

Table 1 Efficacy of rTMS compared to sham treatment.

Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time Drop-out	Outcome	Study quality Comments
			Frequency	Number of pulses per session	Total number of pulses	Intensity			
Avery et al 2006 [10] USA	RCT n=68 Age: 21–65 (mean 44.2) HDRS ₁₇ >17 (mean 23.5) Failed at least two trials with AD Excluded: Bipolar disorder, depression >5 years, personality disorders 31% in the rTMS and 27% in sham group were on concomitant AD	15 sessions within 4 weeks Active: n=35 Sham: n=33 Coil rotated 90° away from the scalp Maintenance treatment with AD for those who responded to treatment	10 Hz	1 600	24 000	110%	Evaluation after 4 weeks. Follow-up 6 months later for those who had responded to rTMS Drop-out rate: 9%	<u>Response rate after 4 weeks</u> Active: 30.6% Sham: 6.1% p=0.008 <u>Remission rate after 4 weeks (HDRS <8)</u> Active: 20.0% Sham: 3.0% p=0.033 <u>Follow-up</u> 44% of the responders in the active group had not relapsed	High
Fitzgerald et al 2003 [11] Australia	RCT n=60 (6 with bipolar disorder, 4 in the sham group). Age: Mean 46 MADRS >20 Failed at least 2 courses of anti- depressants for at least 6 weeks No change in medication	10 sessions LPFC: n=20 RPFC: n=0 Sham: n=20 (further rando- mized to left or right side stimu- lation)	Sham: Coil angled 45° off the skull	LPFC: 1 000 RPFC: 300	LPFC: 10 000 RPFC: 3 000	100%	2 weeks	<u>Change in MADRS score vs baseline</u> LPFC: 36.1–30.8=5.3 RPFC: 37.7–32.2=5.5 Sham: 35.7–35.4=0.3 p=0.005 for rTMS vs sham Trend to less improve- ment for patients with bipolar disorder	High

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Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time Drop-out	Outcome	Study quality Comments
			Frequency	Number of pulses per session	Total number of pulses	Intensity			
Fitzgerald et al 2006 [14] Australia	RCT n=130 Age: Mean 49 Major depression (bipolar, n=25) HDRS ₁₇ >16 (mean 23) Borderline person- ality disorder not excluded. Treatment resistant depression (Thase stage II)	<u>Step 1</u> (right sided rTMS, 110% intensity), 10 sessions 1 Hz: n=67 2 Hz: n=63 <u>Step 2</u> (continued right sided rTMS or left sided rTMS, 100% intensity for those failing step 1), 10 sessions 5 Hz: n=16 10 Hz: n=14	<u>Step 1</u> Right, 1 Hz vs 2 Hz <u>Step 2</u> Continued right side or: Left 5 Hz vs 10 Hz	900 vs 1 800 50	9 000 vs 18 000 9 000, 18 000, 500	110% vs 100% 100%	2 weeks treatment followed by blind assessment and further 2 weeks treatment. Addi- tional 2 weeks for partial responders Drop-out rate: 14%	<u>Response rate</u> <u>after 4 weeks</u> <u>Step 1</u> 1 Hz: 42% 2 Hz: 52% ns <u>Step 2</u> 5 Hz: 6% 10 Hz: 28% ns <u>Remission rate</u> <u>after 4 weeks</u> <u>Step 1</u> 1 Hz: 19% 2 Hz: 32% ns <u>Step 2</u> 5 Hz: 6% 10 Hz: 21% ns <u>Overall sample</u> Response rate: 51% Remission rate: 27%	Moderate for step 1, low for step 2 due to low number of patients
Fitzgerald et al 2006 [12] Australia	RCT n=50 Age: Mean 45 HDRS ₁₇ : Mean 21.0 MADRS >20 (mean 33.6) Treatment resistant depression (Thase stage II)	rTMS: Right side 1 Hz followed by left side 10 Hz: n=25 Sham: Coil angled 45° off the scalp, n=25	1 Hz right side and 10 Hz left side	480 right side and 50 at left side	4 800 to 14 400 pulses right side. 100 to 300 pulses left side	110% right side and 100% left side	Initial assessment after 2 weeks. Responders were offered continued treatment for as long as they improved their scores, up to 6 weeks Drop-out rate: 6%	<u>Response rate</u> <u>after 6 weeks</u> Active: 44% Sham: 8% p<0.05 <u>Remission rate</u> <u>after 6 weeks</u> Active: 36% Sham: 0 p=0.005	High

