

**Appendix 1** to Lai Y, Wang T, Zhang C, et al. Effectiveness and safety of neuroablation for severe and treatment-resistant obsessive-compulsive disorder: a systematic review and meta-analysis. *J Psychiatry Neurosci* 2020.

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Supplemental Digital Content 1. Table. Inclusion criteria and co-intervention of each study.

Supplemental Digital Content 2. Table. Additional characteristics of included studies.

Supplemental Digital Content 3. Figure. Funnel plot for report of response rate. Mean values are plotted against the standard error of each mean.

Supplemental Digital Content 4. Figure. Forest plot of mean reduction in total Y-BOCS score after neuroablation at (A) 12-month follow-up and (B) last follow-up. The diamond at the bottom is the pooled mean and its 95% confidence interval under random effect model. ES: estimated value for mean reduction in total Y-BOCS score.

Supplemental Digital Content 5. Figure. Forest plot of mean percent reduction in total Y-BOCS score after neuroablation at (A) 12-month follow-up and (B) last follow-up. The diamond at the bottom is the pooled mean and its 95% confidence interval under random effect model. ES: estimated value for mean percent reduction in total Y-BOCS score.

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Supplemental Digital Content 6. Figure. Forest plot of mean reduction in total Y-BOCS score at last follow-up in groups with different coverages of internal capsule areas. The diamond at the bottom is the pooled mean and its 95% confidence interval under random effect model. ES: estimated value for mean reduction in total Y-BOCS score.

Supplemental Digital Content 7. Figure. Forest plot of mean percent reduction in total Y-BOCS score at last follow-up in groups with different coverages of internal capsule areas. The diamond at the bottom is the pooled mean and its 95% confidence interval under random effect model. ES: estimated value for mean percent reduction in total Y-BOCS score.

Supplemental Digital Content 8. Figure. Forest plot of response rate at last follow-up as a function of the proportion of patients who received a repeat surgery. The diamond at the bottom is the pooled mean and its 95% confidence interval under random effect model. LFU: last follow-up; SD: standard deviation; ES: estimated value for response rate.

Supplemental Digital Content 9. Table. Meta-regression of continuous predictors for effectiveness.

Supplemental Digital Content 10. Table. Impact of neuroablation on depression and anxiety symptoms.

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Supplemental Digital Content 11. Table. Adverse-event profiles for each dataset.

Supplemental Digital Content 12. Table. Incidence of adverse events as a function of the extent of coverage of internal capsule areas.

**Supplemental Digital Content 1. Table. Inclusion criteria and co-intervention of each study**

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Author	Year	n	Region	Study design	OCD criteria	Selection Criteria	Exclusion Criteria	Co-intervention
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Csigo <sup>15</sup>	2010	5	Hungary	prospective controlled cohort	NR	≥3 SRIs; CBT	NR	meds; CBT (changed to usual practice)
D'Astous <sup>17</sup>	2013	19	Canada	single-arm prospective	DSM-IV	≥3 SRIs, ≥12 weeks; CBT ≥30 h; GAF < 50	NR	NR
Gong <sup>18</sup>	2018	14	China	retrospective controlled cohort	DSM-IV	≥3 SRIs (one clomipramine), ≥12 weeks; CBT>20 hours; <25% reduction in Y-BOCS	NR	3 patients with meds
Gupta <sup>19</sup>	2018	40	USA	single-arm retrospective, multicenter	NR	meds; CBT	organic brain diseases; less than 6 mos' follow-up	meds; CBT (continued)
Irlé <sup>20</sup>	1998	16	Germany	single-arm retrospective	DSM-III-R	meds; psychotherapy; electroconvulsive shock, sleep therapy; chronic	NR	NR
Jung <sup>21</sup>	2006	17	South Korea	single-arm prospective	DSM-IV	substantial reduction in psychosocial functioning; thoroughly addressed comorbid psychiatric condition	organic brain diseases; substance abuse; current axis II diagnosis from clusters A or B, or a current axis III diagnosis with brain pathology	NR
Kim <sup>22</sup>	2002	12	South Korea	single-arm prospective	NR	NR	NR	NR
Kim <sup>23</sup>	2018	11	South Korea	single-arm prospective	DSM-IV	≥ 3 SRIs, ≥ 12 weeks; CBT ≥ 20 sessions; GAF ≤ 50	current or previous psychotic disorder, bipolar disorder or significant cognitive impairment	meds (continued)
Kondziolka <sup>24</sup>	2011	3	USA	single-arm prospective	NR	Y-BOCS stable over the months before radiosurgery	abnormal brain MRI	meds (continued)

