chinese Biomedical Database and China Journal Net) were searched, from their inception until Feb 3, 2017 using the following search terms: (1) English databases: (ECT OR Electric Convulsive Therap* OR Therap*, Electric Convulsive OR Electroshock Therap* OR Convulsive Therap*, Electric) OR Electroconvulsive Therapy OR Electroconvulsive Therapies OR Therap*, Electroconvulsive OR Electric Shock Therap* OR Shock Therap*, Electric OR Therap*, Electric Shock OR Therap*, Electroshock) AND (schizoaffective disorder OR schizophreniform OR Schizophrenic Disorder OR Disorder, Schizophrenic OR Schizophrenic Disorders OR Schizophrenia OR Dementia Praecox) AND (agitation OR exciting OR aggression); (2) Chinese databases: (电休克 OR 电抽搐 OR ECT OR MECT OR 电痉挛) AND (激越 OR 攻击 OR 兴奋） AND 随机 AND (精神分裂症 OR 精神分裂). The search was supplemented by using the "related article" function. Hand-searched reference lists from relevant review articles for additional studies were hand-searched and authors contacted for unpublished data.

2.3 Data extraction

Two independent evaluators (GXJ and ZW) selected studies, extracted data, conducted quality assessment and data synthesis. Any inconsistencies were resolved by discussion to reach consensus or involvement of a third reviewer (XYT).

2.4 Data synthesis and statistical analyses

Clinical outcomes were based on intent-to-treat (ITT) analysis, if available. The meta-analysis was performed using Review Manager (version 5.3) according to the recommendations of the Cochrane Collaboration.[18] To combine studies, the random effects model [19] was used in all cases. For continuous data and dichotomous data, weighted mean differences (WMDs) associated with their 95% confidence intervals (CIs) and risk ratio (RR) ±95% CIs were calculated, respectively. We reported the number-needed-to-treat (NNT) or number-needed-to-harm (NNH) calculated by dividing 1 by the risk difference as soon as RR was significant. One study [11] from the 'ECT alone' group had three study arms. According to the methodology of prior meta-analysis,[20] we should include each of the 2 ECT arms separately in one RCT [11] with 3 treatment arms. Furthermore, the APs monotherapy arm was included twice in the analysis, but half of all patients were randomized to each AP arm in order not to inflate the number of patients in the APs monotherapy arm.

In case of I^2≥50% for the effect of primary outcome on the PANSS total score, a sensitive analysis was conducted by excluding one outlying study [15] with an outlying effect size (ES) of less than -1.24 (i.e.,

more than 1.24 standard deviation superiority of ECT-AP combination) in the 'ECT-AP combination' group. Furthermore, subgroup and meta-regression analyses were conducted to detect the sources of heterogeneity, if possible. Publication bias was assessed using funnel plots and Egger's test.[21] All statistical differences were considered significant when $p<0.05$.

2.5 Assessment of study quality

The Cochrane risk of bias [18] was used to assess the quality of each study. Furthermore, the quality of each study was also assessed with the Jadad scale that assesses study quality on a 5-point scale along the following five domains: "randomization," "double blinding," "description withdrawals and dropouts," "generation of random numbers," and "allocation concealment".[22] The criteria of high and low quality were defined as Jadad score ≥4 and <4, respectively.

2.6 Clinical evidence recommendation

The grading of recommendations assessment, development, and evaluation (GRADE) system [23] was used to judge the quality of clinical evidence recommendations of the meta-analytic results of ECT for agitation in schizophrenia.

3. Results

3.1 Results of the search

Altogether 133 potentially relevant articles from English (n=96) and Chinese databases (n=37) were identified; duplication excluded 14 studies. Of the remaining 119 entries, 112 were determined to be irrelevant after review of the titles and abstracts, a further 7 were removed on the basis of full text review. Finally, 7 RCTs with 8 treatment arms met the selection criteria for the meta-analysis (Figure 1).

3.2 The characteristics of included studies

The seven RCTs lasted an average of 4.3(3.1) weeks (range: 2-8 weeks; median: 2 weeks). The total number of participants in all the studies was 480 (range: 30-100, median: 60). All the RCTs that met our inclusion and exclusion criteria were thus included in the meta-analysis had been conducted in China. Aggregating data across all the reviewed trials: there were 240 patients in ECT monotherapy vs. AP monotherapy (n=135 vs. n=105) comparison and 240 patients in the ECT-AP vs. AP monotherapy (n=120 vs. n=120) comparison (Table 1); patients were on average 34.3(4.5) years old (range: 31.9-43.5 years; median: 32.5 years) in 6 RCTs with available data; 57.6(14.2)% were males (range: 40.0%-80.0%; median: 56.7%); and the mean illness duration with available data (6 RCTs) was 2.7(2.7) years (range: 0.02-6.1 years; median: 2.2 years).

3.3 Assessment of risk of bias and quality assessment

The Cochrane risk of bias was presented in Table 2. 85.7% (6/7) RCTs only mentioned "random" assignment, lacking a detailed description of the method of randomizing and thus were rated as unclear. However, only one RCT [13] using random assignment according to the random number table was rated as low risk. Given that all included studies were open label, the allocation bias, performance bias, and detection bias were rated as high risk. None of the included RCTs presented the study registration materials, which limited us to determine whether or not there was selective reporting (i.e., reporting bias). Furthermore, it was impossible to judge the other types of biases (e.g., drug company sponsorship of the study) due to lack of available evidence. Overall, 7 included RCTs suffered from high risk of bias and were considered as relatively low-quality studies. The Jadad score was 2.0(0.6) (range=1-3, median=2) (Table 1). All RCTs were rated as low quality (Jadad score < 4). Due to pooling of data, less than 3 RCTs with 4 treatment arms were in all forest plots, thus funnel plot analysis to show the presence of risk of publication bias could not be conducted.

