

Berlim MT, Van den Eynde F. Repetitive transcranial magnetic stimulation over the dorsolateral prefrontal cortex for treating posttraumatic stress disorder: an exploratory meta-analysis of randomized, double-blind and sham-controlled trials. Can J Psychiatry. 2014;59(9):487–496.

SUPPLEMENTAL DATA

1. DATABASES SEARCH (1995-2013)

1.1 Electronic Databases – Selection

- MEDLINE: January 1st, 1995 - March 12, 2013
- EMBASE: January 1st, 1996 - March 12, 2013
- PsycINFO: January 1st, 1995 - March 12, 2013
- Cochrane Central Register of Controlled Trials (CENTRAL): January 1st, 1995 - March 12, 2013
- SCOPUS: January 1st, 1996 - March 12, 2013

1.2 Electronic Databases – Syntaxes

1.2.1 MEDLINE (PubMed)

An advanced search was conducted on 2013/03/12 using the following search syntax:

("transcranial magnetic"[TIAB] OR rTMS[TIAB] OR "magnetic stimulation"[TIAB]) AND (stress*[TI] OR PTSD[TI] OR trauma*[TI])

This search retrieved 50 references.

1.2.2 EMBASE (OVID interface)

An advanced search was conducted on 2013/03/12 using the following search syntax:

(transcranial magnetic.ti,ab. or rtms.ti,ab. or magnetic stimulation.ti,ab.) and (ptsd.ti. or stress\$.ti. or tauma\$.ti.) and (English language and yr="1996-Current")

This search retrieved 32 references.

1.2.3 PsycINFO (OVID interface)

An advanced search was conducted on 2013/03/12 using the following syntax:

(transcranial magnetic.ti,ab. or rtms.ti,ab. or magnetic stimulation.ti,ab.) and (ptsd.ti. or stress\$.ti. or trauma\$.ti.) and (English language and yr="1995-Current")

This search retrieved 17 references.

1.2.4 CENTRAL

An advanced search was conducted on 2013/03/12 using the following syntax:

("transcranial magnetic" OR rTMS OR "magnetic stimulation") AND (stress* OR PTSD OR trauma*), from 1995 to 2013 in Trials

This search retrieved 27 references.

1.2.5 SCOPUS

An advanced search was conducted on 2013/03/12 using the following syntax:

TITLE-ABS-KEY("transcranial magnetic" OR rtms OR "magnetic stimulation")
AND TITLE(stress* OR ptsd OR trauma*) AND (LIMIT-TO(LANGUAGE, "English"))
AND (LIMIT-TO(PUBYEAR, 1996-2013))

This search retrieved 74 references.

1.3 *Excluded Studies and Reasons for Exclusion*

1.3.1 MEDLINE, PsycINFO, EMBASE, CENTRAL, and SCOPUS

Searches on MEDLINE, PsycINFO, EMBASE, CENTRAL, and SCOPUS yielded 98 references (after discarding duplicates). Of these, 4 were included in this meta-analysis; please refer to Table 1 for information on excluded studies.

Table 1. MEDLINE, PsycINFO, EMBASE, CENTRAL, and SCOPUS: reasons for exclusion.

REASON FOR EXCLUSION		n
No Primary Data		
Review		14
Comment/editorial/erratum/reply/letter		2
Trial registration		1

With Primary Data	
Case report	4
Open label study	2
Non-treatment rTMS study in subjects with PTSD (e.g., neuroimaging, neuropsychology, neurophysiology, neurochemistry)	2
Treatment of PTSD with another neuromodulation technique (e.g., deep transcranial magnetic stimulation)	1
Study in subjects with other psychiatric disorders (e.g., bipolar disorder)	1
Study in subjects with neurological/urological/orthopedic diseases	49
Studies in healthy subjects	8
Studies in non-humans or using human cells	9
TOTAL	93