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Liu <sup>25</sup>	2008	35	China	prospective controlled cohort	DSM-IV	meds > 5 years; CBT > 5 years	cognitive deficits, severe heart disease or clotting disorders	none (meds were dropped)
Lopes <sup>26</sup>	2014	12	Brazil & USA	randomized controlled trial	DSM-IV	≥ 3 SRIs, ≥ 12 weeks; CBT ≥ 20 h; ≥ 2 augs; CGI not improved	history of head injury; past or general medical condition, or neurological illness with brain compromise; history of physiological effects of a substance; pregnancy or lactation	meds (continued); CBT (3 months after surgery)
Lopes <sup>27</sup>	2009	5	Brazil & USA	single-arm prospective	DSM-IV	≥ 3 SRIs, ≥ 12 weeks; CBT ≥ 20 h; ≥ 2 augs; CGI not improved	history of head injury; past or general medical condition, or neurological illness with brain compromise; history of physiological effects of a substance; pregnancy or lactation	meds (continued)
Montoya <sup>28</sup>	2002	15	USA	single-arm prospective	DSM-III-R/DSM-IV	meds; CBT	NR	NR
Oliver <sup>29</sup>	2003	15	Spain	single-arm prospective	NR	NR	NR	NR
Rasmussen <sup>30</sup>	2018	55	USA	single-arm prospective	DSM-IV or DSM-III-R	≥3 SRIs ≥ 10 weeks; aug of an SSRI with a) lithium, b) neuroleptic, c) clonazepam and d) buspirone; 20 hours of exposure with response prevention; GAF ≤ 45	NR	meds; CBT (continued)

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Ruck <sup>31</sup>	2008	25	Sweden	single-arm retrospective	DSM-III-R or DSM-IV	meds ≥ 5 years; CBT ≥ 5 years	NR	meds (continued)
Sheehan <sup>32</sup>	2013	5	USA	single-arm prospective	NR	all reasonable nonoperative treatments; refused DBS	organic brain diseases	NR
Sheth <sup>33</sup>	2013	64	USA	single-arm prospective	DSM-III, DSM-III-R or DSM-IV	≥3 SRIs; 2 augs ≥ 10 weeks; CBT ≥ 20 h	NR	NR
Spatola <sup>34</sup>	2018	10	Spain	single-arm prospective	NR	NR	abnormal brain MRI	meds (continued)
Yang <sup>35</sup>	2014	19	USA	single-arm retrospective	DSM III, III-R, or IV	≥3 SRIs; 2 augs; CBT	NR	NR
Yin <sup>36</sup>	2018	36	China	single-arm retrospective	DSM IV	≥ 3 SRIs, > 12 weeks; psychotherapy > 6 mos	schizophrenic disorder; bipolar disorder; substance abuse; cluster A or B personality disorder; current severe major depressive episode; abnormal cognitive status	NR
Zhan <sup>37</sup>	2014	53	China	single-arm retrospective	DSM-IV	meds ≥ 3 years; psychotherapy ≥ 3 years; significant reduction in functioning	organic brain diseases; history of personality disorder or substance abuse; cognitive deficits.	NR
Zhang <sup>38</sup>	2013	7	China	single-arm prospective	DSM-IV	1 SSRI + another SSRI or clomipramine, ≥ 2mos; augs; failed to respond to 'exposure and response prevention	organic brain diseases; substance abuse; history of cerebral trauma; marked atrophy	NR

Y-BOCS, Yale-Brown Obsessive-Compulsive Scale; mos, months; aug, augmentation therapy; SRI, serotonin reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors; CBT, cognitive behavioral therapy; CGI, Clinical Global Impression-Improvement Scale; GAF, Global Assessment of Functioning Scale; NR, not reported.

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**Supplemental Digital Content 2. Table. Additional characteristics of included studies**

Author (year, subgroups)	n	Age at surgery (years)*	Duration (years)*	Age at onset (years)*	12-Mo Change in Y-BOCS Score	12-Mo % Change in Y-BOCS Score	LFU Change in Y-BOCS Score	LFU % Change in Y-BOCS Score	Male
Csigo (2010) <sup>15</sup>	5	32.2±6.3; NR	23.2 (SD not reported); NR	9.0±6.7; NR	NR	NR	NR	NR	3
D'Astous (2013) <sup>17</sup>	19	40.8±11.6; 20-60	16.2±8.4; 7-40	14.6 (SD not reported); NR	NR	36.3 (SD not reported)	NR	31 (SD not reported)	7
Gong (2018) <sup>18</sup>	14	31.0±3.1; 18-57	12.6±10.0; 5-32	18.3±6.3; 11-34	NR	NR	NR	NR	5
Gupta (2018) <sup>19</sup>	40	42.5±13.3; 18-75	24.0±13.5; 6-59	18.5 (SD not reported); 5-40	NR	NR	NR	NR	24
Irle (1998, front) <sup>20</sup>	6	35 (median, IQR 11); NR	4 (median, IQR 8); NR	NR; NR	NR	NR	NR	73 (median)	2
Irle (1998, front+dors) <sup>20</sup>	5	33 (median, IQR 12); NR	12 (median, IQR 9); NR	NR; NR	NR	NR	NR	56 (median)	2
Irle (1998, front+pos) <sup>20</sup>	5	37 (median, IQR 13); NR	13 (median, IQR 14); NR	NR; NR	NR	NR	NR	75 (median)	2
Jung (2006) <sup>21</sup>	17	36.1±9.4; NR	10.9±5.2; >3	24.6±9.8; NR	NR	36.0 (SD not reported)	NR	48.0 (SD not reported)	10
Kim (2002) <sup>22</sup>	12	NR; NR	NR; NR	NR; NR	23.6±3.5	68.7±8.0	30.8±3.2	89.0±4.4	NR
Kim (2018) <sup>23</sup>	11	33.0±8.5; 22-44	14.6±4.8; 9-24	18.4±7.5; 9-31	12.5±5.6	-36.1±15.3	13.1±6.7	37.8±18.9	5
Kondziolka (2011) <sup>24</sup>	3	43.7±9.9; 37-55	NR; NR	NR; NR	NR	NR	20.7±10.5	54.2±25.0	1
Liu (2008) <sup>25</sup>	35	29.6±10.6; 18-67	10.8±4.5; 5-32	18.8 (SD not reported); NR	NR	NR	NR	NR	22
Lopes (2014) <sup>26</sup>	12	33.9±10.7; 21-55	18.0±12.3; 5-40	12.6±5.5; 5-22	11.3±11.6	34.9±35.5	15.8±11.5	49.2±35.0	8
Lopes (2009) <sup>27</sup>	5	35.0±11.1; 23-49	17.4±9.4; 5-29	17.6±3.3; 12-20	NR	NR	11.6±11.9	36.4±37.9	2
Montoya (2002) <sup>28</sup>	9	46.3±14.8; 31-77	23.9 (SD not reported, n=15) †; 2-55 (n=15) †	22.4 (SD not reported, n=15); NR	NR	NR	8.6±9.7	27.1±28.1	7
Oliver (2003) <sup>29</sup>	15	34.2±8.2; 23-51	18.1±5.6; 11-26	16.3±9.6; 7-32	NR	NR	14.0±3.6	NR	9