3.4 The improvement of agitation related outcomes

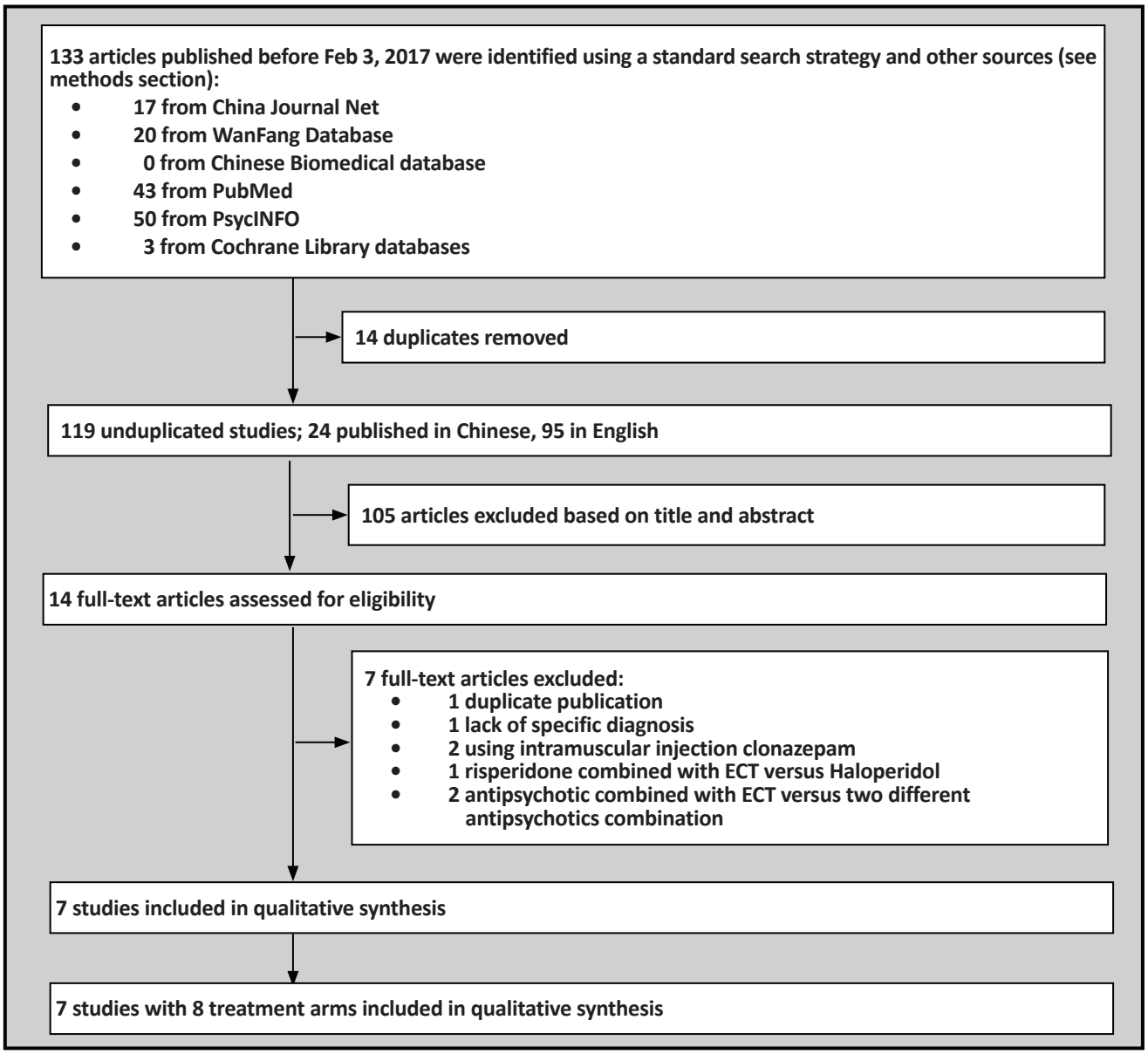
There were differences between the ECT alone vs AP (4 RCTs with 5 treatment arms) and ECT-AP vs AP (3 RCTs) groups. Moreover, the improvement of agitation related outcomes were measured using PANSS in all included RCTs.

ECT alone vs AP: ECT alone was superior to AP monotherapy with respect to PANSS total score (WMD=-7.13, (95%CI: -11.99, -2.27), I^2=0%, p=0.004, Figure 2) and excitement sub-score (WMD=-1.97, (95%CI: -2.87, -1.08), I^2=0%, p<0.0001, Figure 2), but not in the agitation sub-score (WMD=-0.90, p=0.38); ECT alone was superior to AP monotherapy in PANSS total score at 14 days (WMD:-7.13 (95%CI:-11.99, -2.27), p=0.004; I^2=0%, Supplemental Figure 1), but not at 1 and 7 days (WMD:-5.23 to -7.13 (95%CI:-16.86, 4.25), p=0.06 to 0.24; I^2=0% to 77%, Supplemental Figure 1). Furthermore, subgroup and meta-regression analyses could not be performed due to the limited number of RCTs.

Furthermore, ECT alone was superior to AP monotherapy in PANSS excitement sub-score at 7 and 14 days (WMD:-1.97 to -1.92 (95%CI:-3.14, -0.71), p=0.002 to 0.0001; I^2=0%, Supplemental Figure 2), but not at 1 day after ECT treatment (WMD:-1.92 (95%CI:-4.00, 0.17), p=0.07; I^2=35%, Supplemental Figure 2). Among the ECT alone studies one RCT [10] used Clinical Global Impression (CGI) and found an advantageous improvement of psychiatric symptoms in the ECT group at 7 and 14 days.

ECT plus AP vs AP: Regarding the PANSS total score, the ECT-AP combination was superior to AP

Figure 1. Identification of included studies



monotherapy (WMD=-10.40, (95%CI: -19.67, -1.12), I^2=93%, p=0.03, Figure 3), but not in the excitement and agitation sub-scores (WMD=-1.06 to -1.34, p=0.33 to 0.37). The significant difference between the two groups in the PANSS total score disappeared after one outlying study [15] was removed (WMD:-4.23 (95%CI:-8.89, 0.43), p=0.08; I^2=76%). Furthermore, subgroup and meta-regression analyses could not be performed due to the limited number of RCTs.

Furthermore, adding ECT to AP was superior to AP monotherapy at 7 days for the PANSS total score (WMD=-5.01, (95%CI: -9.37, -0.66), I^2=14%, p=0.02, Figure 4), but not to PANSS total score (p=0.15), excitement (p=0.35) and agitation sub-scores (p=0.44) at 14 days (Figures 4).