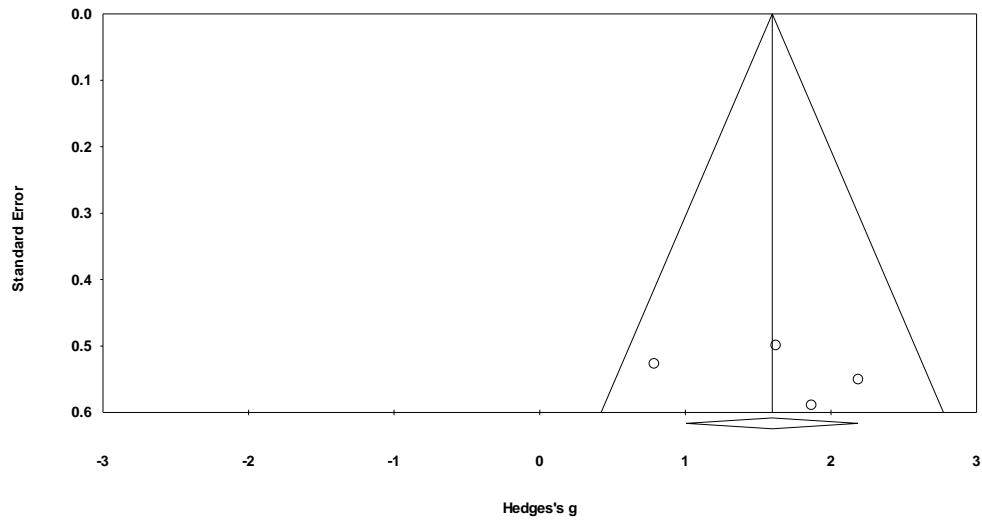
Table 2. MEDLINE, PsycINFO, EMBASE, CENTRAL, and SCOPUS: reasons for exclusion – RCTs on rTMS for PTSD.

Reference	Reason for Exclusion (example)
	2010
Levine et al ¹	n = 7, but ongoing study and no preliminary data available yet
	2009
Osuch et al ²	n = 9, but crossover trial with only ≥ 2 weeks between each trial

2. FUNNEL PLOTS: rTMS APPLIED TO THE RIGHT DLPFC

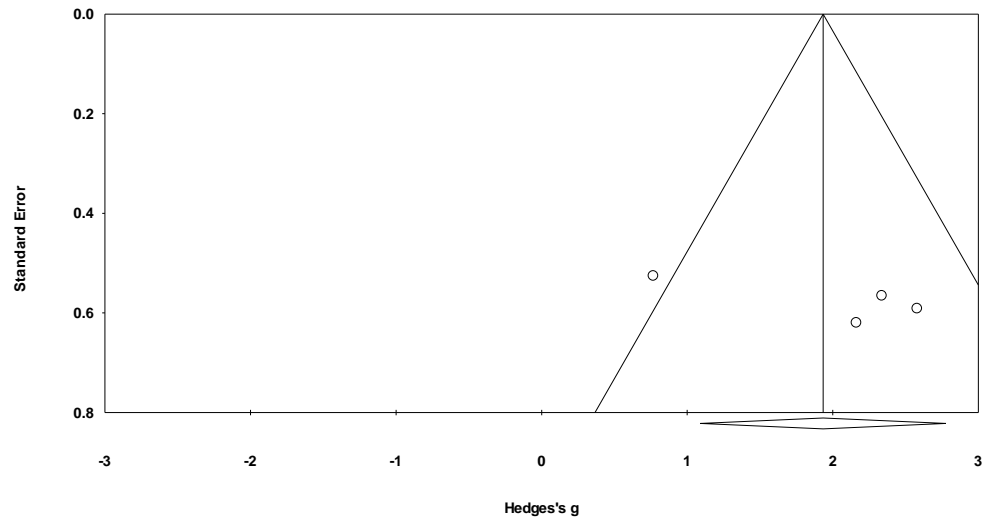
2.1 Pre-Post Clinician-Reported PTSD Symptoms