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Rasmussen (2018, DS) <sup>30</sup>	40	32.8±11.1; 18-65 (n=55) †	12.2 (SD not reported); NR	18.6±7.7; NR	NR	NR	17.4±11.7	NR	25
Rasmussen (2018, SS) <sup>30</sup>	15	35.9±8.7; 18-65 (n=55) †	14.4 (SD not reported); NR	21.5±8.3; NR	NR	NR	NR	NR	10
Ruck (2008, bilat GK) <sup>31</sup>	9	43.9±12.7; 26-68	NR; > 5	NR; NR	16.1±12.1	50.3±36.3	18.5±12.6	55.8±36.3	11 (n=5) †
Ruck (2008, bilat RF) <sup>31</sup>	12	40.2±9.5; 26-53	NR; > 5	NR; NR	15.0±9.1	45.0±29.7	13.8±9.8	41.7±31.4	11 (n=25) †
Ruck (2008, unilat RF) <sup>31</sup>	4	35.3±11.9; 25-52	NR; > 5	NR; NR	13.0±15.8	35.7±45.2	15.0±16.4	44.5±46.3	11 (n=25) †
Sheehan (2013) <sup>32</sup>	5	36.8±7.8; 26-47	20.0±7.3; 12-30	16.8±2.0; 13-19	NR	NR	16.0±7.0	50.0±22.0	3
Sheth (2013, cing/limb) <sup>33</sup>	30	34.7±1.4 (n=64) †; 16–69 (n=64) †	NR; NR	NR; NR	NR	-15.0±20.8	NR	45.0±5.0	42 (n=64) †
Sheth (2013, cing) <sup>33</sup>	34	34.7±1.4 (n=64) †; 16–69 (n=64) †	NR; NR	NR; NR	NR	-36±32.9	NR	28±28.3	42 (n=64) †
Spatola (2018) <sup>34</sup>	10	41.2±10.7; 27-65	15.3±6.8; 6-26	25±10.7; 16-5	NR	NR	18.0±10.6	66.0±31.0	5
Yang (2014, cing) <sup>35</sup>	11	36.9±2.9 (n=18) †; NR	NR; NR	NR; NR	NR	NR	NR	15.7±25.1	10 (n=18) †
Yang (2014, limb) <sup>35</sup>	8	39.3±3.6 (n=11) †; NR	NR; NR	NR; NR	NR	NR	NR	37.7±27.5	5 (n=11) †
Yin (2018) <sup>36</sup>	36	31.2±6.8; 18-45	NR; > 5	NR; NR	NR	NR	13.9±11.1	45.2±32.4	19
Zhan (2014) <sup>37</sup>	53	28.89±9.16; 19-63	8.09±2.99; 5-18	18.8 (SD not reported); NR	NR	NR	NR	NR	32
Zhang (2013) <sup>38</sup>	7	32.4±6.1; 26-44	22.3±7.9; 16-39	10.1 (SD not reported); NR	12.3±2.3	37.7±8.8	12.3±2.3	37.7±8.8	4

DS: double shot group; SS: single shot repeat group; bilat: bilateral; unilat: unilateral; GK: Gamma knife; RF: radiofrequency; cing+: unsuccessful cingulotomy followed by subsequent lesion (a repeat cingulotomy or a subcaudate tractotomy); IQR: interquartile range; NR: not reported.

\*: data were expressed as 'mean±SD; range' unless stated.

†: data reported in a larger population (indicated in the brackets) of the research.