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			Frequency	Number of pulses per session	Total number of pulses	Intensity			
Hausmann et al 2004 [15] Austria	RCT n=41 (6 with bipolar disorder evenly distributed between the groups) Age: Mean 46.5 HDRS ₂₁ : Not defined Antidepressants were washed out at admission	10 sessions (2 weeks) Antidepressant drug therapy was started concomitantly with the rTMS <u>Unilateral stimulation</u> n=12 <u>Bilateral stimulation</u> n=13 <u>Bilateral sham stimulation</u> n=13	<u>Unilateral</u> 20 Hz left DLPFC <u>Bilateral</u> 20 Hz left DLPFC followed by 1 Hz right DLPFC Sham: Coil disconnec- ted from the stimulator and a second coil was held 10 cm from the patient's head	2 000 2 600 for 1 Hz sti- mulation	20 000 26 000 for 1 Hz sti- mulation	100% 120% for 1 Hz sti- mulation	2 weeks	<u>Change in HDRS₂₁</u> Unilateral: 31.6–16.8=14.8 Bilateral: 32.9–18.4=14.5 Sham: 33.7–21.8=11.9 ns	Moderate Randomization procedure not described
Loo et al 2007 [16] Australia	RCT n=40 (4 with bipolar disorder) Age: Mean 47 MADRS ≥25 Less than 2 years duration of depres- sive episode Patients who had failed ECT or more than 2 trials of antidepres- sants were excluded No changes in antide- pressant medication	rTMS given twice daily for 2 weeks followed by 4–6 weeks open phase treatment Active rTMS: n=19 (3 bipolar disorder) Sham rTMS: n=21 (1 bipolar disorder)	10 Hz Sham: Inac- tive coil. Integrity of blinding was tested and satisfactory	1 500	30 000	110%	2 weeks, with follow-up for 5 months	<u>Mean change in MADRS</u> Active rTMS 29.5–18.9=10.6 Sham rTMS 32.6–27.1=5.5 p=0.004 <u>Response rate</u> rTMS: 32% sham rTMS: 14% ns <u>Remission rate</u> Active rTMS: 16% Sham rTMS: 10% ns	Moderate

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Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time Drop-out	Outcome	Study quality Comments
			Frequency	Number of pulses per session	Total number of pulses	Intensity			
McDonald et al 2006 [17] USA	RCT n=62 (8 with bipolar disorder) Age: 18–70 HDRS ₁₇ >20 Referred for ECT. Treatment resistant to >3 antidepressant medications during the present depressive episode (mean 8) 43% had failed pre- vious ECT No antidepressants during the trial	10 Hz for 10 min followed by 1 Hz for 10 min: n=25 1 Hz for 10 min followed by 10 Hz for 10 min: n=25 Sham: n=12	Sham rTMS: Tilting the stimulator at a 90° angle to the scalp	1 600	16 000	110%	2 weeks with 3 monthly follow-up visits for responders Drop-out rate: Not mentioned	<i>Mean change in HDRS₁₇</i> No difference between active and sham rTMS <i>Response rate</i> 10 Hz + 1 Hz: 28% 1 Hz + 10 Hz: 12% Sham: 8% ns <i>Remission rate</i> 10 Hz + 1 Hz: 12% Sham: 0 <i>Follow-up after 3 months</i> No relapse: 2 patients in the 10 Hz + 1 Hz group	Moderate Randomization procedure not described. ITT analysis
Mogg et al 2008 [26] United Kingdom	RCT n=59 Age: >18 MDD (DSM-IV) Stable drug regimen for at least 4 weeks before study entry and throughout the study	10 sessions in 2 weeks Active: n=29 Sham: n=30 Visually and audi- cally identical but without magnetic field	10 Hz left DLPFC	1 000	10 000	120%	End of treatment. Follow-up visits 6 weeks and 4 months later Drop-out rate: 7%	<i>Response rate after 2 weeks</i> Active: 32% Sham: 10% p=0.06 <i>Remission rate after 2 weeks (HDRS₁₇≤8)</i> Active: 25% Sham: 10% ns	Moderate