3.5 Side effects and discontinuation rate

The Treatment Emergent Symptom Scale (TESS) was generally used to assess adverse drug reactions (ADRs) in these RCTs however such data were not available in 1 RCT (Table 1). None of the included RCTs reported the rate or cause of treatment discontinuation.

ECT alone vs APs: Headache (p=0.0001, NNH=3, 95%CI=2-4) was the only ADRs more frequent in the ECT alone group compared to AP monotherapy (Supplemental Figure 3). There was significantly less akathisia (p=0.02, NNH=8, 95%CI=5-17) and electrocardiogram changes (p=0.05) with borderline significance in the ECT alone group compared to the AP group. Meta-analysis of uroclepsia, weight gain, upper

Table 1. Characteristics of the RCTs

Study	N	-Blinding -Setting (%)	Trial Duration (wks)	Country	Patients: -Diagnosis -Criteria -Illness duration (yrs)	Age[a]: years (range)	Sex: Male (%)	Interventions: APs (mg/day); ECT (sessions)	Outcomes	Jadad score
ECT alone vs. APs (trials=4, n=240)										
Guo et al 2009 [10]	60	-Open label -Inpatients (100)	2	China	-Sz -CCMD-3 -Illness duration: 0.66	32.5 (18-50)	n=24 (40%)	1. HAL (10-20); n=30; 2. ECT (8); n=30	PANSS; CGI; TESS	1
Shen et al 2011 [11]	90	-Open label -Inpatients (100)	2	China	-Sz -CCMD-3 (first episode) -Illness duration: 0.17	32.8 (18-59)	n=46 (51%)	1. OLA (5-20); n=30; 2. ECT (etomidate, 6); n=30; 3. ECT (propofol, 6); n=30	PANSS; TESS	2
Yuan et al 2012 [12]	30	-Open label -Inpatients (100)	2	China	-Sz -CCMD-3 -Illness duration: 9.1 days	31.9 (NR)	n=13 (43%)	1. HAL (10-60) ; n=15; 2. ECT (6); n=15	PANSS; TESS	2
Li 2015 [14]	60	-Open label -Inpatients (100)	8	China	-Sz -CCMD-3 -Illness duration: NR	32.4 (20-60)	n=34 (57%)	1.CLZ (50-75) ; n=30; 2. ECT (6-12); n=30	BPRS; TESS	2
ECT+ APs vs. APs (trials=3, n=240)										
Yang et al 2005 [9]	60	-Open label -Inpatients (100)	8	China	-Sz -CCMD-3 (refractory) -Illness duration: 6.1	NR. (NR)	n=38 (63%)	1. CLZ (445); n=30; 2. CLZ (436) + ECT (6-12); n=30	PANSS; TESS	2
Peng et al 2014 [13]	80	-Open label -Inpatients (100)	2	China	-Sz -ICD-10 -Illness duration: 3.8	32.5 (NR)	n=55 (69%)	1. RIS (5.4); n=40; 2. RIS (5.2) + ECT (6-8); n=40	PANSS; TESS	3
Pan 2015 [15]	100	-Open label -Inpatients (100)	8	China	-Sz -ICD-10 -Illness duration: 5.3	43.5 (22-63)	n=80 (80%)	1. AP[b] (NR); n=50; 2. AP[b] (NR) + ECT (8-12); n=50	PANSS;	2

[a]weighted mean; [b]did not report the detailed use of antipsychotics.

APs = antipsychotics; BPRS = Brief Psychiatric Rating Scale; CLZ = Clozapine; CGI = Clinical Global Impression; CCMD-3 = The Chinese Classification of Mental Disorders 3th edition; ECT = Electroconvulsive therapy; HAL = Haloperidol; ICD-10 = International Classification of Diseases, 10th edition; NR = not report; OLA = Olanzapine; PANSS = Positive and Negative Syndrome Scale; RCT = randomized controlled trial; RIS = Risperidone; Sz = schizophrenia; TESS = Treatment Emergent Symptom Scale; yrs = years; wks = weeks.

Table 2. Evaluation of risk of bias in the seven included studies

study	sequence generation	allocation sequence concealment	blinding of participants and personnel	blinding of outcome assessment	incomplete outcome data	selective outcome reporting	other potential threats to validity
Pan 2015 [15]	unclear	high	high	high	low	unclear	unclear
Peng et al 2014 [13]	low	high	high	high	low	high	unclear
Yang et al 2005 [9]	unclear	high	high	high	low	unclear	unclear
Guo et al 2009 [10]	unclear	high	high	high	low	unclear	unclear
Li 2015 [14]	unclear	high	high	high	low	unclear	unclear
Yuan et al 2012 [12]	unclear	high	high	high	unclear	unclear	unclear
Shen et al 2011 [11]	unclear	high	high	high	unclear	unclear	unclear

Figure 2. ECT alone for agitation in schizophrenia: forest plot for the Positive and Negative Syndrome Scale (PANSS) total score and its PANSS excitement and agitation sub-scores at endpoint

