Data Supplement for Carmi et al.,Efficacy and Safety of Deep Transcranial Magnetic Stimulation for Obsessive-Compulsive Disorder: A Prospective Randomized Multicenter Double-Blind Placebo-Controlled Trial. Am J Psychiatry (doi: 10.1176/appi.ajp.2019.18101180)

Missing Data

The primary outcome measure was not evaluated for patients who dropped out prior to randomization. Patients who dropped out after one or more treatments and have data available for the analysis (i.e., at least one post-baseline assessment) of continuous variables were analyzed with a repeated measures analysis of variance model using PROC mixed in SAS, which can handle missing data at random. Therefore, for this evaluation, no imputation of missing data was considered beyond the model estimates. Nevertheless, in a case where the missing at random assumption prove to be incorrect at other time points, a sensitivity analysis using other methods for data imputation, such as last observed carried forward (LOCF), was performed. In the case of binary variables (such as response and remission rates at posttreatment and follow-up assessments), the LOCF method was used.

Analysis of the ITT Data Set

Analysis of the ITT data set shows an average reduction in YBOCS scores of 6.0 points (95% CI: [3.8;8.2]) in the active dTMS group and 4.1 points (95% CI: [1.9;6.2]) in the sham control group. The reductions in YBOCS scores were significant for both groups. While the observed effect size was 0.48, the difference between the slopes of the two groups did not reach statistical significance (p-value: 0.09) in this data set. Nonetheless, improvement in the CGI score was significantly different between the active dTMS and sham groups in this data set. While 48% of the dTMS group were improved (i.e. by 1 or 2 CGI points), only 25% were improved in the sham group (p-value: 0.045).

Finally, the response rate in the active dTMS group (37%) was significantly higher than that of the sham control group (18%); thus, the number needed to treat was 5.3 (p=0.04). The response rate at the 10-week follow up visit was 44% in the active dTMS group and only 22% in the sham control group. This difference was statistically significant (p=0.02).

.

A modified Clinical Global Impressions improvement scale (CGI-I)

The global improvement item requires the clinician to rate how much the patient's illness has improved or worsened relative to a baseline state. Compared to condition at baseline, a patient's illness is compared to change over time, and rated as: very much improved; much improved; moderately improved; minimally improved; no change; minimally worse; moderately worse; much worse; or very much worse. Subjects were assessed for the improvement of illnesses at the baseline visit, at the weekly assessment visits during the treatment period and at the 10 week follow-up visit.

.

TABLE S1.

A. Patients' demographic data.

			DTMS (N=47)	Sham (N=47)	Total (N=94)	p
Age (years)		N	47	47	94	0.0588
		Mean (SD)	41.1 (11.97)	36.5 (11.38)	38.8 (11.85)	
		Median [Range]	39.4 [22.9;68.0]	34.2 [22.2;66.5]	36.0 [22.2;68.0]	
Gender	Male	% (n/N)	57.4% (27/47)	59.6% (28/47)	58.5% (55/94)	1.0000
	Female	% (n/N)	42.6% (20/47)	40.4% (19/47)	41.5% (39/94)	
Race	White	% (n/N)	78.7% (37/47)	87.2% (41/47)	83.0% (78/94)	0.4649
	Hispanic or Latino	% (n/N)	6.4% (3/47)	2.1% (1/47)	4.3% (4/94)	
	Black or African American	% (n/N)	2.1% (1/47)	2.1% (1/47)	2.1% (2/94)	
	Asian	% (n/N)	4.3% (2/47)	4.3% (2/47)	4.3% (4/94)	
	Black or Afro-American; and White (**)	% (n/N)	-	4.3% (2/47)	2.1% (2/94)	
	Hispanic or Latino; and White (**)	% (n/N)	2.1% (1/47)	-	1.1% (1/94)	
	Hispanic or Latino; and Indian or Alaska Native (**)	% (n/N)	2.1% (1/47)	-	1.1% (1/94)	
	Indian or Alaska Native	% (n/N)	4.3% (2/47)	-	2.1% (2/94)	