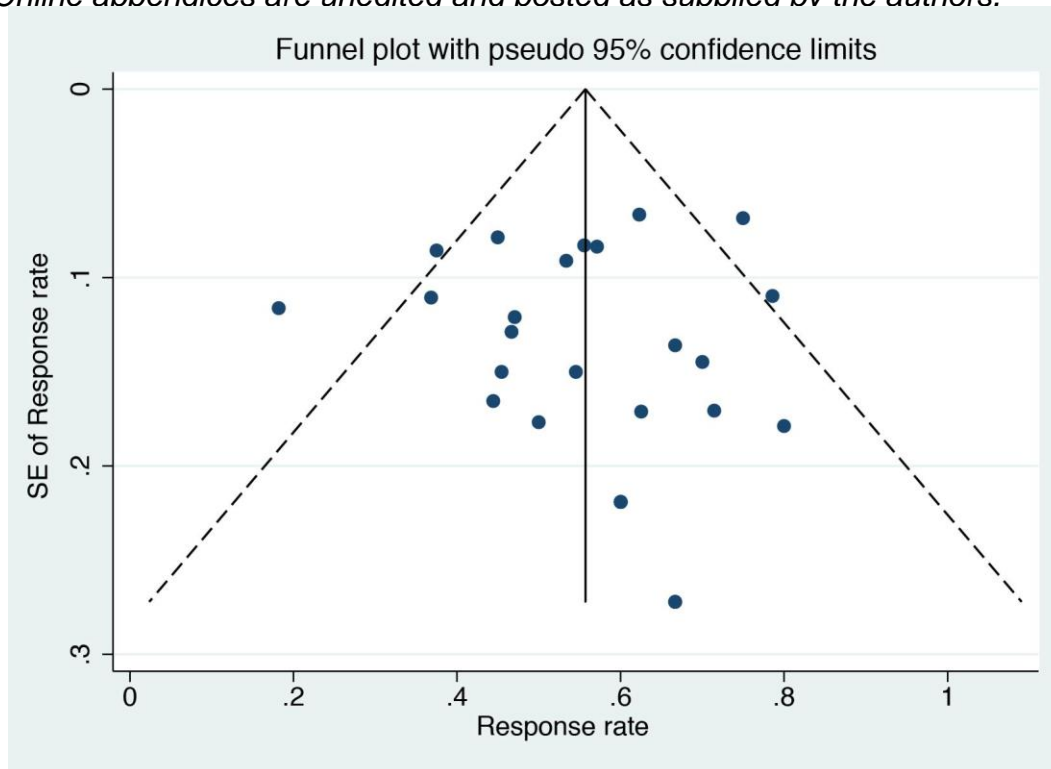


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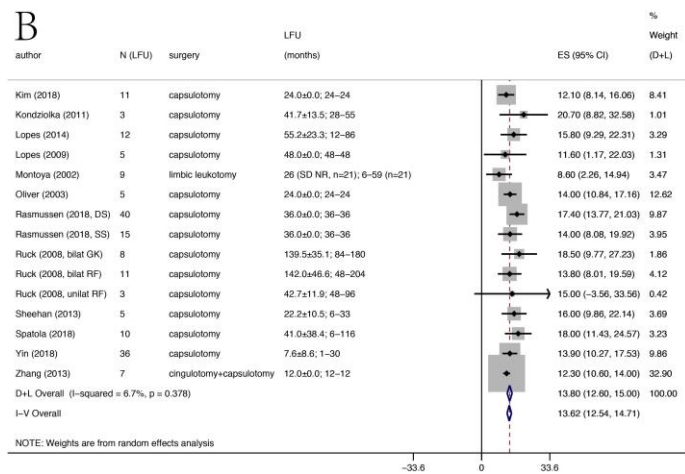
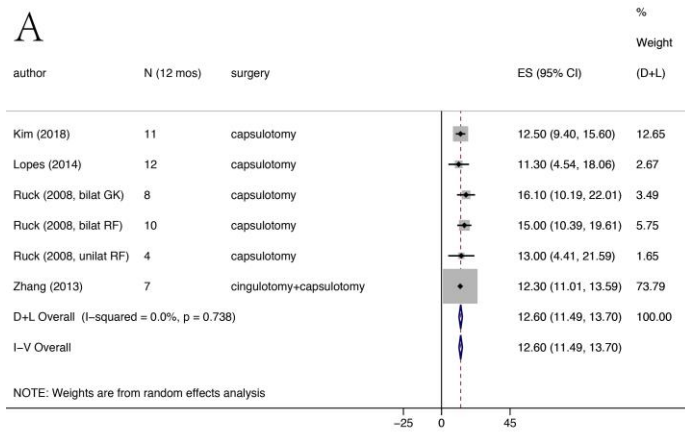