Funnel Plot of Standard Error by Hedges's g



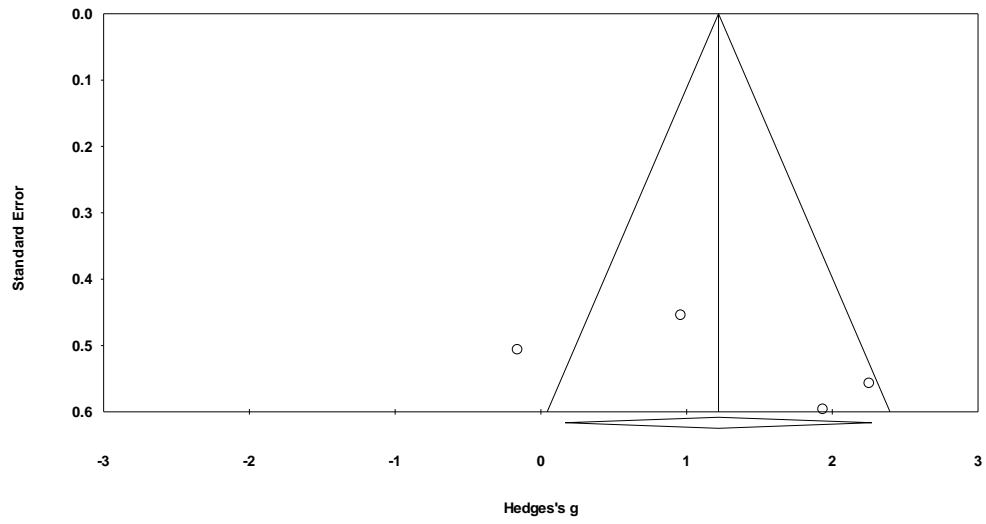
2.2 Pre-Post Self-Reported PTSD Symptoms