Marital Status	Single	% (n/N)	29.8% (14/47)	21.3% (10/47)	25.5% (24/94)	0.3523
	Married	% (n/N)	55.3% (26/47)	70.2% (33/47)	62.8% (59/94)	
	Divorced	% (n/N)	10.6% (5/47)	8.5% (4/47)	9.6% (9/94)	
	Widower	% (n/N)	4.3% (2/47)	-	2.1% (2/94)	
Education	Less than 9 years of education	% (n/N)	-	-	-	0.3161
	9 to 12 years of education	% (n/N)	14.9% (7/47)	6.4% (3/47)	10.6% (10/94)	
	Over 12 years of education	% (n/N)	85.1% (40/47)	93.6% (44/47)	89.4% (84/94)	
Ethnicity	Hispanic or Latino	% (n/N)	6.4% (3/47)	2.1% (1/47)	4.3% (4/94)	0.2350
	Not Hispanic or Latino	% (n/N)	89.4% (42/47)	97.9% (46/47)	93.6% (88/94)	
	Hispanic or Latino; and Not Hispanic or Latino (**)	% (n/N)	4.3% (2/47)	-	2.1% (2/94)	
Dropouts	Subject completed treatment	% (n/N)	89.3% (42/47)	95.7% (45/47)	87/94	
	Subject completed follow-up	% (n/N)	85% (40/47)	96% (44/47)	79/94	

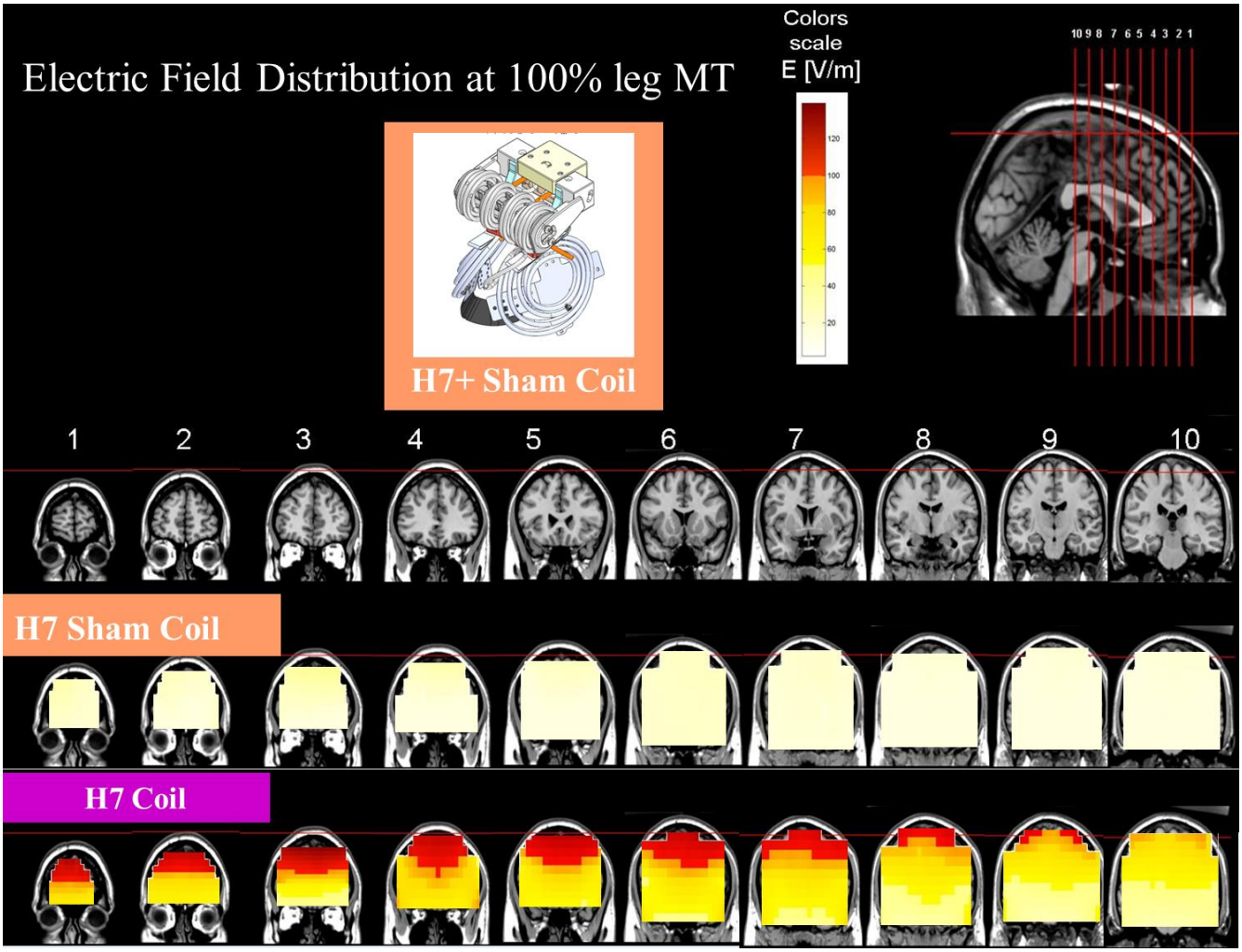
B. SRI drug for depression and other psychiatric medications taken at baseline