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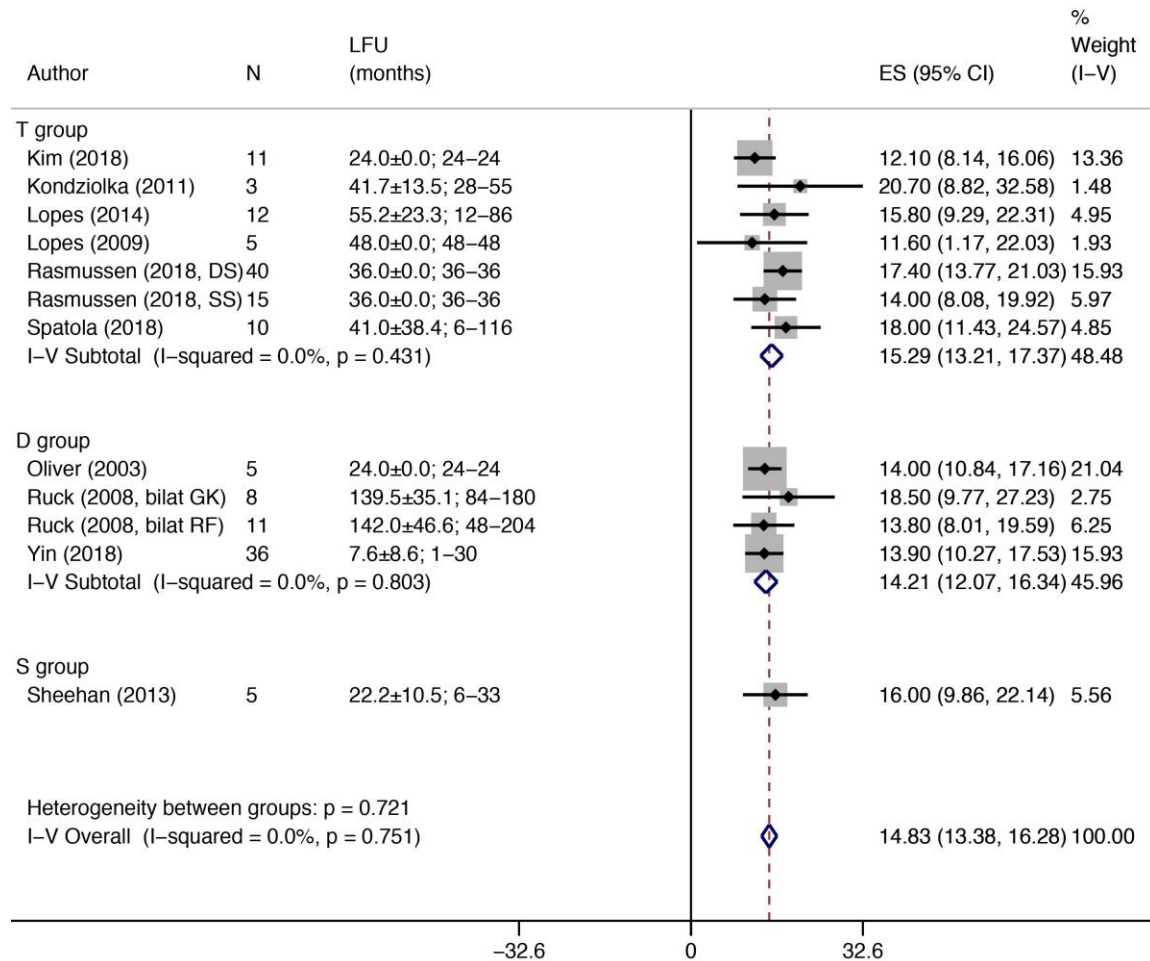


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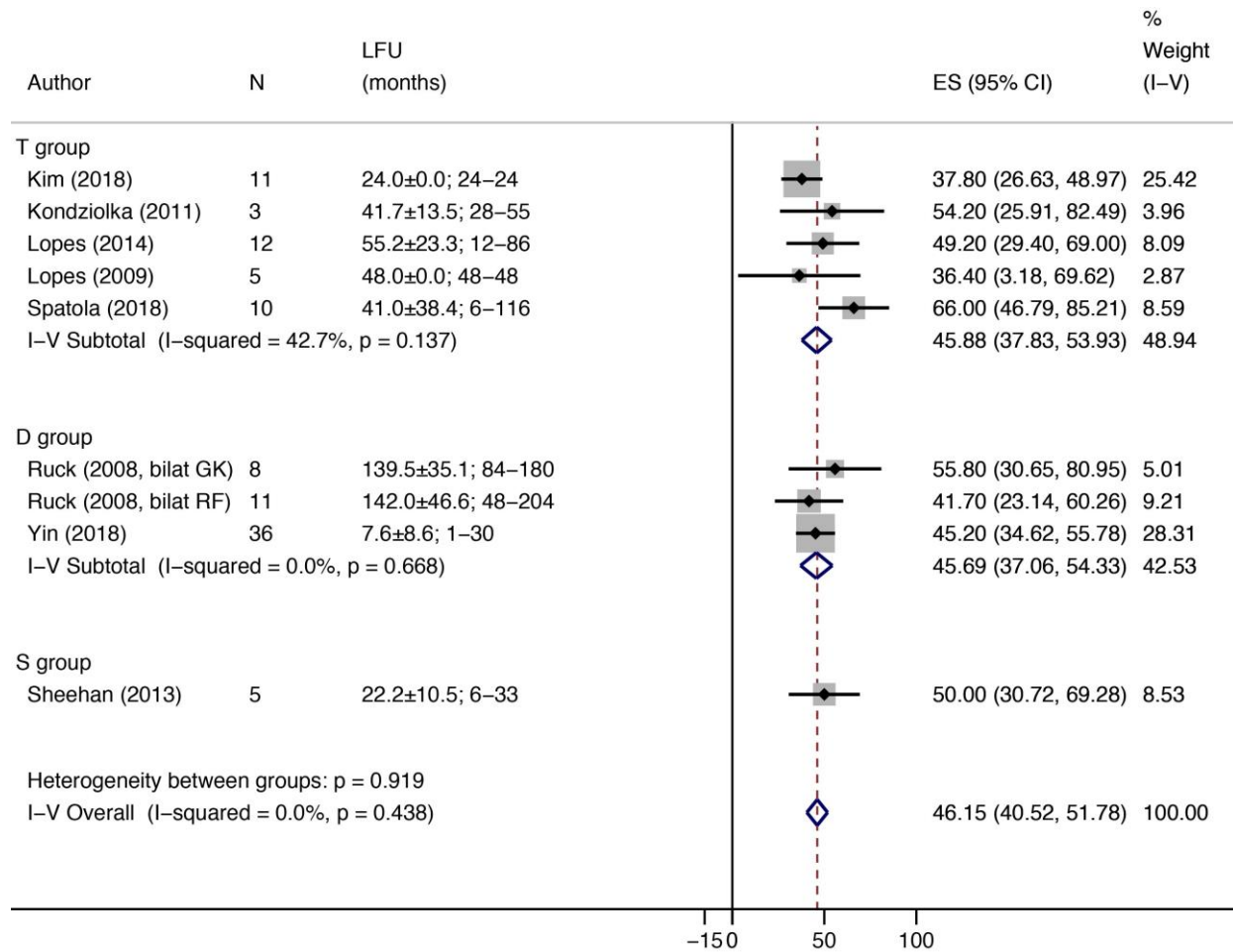