Funnel Plot of Standard Error by Hedges's g



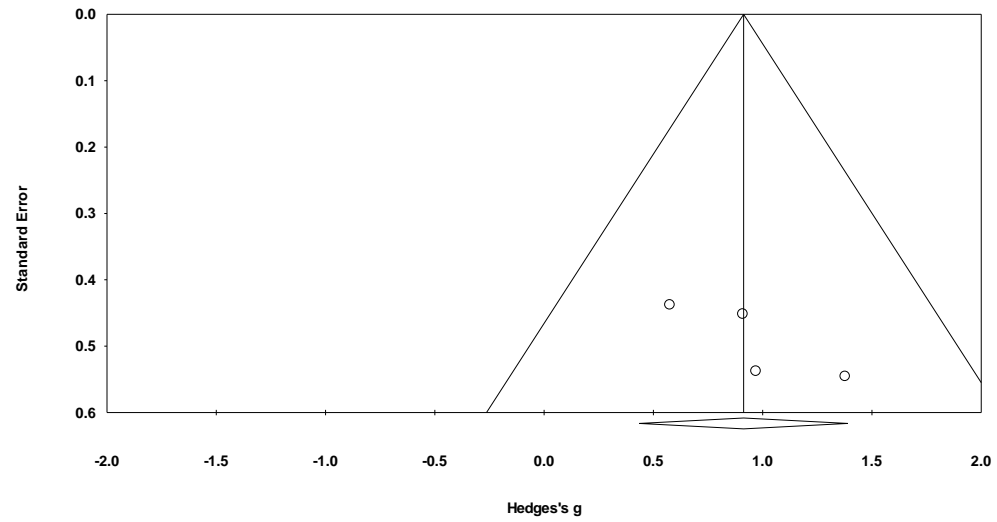
2.3 Pre-Post Overall Anxiety Symptoms

Funnel Plot of Standard Error by Hedges's g

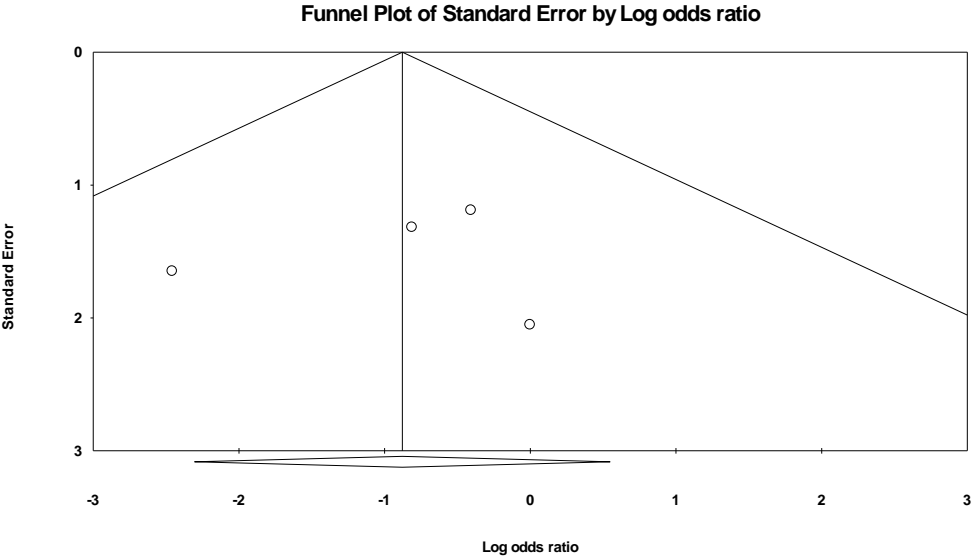


2.4 Pre-Post Depressive Symptoms

Funnel Plot of Standard Error by Hedges's g



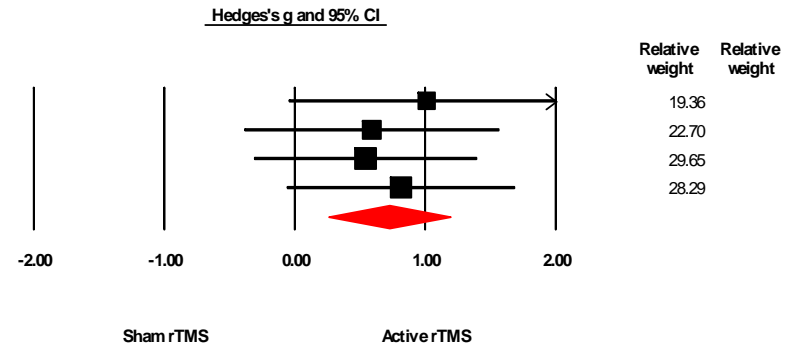
2.5 Dropout Rates



3. FOREST PLOTS: RTMS APPLIED TO THE RIGHT DLPFC

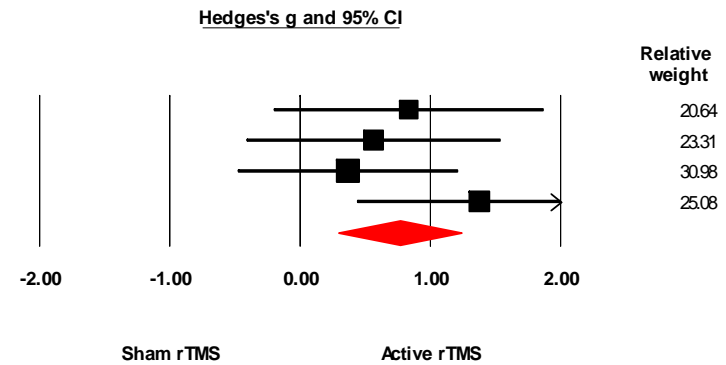
3.1 Baseline Clinician-Reported PTSD Symptoms

Studyname	Statistics for each study							Sample size	
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Active rTMS	Sham rTMS
Cohen et al, 2004a	1.013	0.541	0.292	-0.047	2.072	1.873	0.061	8	6
Cohen et al, 2004b	0.592	0.499	0.249	-0.387	1.570	1.185	0.236	10	6
Boggio et al, 2010	0.544	0.437	0.191	-0.312	1.400	1.245	0.213	10	10
Watts et al, 2012	0.815	0.447	0.200	-0.062	1.691	1.821	0.069	10	10
	0.722	0.238	0.057	0.256	1.188	3.036	0.002	38	32