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Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time Drop-out	Outcome	Study quality Comments
			Frequency	Number of pulses per ses- sion	Total number of pulses	Intensity			
O'Reardon et al 2007 [25] USA, Australia	RCT n=293 Age: 18–70 MDD (DSM-IV) HDRS ₁₇ : ≥20 CGI-S: ≥4 Failed 1–4 anti- depressant treat- ments in this or previous episode Bipolar disorder excluded Lack of response to ECT excluded No antidepressants during the study	30 sessions in 6 weeks Active: n=150 Sham: n=143 Identical with active coil except that it had an em- bedded magnetic shield, giving rise to a weak magnetic field	Left DLPFC Frequency not mentio- ned	3 000	90 000	120%	4 weeks for efficacy measure 6 weeks Drop-out rate: 8%	<u>Response rate at 4 weeks (MADRS)</u> Active: 18.1% Sham: 11% p<0.05 <u>Remission rate at 4 weeks (MADRS)</u> Active: 7.1 Sham: 6.2 p>0.1	Moderate
Rossini et al 2005 [13] Italy	RCT n=99 Age: 18–75 (mean 45) HDRS ₂₁ : ≥21 (mean 25.1) Less than 2 previous failures on AD	10 sessions Active: n=50 Sham: n=49 Patients were further rando- mized between escitalopram sertraline or venlafaxine	15 Hz left Sham given tangentially to the scalp	900	9 000	100%	rTMS + AD given 2 weeks. During the fol- lowing 3 weeks only AD was given Drop-out rate: 10%	<u>Response rate after 2 weeks</u> Active: 51% Sham: 21% p=0.002 <u>Remission rate (HDRS ≤8)</u> Active: 37% Sham: 11% p=0.003	High

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Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time Drop-out	Outcome	Study quality Comments
			Frequency	Number of pulses per ses- sion	Total number of pulses	Intensity			
Rossini et al 2005 [18] Italy	RCT n=54 Age: 18–75 (mean 55) HDRS ₂₁ : >26 (mean 28.6) Drug resistant MD	10 sessions Active 100%: n=18 Active 80%: n=19 Sham: n=17 AD were main- tained during the study	15 Hz Sham: Coil placed on the scalp at a 90° angle	600	6 000	100% vs 80%	2 weeks treat- ment. Follow-up 3 weeks later Drop-out rate: 4%	<u>Response rate</u> <u>after 5 weeks</u> 100% intensity: 61.1% 80% intensity: 27.8% Sham: 6.2% p=0.0008 for difference between 100% intensity and sham. p=0.0044 for difference between 100 and 80% intensity <u>Remission (HDRS ≤8)</u> 100% intensity: 50% 80% intensity: 27.8% Sham: 0 Significance not men- tioned	Moderate
Rumi et al 2005 [19] Brazil	RCT n=46 Age: Mean 39 HDRS ₁₇ at least 22 (mean 30.3) Not drug resistant	20 sessions (4 weeks) Amitriptyline, 110 mg/day was initiated 7 days prior to rTMS Active: n=22 Sham: n=24	Active: 5 Hz Sham: mag- netic field reduced by 95%	1 250	24 500	120%	4 weeks	<u>Response rate</u> Active: 95% Sham: 46% p<0.001 <u>Remission rate</u> Active: 54% Sham: 12% p<0.002	Moderate

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Table 1 continued

Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time Drop-out	Outcome	Study quality Comments
			Frequency	Number of pulses per ses- sion	Total number of pulses	Intensity			
Stern et al 2007 [20] USA	RCT n=45 (bipolar disorder excluded) Age: 21–80 HDRS ₂₁ : >20 Referred for ECT, having failed an adequate course of antidepressant medication Antidepressants discontinued	10 sessions 10 Hz left rTMS: n=10 1 Hz left rTMS: n=10 1 Hz right rTMS: n=10 Sham: n=15	Sham rTMS: The coil was orien- ted perpen- dicularly to the scalp	1 600	16 000	110%	2 weeks + 4 weeks open follow-up	<u>Change in HDRS₂₁ after 2 weeks vs baseline</u> 10 Hz: 27.8–15.1=12.7 1 Hz left: 27.6–27.6=0 1 Hz right: 27.9–15.8= 12.1 Sham: 27.4–26.7=0.7 p=0.0001 <u>Response rate</u> 10 Hz: 50% 1 Hz left: 0 1 Hz right: 50% Sham: 0 <u>Remission rate</u> 10 Hz: 33,3% 1 Hz left: 0 1 Hz right: 10% Sham: 0	Moderate Completer analysis only