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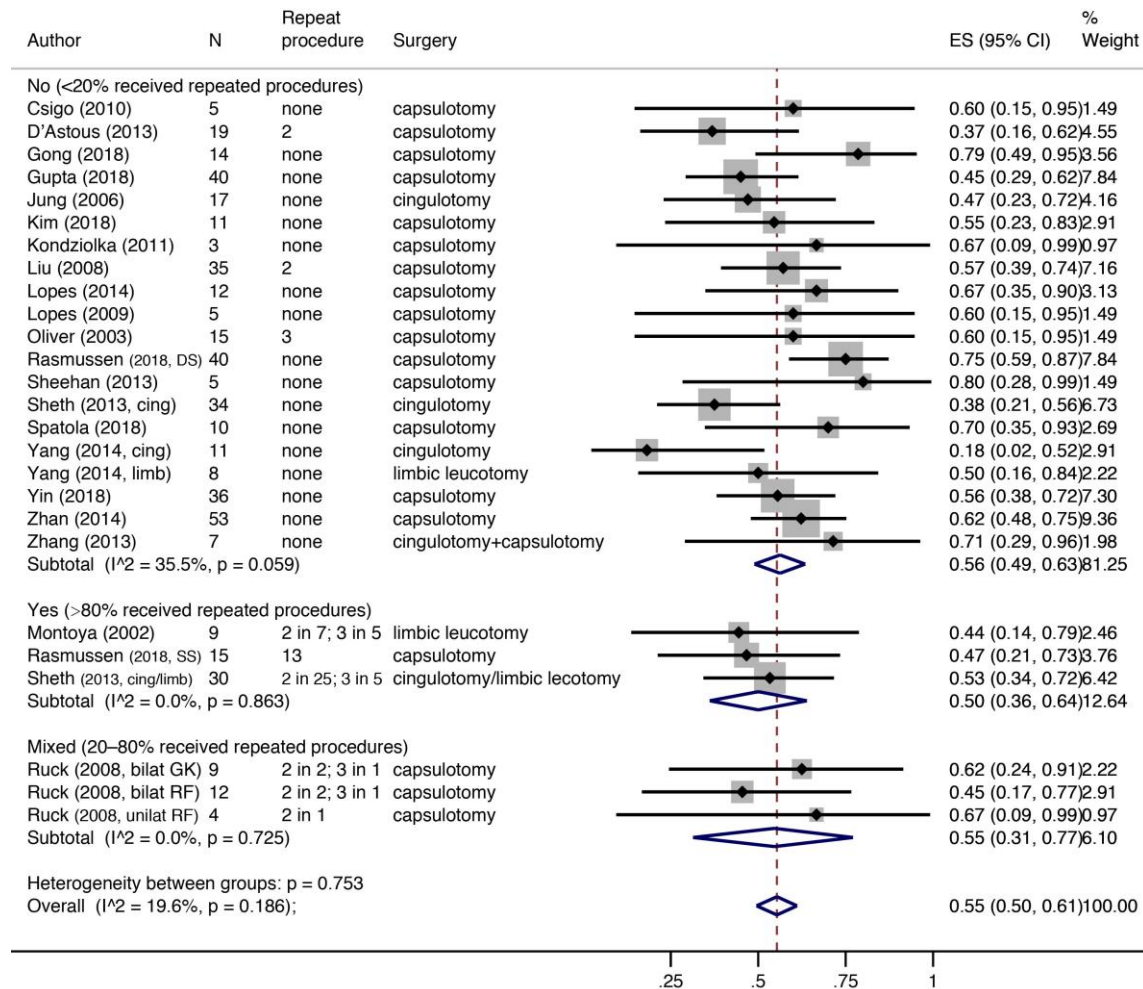


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**Supplemental Digital Content 9. Table. Meta-regression searching for predictors of effectiveness.**