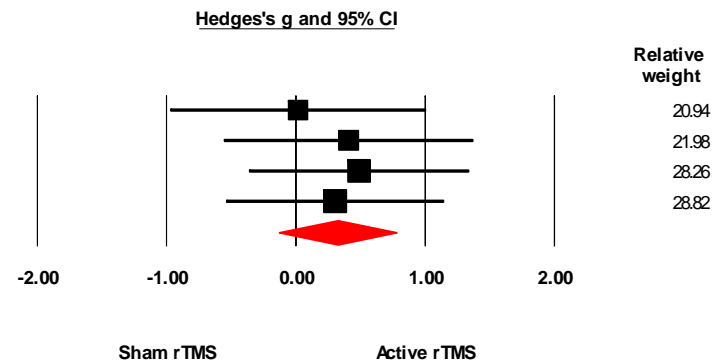
3.2 Baseline Patient-Reported PTSD Symptoms

Study name	Statistics for each study							Sample size	
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Active rTMS	Sham rTMS
Cohen et al, 2004a	0.834	0.530	0.280	-0.204	1.873	1.576	0.115	8	6
Cohen et al, 2004b	0.564	0.498	0.248	-0.412	1.541	1.133	0.257	10	6
Boggio et al, 2010	0.368	0.432	0.187	-0.480	1.215	0.851	0.395	10	10
Watts et al, 2012	1.376	0.480	0.231	0.435	2.318	2.865	0.004	10	10
	0.763	0.241	0.058	0.291	1.234	3.171	0.002	38	32