AD = Antidepressive drugs; CGI-S = Clinician's global impressions severity scale; DLPFC = Dorsolateral left prefrontal cortex; DSM-IV = Diagnostic and statistical manual of mental disorders; ECT = Electroconvulsive therapy; HDRS = Hamilton depression rating scale; Hz = Hertz; ITT = Intention to treat; LPFC = Left prefrontal cortex; MADRS = Montgomery-Åsberg depression rating scale; MD = Major depression; MDD = Major depression disorder; n = Number; ns = Not significant; RCT = Randomized controlled trial; RPFC = Right prefrontal cortex; rTMS = Repetitive transcranial magnetic stimulation

Table 2 Efficacy of rTMS compared to ECT.

Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time	Outcome	Study quality Comments
			Frequency	Number of pulses per session	Total number of pulses	Intensity			
McLoughlin et al 2007 [22] United Kingdom and Eranti et al 2007 [21] United Kingdom	RCT, aim to show equivalence n=46 Age: >18 (mean 65) HDRS ₁₇ : Mean 24.4 Referral by consul- tant psychiatrist for ECT Excluded: ECT or rTMS in the previous 6 months, dementia or other axis I diagnosis No medication changes	<i>rTMS</i> n=24 15 daily sessions (weekdays) <i>ECT</i> n=22 Twice weekly, number of treat- ments depended of the patients' responses	DLPFC: 10 Hz	1 000	15 000	110% w	Treatment completed and follow-up after 2–3 days and after 6 months	<i>Mean reduction in HDRS₁₇</i> rTMS: 5.4 ECT: 14.1 p=0.002 <i>Response rate</i> rTMS: 16,7% ECT: 59.1% p=0.005 <i>Remission (HDRS ≤8)</i> rTMS: 16.7% ECT: 59.1% After 6 months: HDRS ₁₇ score did not differ between groups (mean score 13.5)	Moderate Well designed study, but blinding could not be maintained and 25% of the rTMS group discontinued due to perceived lack of effect Only 43% of eligible patients consented to participate

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Table 2 continued

Author Year Reference Country	Study design Population	Intervention	rTMS data		rTMS data		Observation time	Outcome	Study quality Comments
			Frequency	Number of pulses per session	Total number of pulses	Intensity			
Grunhaus et al 2003 [24] Israel	RCT n=40 Age: At least 19 (mean 59.5) HDRS ₁₇ : >18 (mean 25) Referral for ECT Excluded: Additio- nal axis I diagnoses. Tapering of psycho- tropic medication, only lorazepam was allowed	rTMS: n=20 Number of treatments: 20 (4 weeks) ECT: n=20 According to APA guidelines, number of treat- ments ≥6 (unless an early response was seen)	DLPFC: 10 Hz	1 200	24 000	90%	Baseline, after 2 weeks, after 4 weeks	<u>Decrease in HDRS₁₇</u> rTMS: 24.4–13.3=11.1 ECT: 25.5–13.2=12.3 ns <u>Response rate</u> rTMS: 55% ECT: 60% ns <u>Remission rate (HDRS₁₇ < 8)</u> rTMS: 30% ECT: 30%	Moderate Groups unbalanced with respect to GAF and BPRS

APA = American psychiatric association; BPRS = Brief psychiatric rating scale;
DLPFC = Dorsolateral left prefrontal cortex; ECT = Electroconvulsive therapy;
GAF = Global assessment of functioning scale; HDRS = Hamilton depression rating
scale; Hz = Hertz; n = Number; ns = Not significant; RCT = Randomized controlled
trial; rTMS = Repetitive transcranial magnetic stimulation

Table 3 Safety of rTMS compared to sham treatment or ECT.

Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Avery et al 2006 [10] USA	RCT n=68 Age: 21–65 Recruited through referral and adver- tisements Failed at least 2 trials with AD HDRS ₁₇ : >17	15 sessions within 4 weeks rTMS: n=35 Sham rTMS: n=33 Coil rotated 90° away from the scalp	10 Hz 1 600 pulses/session 110% MT	Evaluation after 4 weeks. Follow-up 6 months later for those who had respon- ded to rTMS	<u>Adverse events</u> No significant difference between rTMS and sham in SAFTEE score <u>Pain at the stimulation site</u> rTMS: 41% Sham: none <u>Cognitive function</u> No significant difference between rTMS and sham	High
Eranti et al 2007 [21] United Kingdom	RCT, aim to show equivalence n=46 Age: >18 (mean 65) Referral by consultant psychiatrist for ECT	rTMS: n=24 15 daily sessions (weekdays) ECT: n=22 Twice weekly, number of treat- ments depended of the patients' responses	DLPFC: 10 Hz 1 000 pulses/session 10% MT	After treatment. Follow-up after 2–3 days and after 6 months	<u>Adverse events</u> Significantly lower side effect scores in the ECT group <u>Cognitive function</u> No difference in CAMCOG or MMSE between groups	Moderate 27% drop-out in the rTMS group and no drop-out in the ECT group
Fitzgerald et al 2003 [11] Australia	RCT n=60 (6 with bipolar disorder, 4 in the sham group) Age: Mean 46 MADRS: >20 Failed at least 2 courses of antidepressants for at least 6 weeks No change in medication	10 sessions LPFC: n=20 RPFC: n=20 Sham: n=20 (Further randomized to left or right side stimulation)			<u>Rate of adverse events</u> Local pain: 11% Headache: 10% Manic episode: 1 patient with bipolar disorder Assessment of cognitive functions: No deterioration	High

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Table 3 continued

Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Fitzgerald et al 2006 [14] Australia	RCT n=130 Major depression (bipolar, n=25) HDRS ₁₇ : >16 Borderline not excluded. Treatment resistant (Thase stage II)	<u>Step 1</u> (right sided rTMS, 110% intensity), 10 sessions 1 Hz: n=67 2 Hz: n=63 <u>Step 2</u> (continued right sided rTMS or left sided rTMS), 10 sessions 5 Hz: n=16 10 Hz: n=14	Right: 1 Hz, 900 pulses/session 2 Hz, 1 800 pulses/session 110% MT Left: 5 Hz, 500 pulses/session 10 Hz 500 pulses/session 100% MT	Blind assessment after 2 weeks. Maximum treat- ment time 6 weeks	<u>Rate of adverse events</u> Not specified. 1 case of hypomania recorded	Moderate Drop-out rate: 2/130 failed the first step. 18/130 withdrew after first step
Fitzgerald et al 2006 [12] Australia	RCT n=50 Treatment resistant depression MADRS: >20	rTMS: Right side followed by left side, n=25 Sham: Coil angled 45° off the scalp, n=25	Right: 1 Hz 480 pulses/session 100% MT Left: 10 Hz 50 pulses/session 100% MT	Initial assessment after 2 weeks. Initial responders were offered continued treatment for as long as they improved their scores, up to 6 weeks	<u>Headache</u> rTMS: 20% Sham: 12% <u>Nausea</u> rTMS: 12% Sham: None <u>Cognitive function</u> No significant reduction in cognitive performance, measured by 5 different tests	High
Hansen et al 2004 [30] Denmark	RCT n=15 (3 with bipolar disorder, all in the sham group) Age: 38–62	15 sessions, add-on to antidepressant drugs Active rTMS: n=6 Sham: n=7	Left: 10 Hz 200 pulses/session 90% MT		<u>Rate of adverse events</u> Pain: 5/8 in the rTMS group; 3/8 withdrew	Low