<b>Covariates</b>	<b>Coefficient</b>	<b>Std. Err.</b>	<b>t</b>	<b>p</b>
<i>Mean reduction in Y-BOCS</i>				
Mean last follow-up month	-0.0492277	0.1449302	-0.34	0.751
Mean age at surgery	1.52649	1.501641	1.02	0.367
Mean disease onset age	-1.569232	1.372589	-1.14	0.317
Mean duration of illness	-1.937321	1.517125	-1.28	0.271
Mean pre-operative Y-BOCS scale	-0.3553594	0.5584496	-0.64	0.559
<i>Mean percent reduction in Y-BOCS</i>				
Mean last follow-up month	0.0198591	0.0310949	0.64	0.638
Mean age at surgery	-0.0462007	0.1897537	-0.24	0.848
Mean disease onset age	0.1322882	0.2725361	0.49	0.712
Mean duration of illness	0.2588457	0.4605269	0.56	0.674
Mean pre-operative Y-BOCS scale	0.4843047	0.6243295	0.78	0.580
<i>Last follow-up's response rate</i>				
Mean last follow-up month	-0.0024244	0.0031249	-0.78	0.454
Mean age at surgery	-0.0139003	0.0260059	-0.53	0.604
Mean disease onset age	-0.0044235	0.0243867	-0.18	0.859
Mean duration of illness	-0.0041306	0.0255193	-0.16	0.874
Mean pre-operative Y-BOCS scale	0.0048177	0.0097662	0.49	0.631

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**Supplemental Digital Content 10. Table. Impact of neuroablation on depression and anxiety symptoms.**

Author	Year	n	Depression					Anxiety					
			Scale	Baseline score	LFU score	P value	Statistical method	Scale	Baseline score	LFU score	P value	Statistical method	
Csigo	2010	5	HAM-D	22.6±13.7	7.2±4.7	p>0.05	Wilcoxon	HAM-A	21.2±7.2	11.0±7.9	0.001	Wilcoxon	
Gupta	2018	40	BDI	NR	NR (n=30)	p>0.05	MH	BAI	NR	NR (n=25)	p<0.005	MH	
Jung	2006	17	HAM-D	23.9±11.5	12±7.4	0.003	Wilcoxon	HAM-A	16.8±8	7.2±6.1	0.005	Wilcoxon	
Kim	2018	11	HAM-D	19.0±5.3	7.6±5.3	0.001	Wilcoxon	HAM-A	22.4±5.9	7.9±3.9	0.001	Wilcoxon	
Liu	2008	35	HAM-D	7.4±3.4	2.4±2.1	<0.001	t-test	HAM-A	17.4±3.1	4.0±2.4	<0.001	t-test	
Lopes	2014	11	BDI	23.8±13.0	15.3±13.8	0.137	Wilcoxon	BAI	19.4±15.4	9.5±13.0	0.052	Wilcoxon	
Lopes	2009	5	BDI	25.2±10.0	16.6±13.2	0.313	Wilcoxon	BAI	27.6±11.5	12.6±8.1	0.063	Wilcoxon	
Oliver	2003	18	HAM-D	NR	NR	0.415	NR	NR	NR	NR	NR	NR	NR
			BDI	20.06 (SD not reported)	11 (SD not reported)	0.038	NR	NR	NR	NR	NR	NR	NR
Rasmussen (DS)	2018	40	HAM-D	27.7±9.7	15.8±10.8 (n=32)	<0.001	regressoin	HAM-A	20.0±9.5	11.3±6.7 (n=32)	<0.001	regressoin	
Rasmussen (SS)	2018	15	HAM-D	24.3±8.7	17.1±13.1 (n=14)	0.01	regressoin	HAM-A	19.3±8.5	12.2±8.9 (n=14)	0.006	regressoin	
Ruck (bilat GK)	2008	9	MADRS	20.1±5.8	7.2±6.3	<0.05	Wilcoxon	BSA	21.3±4.4	7.4±5.7	<0.05	Wilcoxon	

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Ruck (bilat RF)	2008	12	MADRS	20.9±8.8	10.1±5.4	<0.01	Wilcoxon	BSA	15.8±6.5	10.9±5.3	p>0.05	Wilcoxon
Ruck (unilat RF)	2008	4	MADRS	25.0±8.7	12.3±3.1	p>0.05	Wilcoxon	BSA	17.3±10.1	11.0±1.7	p>0.05	Wilcoxon
Sheth (cing+)	2013	30	BDI	29.7±12.0	17.4±14.0 (n= 27)	NR	NR	NR	NR	NR	NR	NR
Sheth (cing)	2013	34	BDI	24.3±10.5	21.3±14.7 (n=32)	NR	NR	NR	NR	NR	NR	NR
Spatola	2018	10	BDI	23.4±9.9	9±6.5	0.006	Wilcoxon	STAI-T	64.2±9.4	47.2±13.9	0.022	Wilcoxon
								STAI-S	54.3±15.8	43±4.4	0.018	Wilcoxon
Yin	2018	36	HAM-D	13.8±7.4	8.3±6.5	<0.001	Wilcoxon	HAM-A	15.0±8.6	9.2±7.6	<0.001	Wilcoxon
Zhan	2014	53	HAM-D	14.8±7.3	5.0±3.7	p<0.05	NR	HAM-A	16.8±6.2	4.3±3.2	p<0.05	NR
Zhang	2013	7	HAM-D	21.5±5.8	13.9±7.9	0.008	Wilcoxon	HAM-A	22.2±6.7	13.7±5.1	0.063	Wilcoxon

LFU: last follow-up; DS: double shot group; SS: single shot repeat group; bilat: bilateral; unilat: unilateral; GK: Gamma knife; RF: radiofrequency; cing+: cingulotomy followed by a repeat cingulotomy or a subcaudate tractotomy; NR: not reported; Wilcoxon: Wilcoxon signed-rank sum tests; MH: the Mann–Whitney test; regression: linear mixed effects regression models; HAMA-D, Hamilton Depression Scale; Hamilton Anxiety Scale; BDI, Beck's depression index; BAI, Beck's anxiety index; MADRS, Montgomery- Åsberg Depression Rating Scale; BSA, Brief Scale of Anxiety; STAI-T, State-Trait Anxiety Inventory-Trait; STAI-S, State-Trait Anxiety Inventory-State.