		DTMS (N=47)			Sham (N=47)			Total (N=94)		
		# of reports	# of subjects	Incidence	# of reports	# of subjects	Incidence	# of reports	# of subjects	Incidence
Medication Type	Generic Name									
All	All	100	45	95.74%	81	42	89.36%	181	87	92.55%
SSRI Medications	All	44	42	89.36%	45	41	87.23%	89	83	88.30%
	Citalopram	.	.	.	1	1	2.13%	1	1	1.06%
	Escitalopram	4	4	8.51%	6	6	12.77%	10	10	10.64%
	Fluoxetine	11	11	23.40%	12	11	23.40%	23	22	23.40%
	Fluvoxamine	14	13	27.66%	9	7	14.89%	23	20	21.28%
	Paroxetine	5	5	10.64%	5	5	10.64%	10	10	10.64%
	Sertraline	10	9	19.15%	12	11	23.40%	22	20	21.28%
Antidepressant Medications	All	5	4	8.51%	2	2	4.26%	7	6	6.38%
	Bupropion	1	1	2.13%	1	1	2.13%	2	2	2.13%
	Duloxetine	1	1	2.13%	.	.	.	1	1	1.06%
	Sertraline	.	.	.	1	1	2.13%	1	1	1.06%
	Trazodone	1	1	2.13%	.	.	.	1	1	1.06%
	Venlafaxine	2	2	4.26%	.	.	.	2	2	2.13%
Other Psychiatric Medications	All	51	28	59.57%	34	20	42.55%	85	48	51.06%
	Albuterol	.	.	.	1	1	2.13%	1	1	1.06%
	Alprazolam	5	5	10.64%	1	1	2.13%	6	6	6.38%
	Aripiprazole	3	2	4.26%	2	1	2.13%	5	3	3.19%
	Buprenorphine	.	.	.	2	2	4.26%	2	2	2.13%
	Buspirone	2	1	2.13%	.	.	.	2	1	1.06%
	Clonazepam	12	11	23.40%	10	8	17.02%	22	19	20.21%
	Clonidine	1	1	2.13%	2	2	4.26%	3	3	3.19%
	Dexmethylphenidate	.	.	.	1	1	2.13%	1	1	1.06%
	Diazepam	1	1	2.13%	.	.	.	1	1	1.06%
	Eszopiclone	1	1	2.13%	.	.	.	1	1	1.06%
	Gabapentin	2	2	4.26%	.	.	.	2	2	2.13%
	Guanfacine	2	2	4.26%	.	.	.	2	2	2.13%
	Haloperidol lactate	1	1	2.13%	.	.	.	1	1	1.06%
	Lamotrigine	2	2	4.26%	1	1	2.13%	3	3	3.19%
	Lorazepam	5	5	10.64%	1	1	2.13%	6	6	6.38%
	Melatonin	.	.	.	1	1	2.13%	1	1	1.06%
	Memantine	.	.	.	1	1	2.13%	1	1	1.06%
	Olanzapine	1	1	2.13%	.	.	.	1	1	1.06%
	Prazosin	.	.	.	1	1	2.13%	1	1	1.06%
	Quetiapine	4	4	8.51%	3	3	6.38%	7	7	7.45%
	Risperidone	3	3	6.38%	3	3	6.38%	6	6	6.38%
	Temazepam	2	1	2.13%	.	.	.	2	1	1.06%
	Topiramate	.	.	.	2	2	4.26%	2	2	2.13%
	Trazodone	1	1	2.13%	.	.	.	1	1	1.06%
	Zolpidem	3	2	4.26%	2	2	4.26%	5	4	4.26%