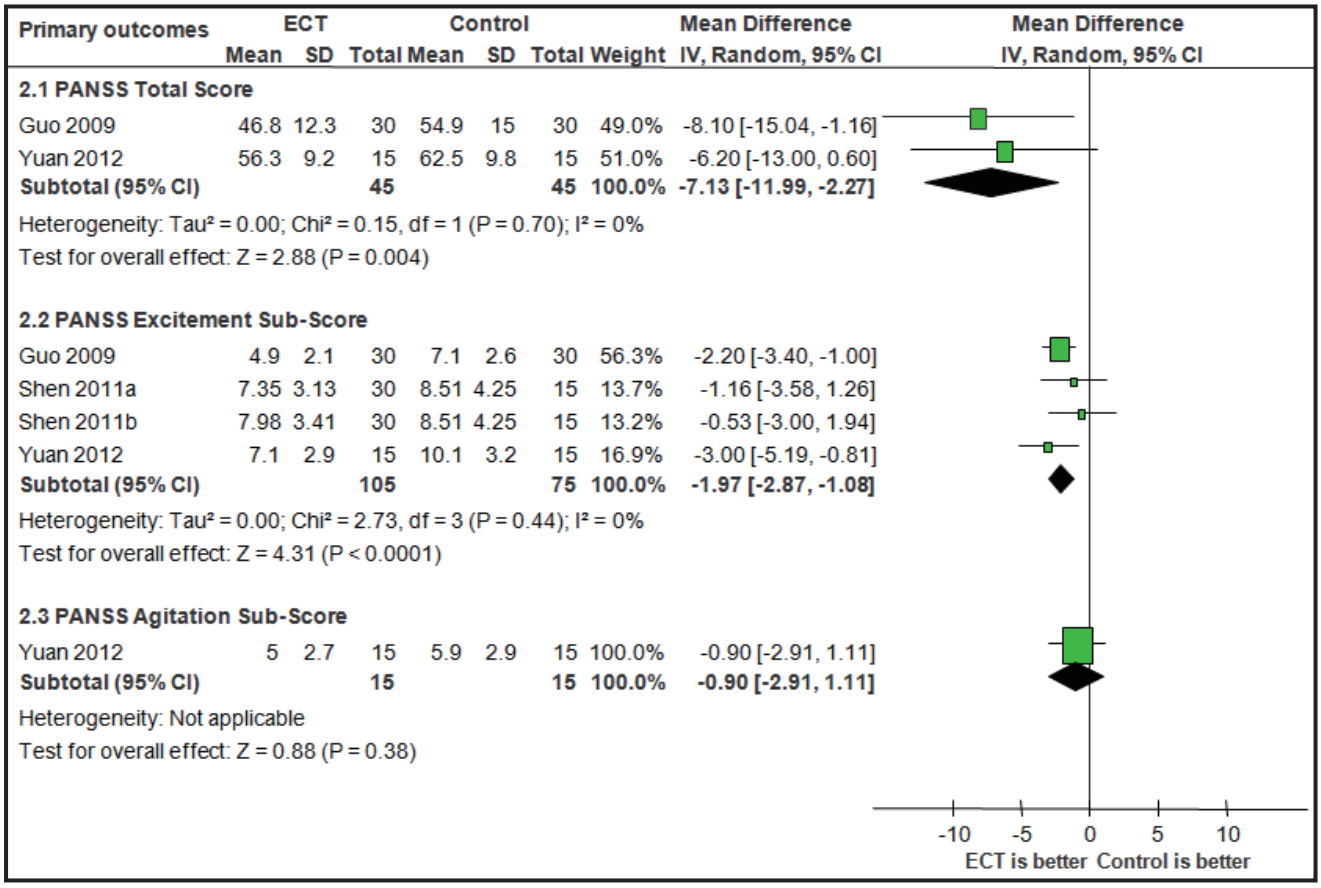
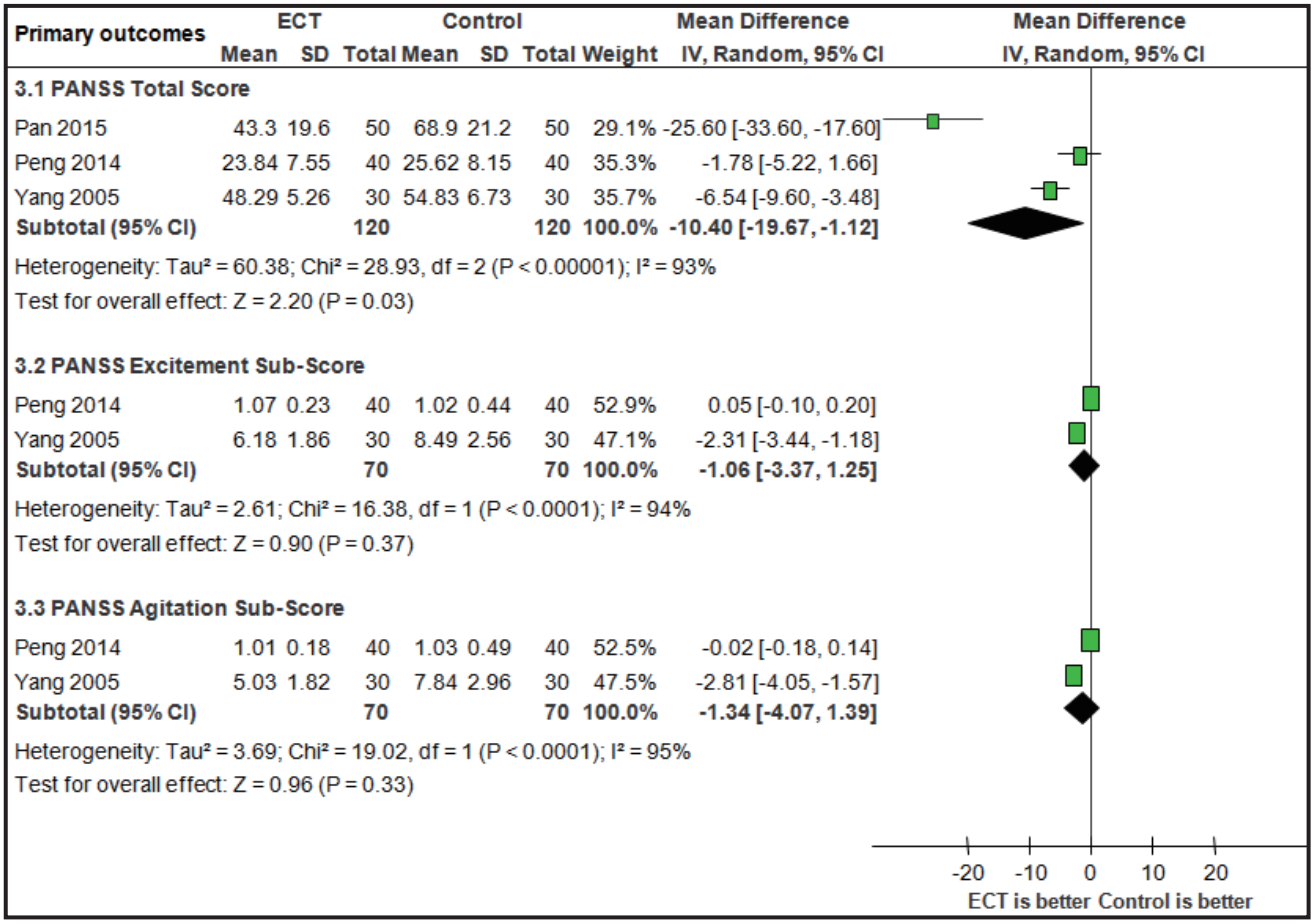


Figure 3. Add-on ECT to antipsychotics for agitation in schizophrenia: forest plot for the Positive and Negative Syndrome Scale (PANSS) total score and its excitement and agitation sub-scores at endpoint



respiratory infections, tremor, dry mouth, insomnia, and electroencephalography changes did not differ between the groups (Supplemental Figure 3).