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Table 3 continued

Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Hausmann et al 2004 [15] Austria	RCT n=41 (6 with bipolar disorder evenly distri- buted between the groups) Age: Mean 46,5 HDRS ₂₁ : Not defined Antidepressants were washed out at admission	10 sessions (2 weeks) Antidepressant drug therapy was started concomitantly with the rTMS Unilateral stimulation: n=12 Bilateral stimulation: n=13 Bilateral sham stimu- lation: n=13			<u>Rate of adverse events</u> Headache: 5% Manic symptoms: 1 patient <u>Assessment of cognitive function</u> No deterioration	Moderate
Isenberg et al 2005 [35] USA	RCT n=28	10 sessions rTMS Right side: n=14 Left side: n=14	Right: 1 Hz 120 pulses/session 110% MT Left: 20 Hz 2 000 pulses/session 80% MT	Initial assessment after 2 weeks, follow-up after 1 month	<u>Rate of adverse events</u> Pain: 36% Headache: 25% No difference between groups <u>Cognitive function</u> MMSE not affected by rTMS	Low
Janicak et al 2008 [7] Multicenter trials in USA and Australia	3 studies: 1. RCT n=293 (O'Reardon 2007 [25]) 2. Open-label trial for patients that had not benefitted from their assigned treatment n=158 3. Open-label durability of effect from studies 1 or 2 n=136	30 sessions Active: n=150 Sham: n=143	Left: 3 000 pulses/ session 120% MT Participants in both study 1 and 2 could receive 216 000 pulses 10 000 sessions were given totally	Drop-out rate: Study 1: 8% Study 2: 17.7% Study 3: 34.6%	<u>Adverse events</u> <u>Study 1</u> Headache: 58.2 vs 55.1% Application site pain: 35.8 vs 3.8% <u>Study 2</u> Headache: 47.9 vs 45.9% Application site pain: 11 vs 31.8% <u>Exacerbation of depression</u> 10 events in the sham group and 1 event in the active group <u>Assessment of cognitive function</u> No change in global cognitive func- tion, short-term and delayed recall and retrieval of long-term autobio- graphical memory	

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Table 3 continued

Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Januel et al 2006 [36] France	n=27 Age: 18–65 Unipolar depression HDRS ₁₇ : >18 None medication resistant, no AD	16 sessions rTMS: n=11 Sham: No magnetic field n=16	1 Hz 120 pulses/session 90% MT	Cognitive function was assessed after 2 weeks	<u>Headache</u> rTMS: 8% <u>Cognitive function</u> No difference between the groups in 5 tests	Low
Loo et al 2007 [16] Australia	n=40 Age: Mean 47 MADRS ≥25 Less than 2 years duration of depressive episode Patients who had failed ECT or more than 2 trials of antidepressants were excluded No changes in anti- depressant medication	rTMS given twice daily for 2 weeks Active rTMS: n=19 Sham rTMS: n=21			<u>Rate of adverse events</u> Active rTMS Pain: 80% Headache: 42% Sham rTMS Pain: 0 Headache: 0 <u>Neuropsychological assessment</u> No significant adverse effects although a worsening was seen in the TMT A test	Moderate
McDonald et al 2006 [17] United Kingdom	RCT n=62 Age: 18–70 HDRS ₁₇ : >20 Referred for ECT. Treatment resistant to >3 antidepressant medications during the present depressive episode (mean 8). 43% had failed previous ECT No antidepressants during the trial	10 Hz followed by 1 Hz: n=25 1 Hz followed by 10 Hz: n=25 Sham: n=12			<u>Rate of adverse events</u> Not stated <u>Assessment of cognitive functions</u> No difference between groups	Moderate