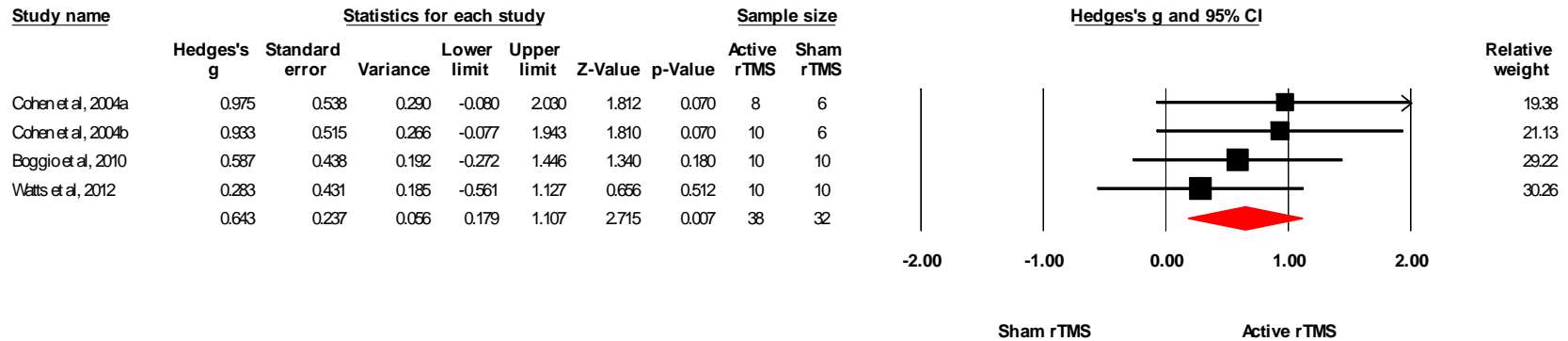


3.3 Baseline Overall Anxiety Symptoms

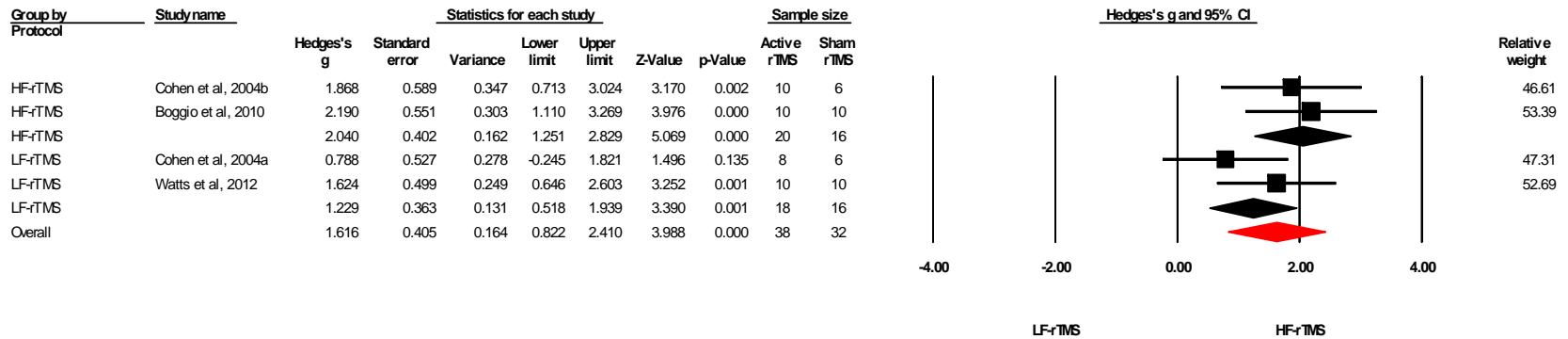
Study name	Statistics for each study							Sample size	
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Active rTMS	Sham rTMS
Cohen et al, 2004a	0.017	0.506	0.256	-0.974	1.008	0.034	0.973	8	6
Cohen et al, 2004b	0.409	0.494	0.244	-0.559	1.376	0.828	0.408	10	6
Boggio et al, 2010	0.490	0.435	0.189	-0.364	1.343	1.125	0.261	10	10
Watts et al, 2012	0.304	0.431	0.186	-0.541	1.148	0.704	0.481	10	10
	0.319	0.231	0.054	-0.134	0.773	1.380	0.168	38	32