ECT plus AP vs AP: Only two RCTs [9,13] reported the ADRs without meta-analyzable data.

3.6 Clinical evidence recommendation

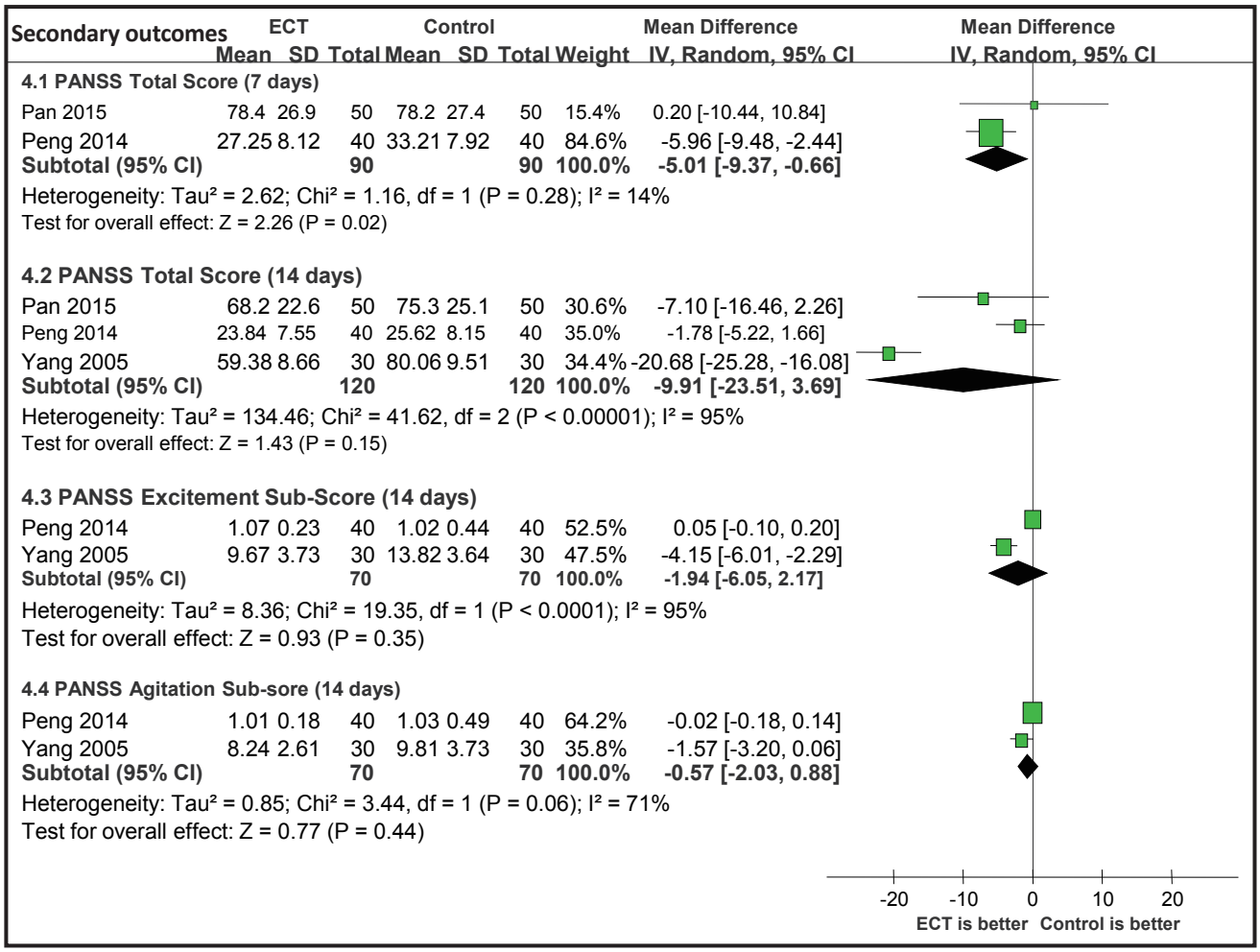
Clinical evidence recommendation of the main meta-analytic outcomes based on the GRADE approach showed some limitations of risk of bias, inconsistency and publishing bias, and no obvious indirectness or imprecision. According to the above assessments, the quality of evidence of 8 outcomes presented in Table 3 and ranged from ‘‘very low’’ (37.5%), “low” (50%), to ‘‘high’’ (12.5%).

4. Discussion

4.1 Main findings

Despite a systematic literature search in both English and Chinese-language databases, we only identified 7 RCTs with 8 treatment arms that examined the efficacy and safety of using ECT for the treatment of agitation in 480 patients with schizophrenia who are currently using APs. All included RCTs were open label and the assessment of outcomes was not blinded in all trials. Furthermore, the quality of all included RCTs was rated as ‘low quality’ based on Jadad scale. Overall, the results suggest that both ECT alone and the ECT-AP combination over 2 to 8 weeks had superior efficacy to AP monotherapy regarding the reduction in PANSS total score, but not in the agitation sub-score. ECT and ECT-AP combination were both safe and well tolerated. The reduction in the total PANSS score with ECT alone was superior to AP monotherapy as early as at 1 day with a moderate effect size of -0.52, which increased to a relatively larger effect size of -0.60 after 14 days. The ECT-AP combinations were significantly superior to AP monotherapy with respect to PANSS total score at 7 days with a small effect size of -0.36. However, 35 patients reported headache (38.9% vs. 0% on APs monotherapy, NNH=3), which was significantly more common in the ECT alone group. These adverse effects were transient and mild.[10,11]