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Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Mogg et al 2008 [26] United Kingdom	RCT n=59 Age: >18 MDD (DSM-IV) Stable drug regimen for at least 4 weeks before study entry and throughout the study	10 sessions Active: n=29 Sham: n=30	10 Hz left 1 000 pulses/session 120% MT	2 weeks	<u>Adverse events</u> 1 case of seizures in the sham group <u>Assessment of cognitive function</u> No differences between the groups in 6 neuropsychiatric tests measured up to 4 months after end of treatment	High
Mosimann et al 2004 [37] Switzerland	RCT n=24 Age: 40–90 Treatment resistant depression. Referred from primary care or psychiatry. Bipolar disease included	10 sessions rTMS: n=15 Sham: n=9	20 Hz 1 600 pulses/session 100% MT	2 weeks	<u>Adverse events</u> rTMS: 47% Sham: 56% <u>Assessment of cognitive function</u> No deterioration	Low
Rosa et al 2006 [38] Brazil	RCT n=42 Age: Mean 43.6 Unipolar depression HDRS ₁₇ : >22 Referred for ECT AD, mood stabilizers and antipsychotics were not allowed during the study	rTMS: 20 sessions, 10 Hz, 25 trains, 10 sec (total 50 000 pulses), n=22 ECT: According to APA 2001, n=20	10 Hz 2 500 pulses/session 100% MT	2 and 4 weeks	<u>Cognitive function</u> No significant differences between the groups Trend of worsening for the ECT group and trend of improvement for the rTMS group	Low
Rossini et al 2005 [13] Italy	RCT n=99 HDRS ₂₁ : ≥21 Less than 2 failures on AD	10 sessions Active: n=50 Sham: n=49	15 Hz 900 pulses/session 100% MT	rTMS + AD given 2 weeks	<u>Rate of adverse events</u> Not clearly described	Low

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Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Rossini et al 2005 [18] Italy	RCT n=54 Age: 18–75 Drug resistant MD HDRS ₂₁ : >26	10 sessions Active 100% MT: n=18 Active 80% MT: n=19 Sham: n=17	15 Hz 600 pulses/session 100% MT or 80% MT	2 weeks treatment. Follow-up 3 weeks later	<u>Rate of adverse events</u> rTMS: Headache 11%, pain 8%	Moderate
Rumi et al 2005 [19] Brazil	RCT n=46 HDRS ₁₇ : ≥22 (mean 29) Age: Mean 39 Outpatients	20 sessions + amitriptyline, 110 mg/day rTMS: n=22 Sham rTMS: n=24	5 Hz 1 250 pulses/session 120% MT		<u>Headache</u> rTMS: 95% Sham: 91% <u>Pain</u> rTMS: 95% Sham: 70% p<0.001	Moderate
Schulze- Rauschenbach et al 2005 [23] Germany	Open study n=45	rTMS: n=16 ECT: n=14 Healthy control: n=15	10 Hz 4–600 pulses/session 100% MT ECT according to APA guidelines 1990	Mean 10.8 treatments rTMS Mean 9.9 treatments ECT	<u>Cognitive function</u> No difference in MMSE. Significant differences favouring rTMS in 5 measures of long-term memory recall or recognition	Low
Stern et al 2007 [20] USA	RCT n=45 (bipolar disorder excluded) Age: 21–80 HDRS ₂₁ : >20 Referred for ECT, having failed an ade- quate course of anti- depressant medication Antidepressants discontinued	10 sessions 10 Hz left rTMS: n=10 1 Hz left rTMS: n=10 1 Hz right rTMS: n=10 Sham: n=15			<u>Rate of adverse events</u> Headache: 20% 30% of the patients in the groups without effect withdrew due to adverse events; none in the groups with effect	Low

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Author Year Reference Country	Study design Population	Intervention	rTMS data	Observation time	Outcome	Study quality Comments
Su et al 2005 [31] Taiwan	RCT n=33 (2 with bipolar disorder) Age: 43 HDRS ₂₁ : >18 Failed at least 2 adequate trials of antidepressant medications for >6 weeks No change in medication	10 sessions rTMS 20 Hz: n=10 rTMS 5 Hz: n=12 Sham: n=11			<u>Rate of adverse events</u> Headache: 15% Pain: 6% (patients dropped out) Hypomania: 1 patient with bipolar disorder	Low

AD = Antidepressive drugs; APA = American psychiatry association; CAMCOG = Cambridge cognitive examination; DLPFC = Dorsolateral left prefrontal cortex; DSM = Diagnostic and statistical manual of mental disorders; ECT= Electroconvulsive therapy; HDRS = Hamilton depression rating scale; Hz = Hertz; LPFC = Left prefrontal cortex; MADRS = Montgomery-Åsberg depression rating scale; MD = Major depression; MDD = Major depressive disorder; MMSE= Mini mental state examination; MT = Motor threshold; n = Number; RCT = Randomized controlled trial; RPFC = Right prefrontal cortex; rTMS = Repetitive transcranial magnetic stimulation; SAFTEE = Systematic assessment for treatment emergent events; TMT A = Trail making test A