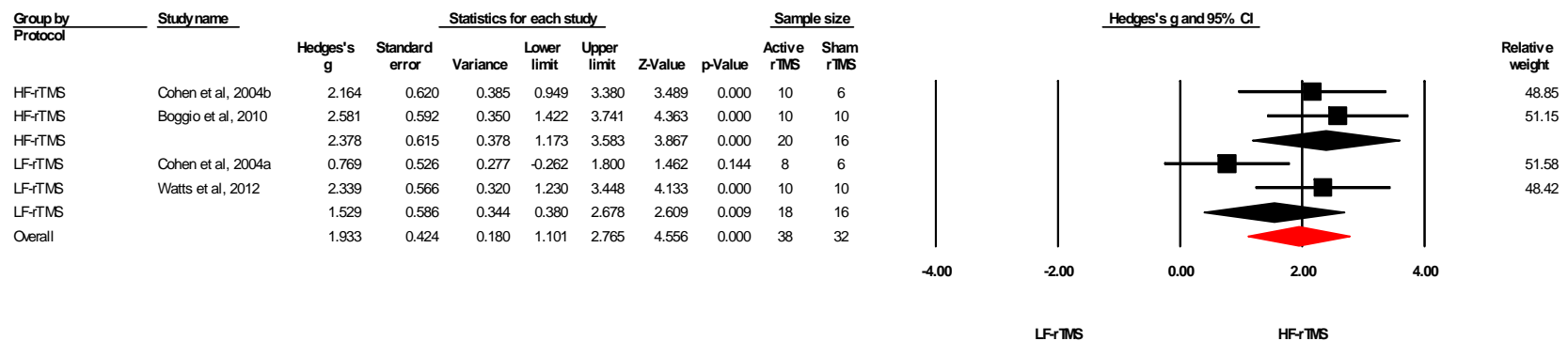
3.4 Baseline Depressive Symptoms



3.5 Subgroup Analysis - HF-rTMS vs. LF-rTMS: Pre-Post Clinician-Reported PTSD Symptoms

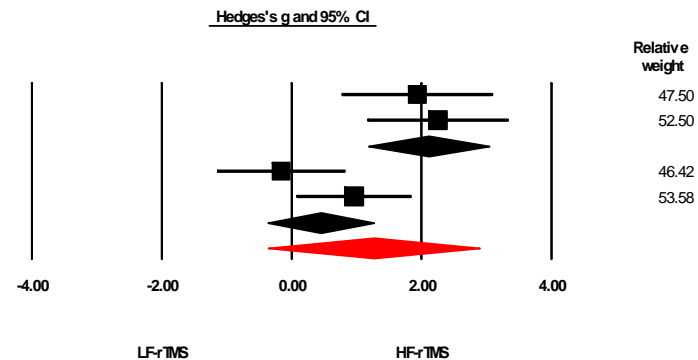


3.6 Subgroup Analysis - HF-rTMS vs. LF-rTMS: Pre-Post Patient-Reported PTSD Symptoms



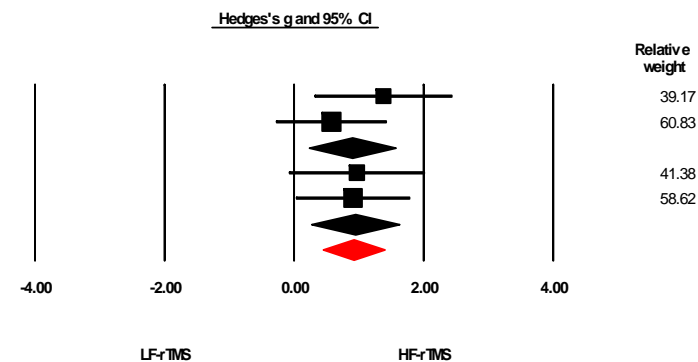
3.7 Subgroup Analysis - HF-rTMS vs. LF-rTMS: Pre-Post Overall Anxiety Symptoms

Group by Protocol	Study name	Statistics for each study							Sample size	
		Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Active rTMS	Sham rTMS
HF-rTMS	Cohen et al., 2004b	1.936	0.596	0.356	0.768	3.105	3.247	0.001	10	6
HF-rTMS	Boggio et al., 2010	2.255	0.557	0.311	1.162	3.347	4.046	0.000	10	10
HF-rTMS		2.103	0.474	0.225	1.174	3.033	4.436	0.000	20	16
LF-rTMS	Cohen et al., 2004a	-0.159	0.506	0.257	-1.151	0.834	-0.314	0.754	8	6
LF-rTMS	Watts et al., 2012	0.961	0.454	0.207	0.071	1.852	2.115	0.034	10	10
LF-rTMS		0.441	0.417	0.174	-0.376	1.258	1.059	0.290	18	16
Overall		1.257	0.831	0.690	-0.371	2.885	1.513	0.130	38	32



3.8 Subgroup Analysis - HF-rTMS vs. LF-rTMS: Pre-Post Depressive Symptoms

Group by Protocol	Study name	Statistics for each study							Sample size	
		Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Active rTMS	Sham rTMS
HF-rTMS	Cohen et al., 2004b	1.378	0.546	0.298	0.309	2.448	2.526	0.012	10	6
HF-rTMS	Boggio et al., 2010	0.576	0.438	0.192	-0.282	1.435	1.316	0.188	10	10
HF-rTMS		0.891	0.342	0.117	0.221	1.560	2.608	0.009	20	16
LF-rTMS	Cohen et al., 2004a	0.970	0.538	0.289	-0.084	2.024	1.804	0.071	8	6
LF-rTMS	Watts et al., 2012	0.910	0.452	0.204	0.025	1.796	2.014	0.044	10	10
LF-rTMS		0.935	0.346	0.120	0.257	1.613	2.703	0.007	18	16
Overall		0.913	0.243	0.059	0.436	1.389	3.755	0.000	38	32



4. REFERENCES

1. Levine J, Gauchman T, Grisaru N. High frequency TMS effect over right versus left prefrontal cortex, each with or without exposure to traumatic stimuli on PTSD flashbacks. *Int J Neuropsychopharmacol.* 2010;13:210.
2. Osuch EA, Benson BE, Luckenbaugh DA, Geraci M, Post RM, McCann U. Repetitive TMS combined with exposure therapy for PTSD: a preliminary study. *J Anxiety Disord.* 2009;23:54-9.