Figure 4. Add-on ECT to antipsychotics for agitation in schizophrenia: forest plot for the Positive and Negative Syndrome Scale (PANSS) total score at 7 and 14 days as well as PANSS agitation and excitement sub-score at 14 days



4.2 Limitations

Several limitations need to be acknowledged. First, 7 RCTs (100%) reviewed were rated as low quality and the strength of the evidence for 87.5% outcomes was rated as "very low" or "low" according to the GRADE approach. However, strong recommendations does not necessarily imply high quality evidence and low quality evidence can still result in strong recommendations.[23] Further, the RCTs were inconsistent in their methodology with respect to sampling and the delivery of ECT and the type and dose of antipsychotic medications. Subgroup analyses and meta-regression cannot be employed to lessen the heterogeneity of primary outcomes. Second, data regarding the cognitive effects of ECT were not systematically assessed in the included studies. In addition, agitation, the target symptom in this study, was evaluated with a single item in the PANSS, rather than with a standardized rating scale. Furthermore, some more variables potentially associated with agitation, such as the quality of care and patients' education, were not assessed in included studies. Third, treatment adherence was not routinely assessed or reported. In particular, the ECT dose-response effects on agitation when used as monotherapy or/and co-treatment in agitation patients with schizophrenia, definitely needs to be more fully evaluated. Finally, all studies were conducted in China thus the findings need to be replicated in other countries.

4.3 Implications

Although this paper included 7 low quality RCTs with small samples and the methodological limitations [23] identified, the thorough methodology of this meta-analysis included the assessment of quality using the Cochrane risk of bias,[18] Jadad scale [22], and GRADE system.[23] The heterogeneity of PANSS total score assessed by I^2 decreased from 93% to 76% after removing one outlying study;[15] in addition, the significance disappeared, which could be due

Table 3. GRADE Analyses for main primary and secondary outcomes: ECT for agitation in schizophrenia

Outcomes	N (arms)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Large effect	Overall quality of evidence[a]
ECT alone vs. APs								
PANSS total score	90 (2)	Serious[b]	No	No	No	Serious[d]	No	Low
PANSS excitement sub-score	180 (4)	Serious[b]	No	No	No	Serious[d]	No	Low
PANSS agitation sub-score	30 (1)	Serious[b]	No	No	No	Serious[d]	No	Low
Headache	180 (3)	Serious[b]	No	No	No	Serious[d]	Very large[e]	High
Akathisia	180 (3)	Serious[b]	No	No	No	Serious[d]	No	Low
ECT+ APs vs. APs								
PANSS total score	240 (3)	Serious[b]	Serious[c]	No	No	Serious[d]	No	Very Low
PANSS excitement sub-score	140 (2)	Serious[b]	Serious[c]	No	No	Serious[d]	No	Very Low
PANSS agitation sub-score	140 (2)	Serious[b]	Serious[c]	No	No	Serious[d]	No	Very Low

APs = antipsychotics; ECT = Electroconvulsive therapy; GRADE = grading of recommendations assessment, development, and evaluation; PANSS = Positive and Negative Syndrome Scale

[a]GRADE Working Group grades of evidence: High quality=further research is very unlikely to change our confidence in the estimate of effect. Moderate quality=further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality=further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality=we are very uncertain about the estimate.

[b]All studies reported as having a serious bias used a open label method, only mentioned random allocation without describing the method and withdrawal from the study.

[c]All studies reported as having a serious inconsistency had I^2> 50%.

[d]For continuous outcomes, N < 400; For dichotomous outcomes, N<300.

[e]The results of meta-analytic outcomes: RR>5 or <0.2

to the decreased sample size thereby reducing the power detecting significant results. The previous meta-analyses[24-25] supported our interpretation that adjunctive ECT can be an efficacious treatment for improving total psychopathology in schizophrenia patients. Agitation poses a significant challenge in the treatment of schizophrenia.[1] However, the current meta-analysis of 7 relatively low quality RCTs showed that both ECT alone and the ECT-AP combination are ineffective treatments for agitation in 480 Chinese schizophrenia patients. This meta-analysis indicates that other symptoms (e.g. hallucination, delusion, etc.) maybe respond better to ECT when compared with agitation related outcomes in schizophrenia patients.

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Conflicts of interest statement

The authors declare that they have no conflicts of interest concerning this article.

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电休克治疗用于精神分裂症的激越症状：随机对照试验的 meta 分析

顾小静，郑伟，郭彤，Gabor S. Ungvari，Helen F.K. Chiu，操小兰，Carl D'Arcy，孟祥飞，宁玉萍，项玉涛

背景：躁动在精神分裂症治疗中是一个重大挑战。电休克疗法（ECT）对各种精神疾病是一种快速、有效、和安全的治疗，但 ECT 对精神分裂症的躁动治疗的相关 meta 分析还尚未报道。

目标：系统地评估单一使用 ECT 或 ECT 合并使用其他抗精神病药物（APs）的对精神分裂症的躁动治疗的有效性和安全性。

方法：进行随机对照试验（RCT）的系统文献搜索。两名独立评估者筛选研究、提取结果数据与现有数据的安全性、进行质量评估和数据合成。采用建议、评估、开发、和评价的工作组等级（GRADE）来判断主要成果的证据的总体水平。

结果：一共确定了中国有七个 RCTs，包括 ECT 单一使用（4 个 RCTs 有 5 个治疗组，n = 240）和 ECT-APs 合并使用（3 个 RCTs，n = 240）。研究对象平均年龄 34.3（4.5）岁，平均治疗时间为 4.3（3.1）周。所有 7 个 RCTs 非盲法，并且根据 Jadad 量表 7 项 RCTs 均被评为低质量。样本的 Meta 分析发现与 APs 单一治疗相比，单一使用 ECT 或 ECT-APs 合并使用阳性和阴性症状量表（PANSS）的躁动子因子评分改善均无显著性差异（ECT 单一使用 : weighted mean difference（WMD）=-0.90, 95% confidence interval (CI): (-2.91, 1.11), p=0.38; ECT-APs 合并使用：WMD=-1.34, (95%CI: -4.07, 1.39), p=0.33）。然而，PANSS 总分（WMD=-7.13, I^2=0%, p=0.004）和兴奋子因子评分（WMD=-1.97, p<0.0001）、ECT 治疗 14 天后的 PANSS 总分（WMD=-7.13, I^2=0%, p=0.004）和第 7 天和第 14 天的兴奋子因子评分（WMD=-1.97 to -1.92, p=0.002 to 0.0001）均显示单一使用 ECT 优于 APs 单一治疗。ECT-APs 合并治疗结束时（WMD=-10.40, p=0.03）和治疗后 7 天（WMD=-5.01, p=0.02）的 PANSS 总分显示均优于 APs 单药治疗。头痛（p=0.0001, number-needed-to-harm (NNH)=3, 95%CI=2-4）是唯一的 ECT 单一治疗后不良反应，并且 ECT 单一治疗组比 APs 单药治疗发生的更频繁。根据 GRADE 方法，主要结果的证据水平被评为“非常低”（37.5%）和“低”（50%）。