TABLE S2. List of subjects excluded from analyses (ITT-> mITT)

Subject ID	Reason for Exclusion
NS-03	Subject did not meet Inclusion Criteria #5 - *subjects are maintained on SSRI medications at a stable therapeutic dosage for at least 2 months prior to study entry.* Subject's SSRI (Fluvoxamine) medication dose was increased, 3 days prior to the screening visit. This was revealed and documented as a protocol deviation during a monitoring visit in May 2015.
NS-04	Subject did not meet Inclusion Criteria #5 - *subjects are maintained on SSRI medications at a stable therapeutic dosage for at least 2 months prior to study entry.* Subject's SSRI (Sertraline) medication dose was increased from 175mg to 200mg, 1 week prior to the screening visit. This was revealed and documented as a protocol deviation during a monitoring visit in May 2015.
NS-06	Subject did not meet Inclusion Criteria #5 - *subjects are maintained on SSRI medications at a stable therapeutic dosage for at least 2 months prior to study entry.* Subject's medication dose (Ondansetron, although taken for vomiting and nausea, is a potent serotonergic drug like SSRIs, which has been recommended as augmentation for resistant OCD patients) was taken at baseline before initiation of dTMS treatments and then again at 2 weeks. This was revealed during the final centralized monitoring processes in March-May, 2017.
UC-04	Subject did not meet Exclusion Criteria #2 - *Subjects diagnosed according to the SCID II as suffering from severe Personality Disorder (excluding Obsessive Compulsive Personality Disorder) or hospitalized due to exacerbation related to borderline personality disorder*. Subject suffered from severe personality disorders. This was revealed during a monitoring visit in July 2016 and documented in August 2016 as a protocol deviation. Subject's SCID Axis II completed forms indicated a severe personality disorder. The study rater indicated that this didn't appear severe at the time of recruitment, but were shown throughout the study to be severe. As this subject apparently suffered from severe personality disorder prior to commencement of the study, and this is a study exclusion criteria, the subject should not have been recruited to the study and was documented as a protocol deviation.
CH-07	Subject did not meet Inclusion Criteria #5 - *subjects are maintained on SSRI medications (with or without additional antidepressant or psychotropic augmentation for treatment of OCD), at a stable therapeutic dosage for at least 2 months prior to study entry and for the duration of the trial and/or subjects are maintained on psychotherapeutic behavioral intervention therapy. Subjects undergoing CBT treatment must be in the maintenance stage (i.e., not during the assessment or skills acquisition or training stages)*. This inclusion criteria requires that subjects are currently either taking SSRI medications or are undergoing CBT treatment (in the maintenance phase), but have been treated with SSRI medications previously in their treatment history. Although, CH-07 was undergoing CBT maintenance treatment, the subject did not have a history of taking any OCD medications, including SSRIs or others. This was revealed during a site visit by the study expert rater early on in the study, in November, 2014. Subsequent to this discovery, a newsletter went out to all sites with a clarification of this Inclusion Criteria and no further subjects were mistakenly enrolled.

FIGURE S1. Coil design and colored electric field maps for active and sham H7 coils



The H7 coil consists of 16 windings arranged in two groups (8 in each group). The windings are flexible and designed conform to the human head. The maps indicate the Active and Sham's electric fields (with absolute magnitude in each pixel), following stimulation equivalent to 100% of the average leg motor threshold, for 14 coronal slices 1 cm apart. Red pixels indicate regions with field intensity above the threshold for neuronal activation (100 V/m).