结论：基于中国 7 个 RCTs 合并的数据发现 ECT 单一治疗或 ECT-APs 合并治疗在精神分裂症患者的躁动治疗中并没有优势。然而，ECT 单一治疗或 ECT-APs 合并治疗均与 PANSS 总分减低显著有关。需要高质量的 RCTs 验证目前的解释。

关键词：电休克治疗；躁动；精神分裂症；头痛，meta 分析

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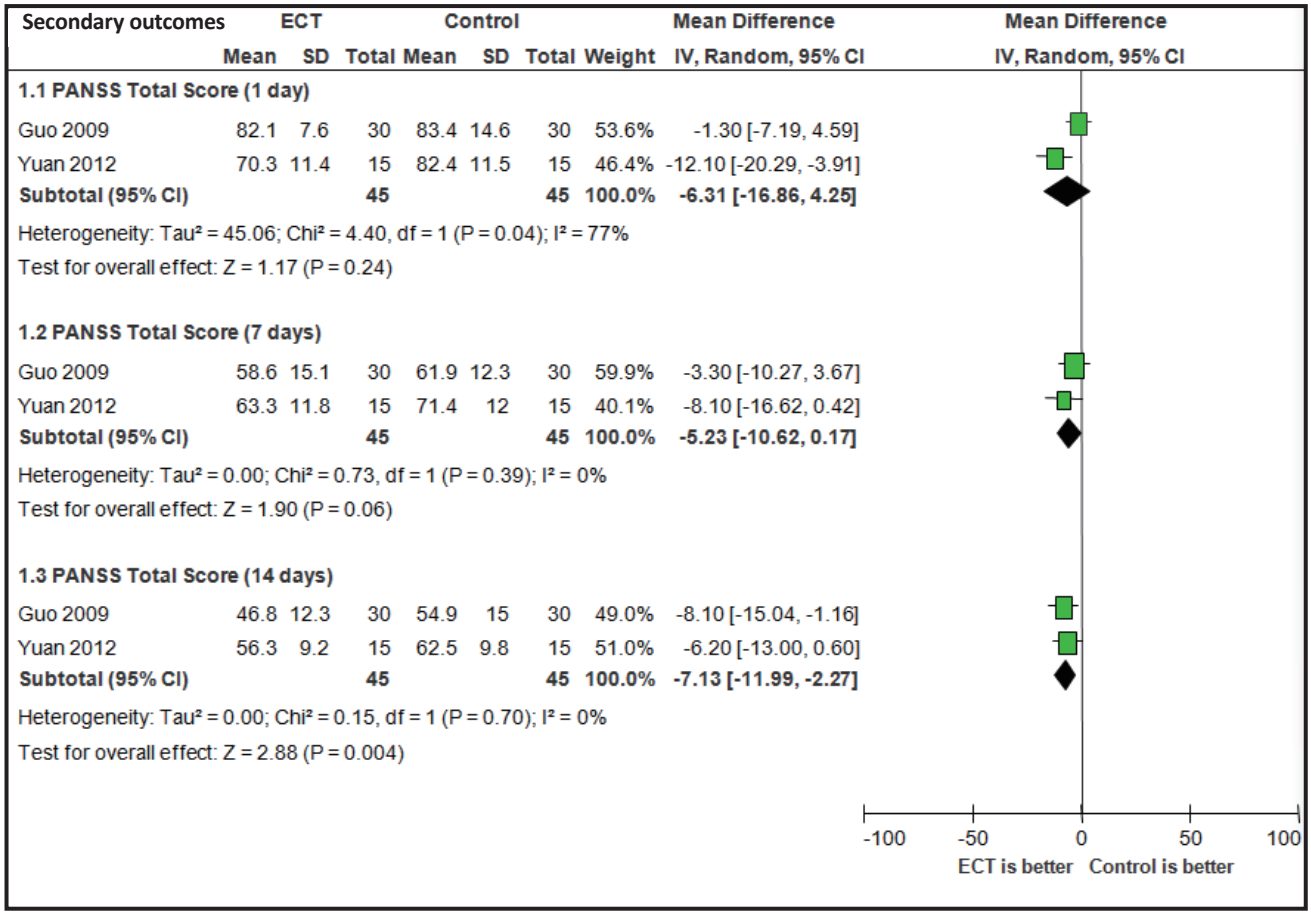
Xiao-jing Gu obtained a bachelor's degree in 2009 and a master's degree in psychiatry and mental health from the Capital Medical University in Beijing in 2012. Since then she has been working as a resident physician in the Second Affiliated Clinical College of Xinxiang Medical University, Henan Mental Hospital. Her research interests are depression and schizophrenia.

Wei Zheng obtained a bachelor's degree from Hebei Medical University in 2012 and a master's degree in psychiatry and mental health from the Capital Medical University in Beijing in 2015. Since then he has been working as a resident physician in the Department of Psychiatry in the Guangzhou Huiai Hospital. He is currently a PhD Candidate at the Affiliated Brain Hospital of Guangzhou Medical University (Guangzhou Huiai Hospital). His research interests are depression and schizophrenia.

Supplemental Figure 1. ECT alone for agitation in schizophrenia: forest plot for the Positive and Negative Syndrome Scale (PANSS) total score at 1, 7, and 14 days



Notice for soliciting papers for the 14th academic conference of the Chinese Society of Neuroscience & Psychiatry (CSNP)

"The 14th annual academic conference of the Chinese Society of Neuroscience & Psychiatry", which is hosted by CSNP, and undertaken by Mental Health Center of Shanghai Jiao Tong University's medical school and Shandong Mental Health Center, will be held in the Luneng Hilton Hotel in Jinan, Shandong, from 29th June to 1st July, 2017.

The present society welcomes paper submissions and conference participations. The conference affair group accepts abstracts (objectives, methods, results and conclusions) under 1000 words. The website used for paper submissions and registrations is http://61.147.124.137:8088/2017/default.aspx. The academic committee of this conference will review papers and select high quality reports for presentation at the conference. We look forward to your participation and support! The deadline for paper submission is 1st June, 2017.

We welcome colleagues from all over China and abroad to participate in this conference held in scenic Jinan. We are looking forward to a lively discussion on developments in the field.

Dates: 29th June to 1st July, 2017 (check in on 29th June)

Address: Luneng Hilton Hotel in Jinan, Shandong, No.2888 South Erhuan Lu, Central District in Jinan

Cost arrangement: The registration fee, travel fee and accommodation fee are at your own expense. The registration fee is 1000 yuan (Shandong representatives and graduate students with student IDs can pay half of the registration fee). The accommodation fee from 30th June to 1st July 2017 is 500 yuan per standard room.

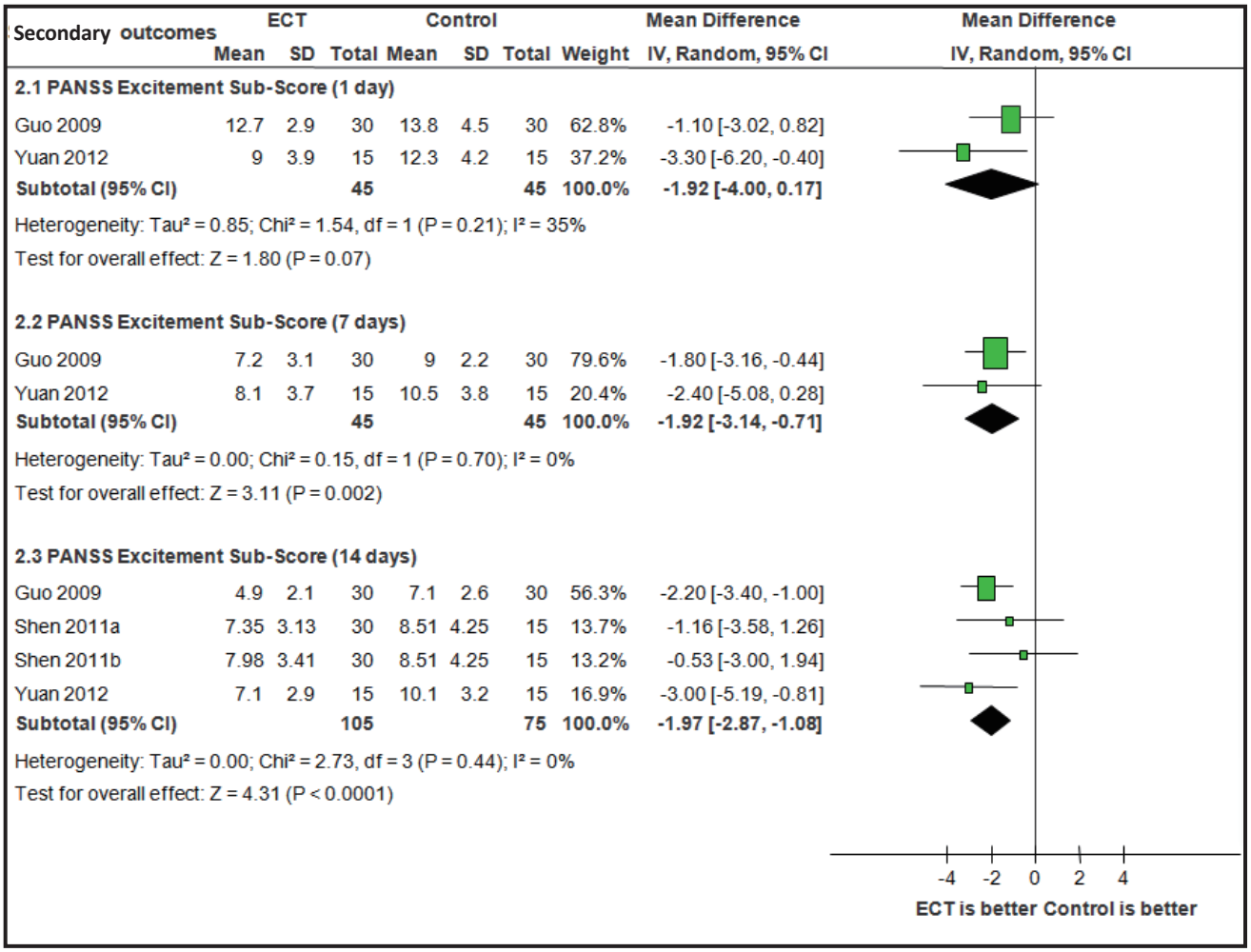
Contact: Ruizhi Mao 18221768225

E-mail: csnpmeeting@163.com

Chinese Society of Neuroscience & Psychiatry

4th February 2017

Supplemental Figure 2. ECT alone for agitation in schizophrenia: forest plot for the Positive and Negative Syndrome Scale (PANSS) excitement sub-score at 1, 7, and 14 days



Erratum

Li HB, Wang Y, Jiang J, Li W, Li CB. Effects of transcranial direct current stimulation (tDCS) for auditory hallucinations: A systematic review. *Shanghai Arch Psychiatry*. 2016; **28**(6):301-308. doi: http://dx.doi.org/10.11919/j.issn.1002-0829.216121

In the Figure 1 (identification of included studies) of the paper, the number in the first box "304 potential articles published before 13 February 2016 were identified…" should be "432 potential articles published before 13 February 2016 were identified…". This change was been made to the online version on the *Shanghai Archives of Psychiatry* website as of 10 Jan, 2017.

Supplemental Figure 3. ECT alone for agitation in schizophrenia: forest plot for adverse events