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**Supplemental Digital Content 11. Table. Adverse-event profiles for each dataset.**

Author	Year	n	Mild and transient adverse events			Permanent or serious adverse events*	
			Event	Time to resolution	No.	Event	No.
Csigo	2010	5	urinary incontinence	temporary	2	weight gain	2
			fever	several days	3		
			sleepiness	4 days	1		
			depression	10 days	2		
D'Astous	2013	19	intracranial hemorrhage	NR	3	hemiplegia	1
			frontal syndrome	NR	5	cognitive defect	1
			urinary incontinence	NR	1		
			pneumonia	NR	1		
			urinary infection	NR	1		
			deep vein thrombosis	NR	3		
Gong	2018	14	urinary incontinence	2-3 d	2	personality changes (lack of interest, inappropriate laughter, and decreased motivation)	3
			hypersomnia	few days	6	sexual disinhibition	1
			childish behavior	3 mos	6	significant changes in weight	0
			hallucination	1 mos	4		
			sexual disinhibition	6 mos	1		
Gupta	2018	40	radiation-induced changes including cyst formation <sup>†</sup>	NR	1		
			suicidal ideations (depression)	NR	3		

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			severe mood swings	NR	2		
			mild to moderate mood swings	NR	5		
			insomnia	NR	5		
			headaches	NR	3		
			weight changes	NR	8		
Irle	1998	16	NR	NR		substance dependence (alcohol or benzodiazepines)	8
Jung	2006	17	immediate memory dysfunction	<2 mos	3	none	
Kim	2018	11	headache (during sonication > 50°C)	NR	7	no significant changes in weight	
			vestibular symptoms (nausea, vomiting or dizziness)	during sonication	5		
			anxiety	NR	3		
			stomach upset	NR	2		
Kim	2002	12	incontinence (among all surgery patients, included aggressive and depression)	NR	1		
Kondziolka	2011	3	none			none	
Liu	2008	35	urinary incontinence	3–5 days	3	ICH requiring ventricular drainage	1
			acute confusion	3–5 days	3	personality change (apathy, abulia, loss of interest)	2
			mild cognitive deficits and transient dementia	3–10 days	9	weight loss	1
						severe personality change	0
						cognitive impairment	0
						hemiparesis	0
						aphasia	0

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Lopes	2014	12	insomnia	NR	2		
			mania/hypomania	NR	2		
			visual hallucination	few hours	1		
			headache	episodic	5		
			slurred speech	2-3 d	2		
			muscle pain	4 d	1		
			nausea/vomiting	NR	7		
			abdominal discomfort	3 d	1		
			increased appetite	NR	7		
			increased weight	NR	7		
			skin paresthesia	1-4 w	9		
			pain/edema on the skin	1-2 w	4		
			sialorrhea	3 d	1		
			sore throat	7 d	1		
			memory deficits and executive function impairment	5 mos	1		
			radiation-induced perilesional edema	NR	1		
Lopes	2009	5	headaches, NSAID responsive	Days to weeks	3	considerable weight gain	1
			lightheadedness/vertigo	Days to weeks	4	episodic headaches, requiring steroids	1
			weight changes	Days to weeks	3		
			episodic nausea/vomiting	Days to weeks	2		
Montoya	2002	15 (advers)	incontinence	NR	2	incontinence	3

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			e effects reporte d in n=21, include d MDD)				
			short-term memory disorder	NR	3	short-term memory disorder	2
			headache	< 48h	1	headache	1
			generalized seizures (no seizure history)	NR	3	complex partial seizures (no seizure history)	1
			low-grade fever	< 48h	2	suicide	1
			nausea/vomiting	< 48h	common	intracranial hemorrhage	0
			somnolence	several days	6	deaths attributable to surgery	0
			apathy	several days	5		
Oliver	2003	15	postoperative wound infection	NR	1		
			hallucinations	NR	1	progressive behavior disorder (from postoperative brain edema)	1
			epileptic seizure	NR	1		
			postoperative brain edema	NR	1		
Rasmussen	2018	55	nausea and vomiting (double shot group)	intravenous dexamethasone prophylactically immediately before the	some**	brain cysts	3 <sup>c</sup>

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			procedure			
			postoperative headache	2-5 d	most**	
			significant interstitial edema (radiation-induced lesion) with headache without additional complications	1 mos	5	
			asymptomatic lacunar infarcts of the caudate	NR	6	
			manic episodes (patients with manic history)	NR	3	
Ruck (bilat GK)	2008	9	none			radiation necrosis 1
						apathy 2
						memory problems 1
						executive dysfunction 1
						edema 1
						urinary incontinence 1
						seizure 1
						sexual disinhibition 1
						urinary incontinence 1
						sexual disinhibition 1
Ruck (bilat RF)	2008	12				
Ruck (unilat RF)	2008	4			0	0
Sheehan	2013	5	no significant adverse event			no significant adverse event
Sheth	2013	64	postop memory dysfunction	days to mos	5	seizure disorder requiring AED 1
			urinary retention	days	2	subdural empyema requiring 1

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					surgical evacuation		
			worsened preexisting urinary incontinence	NR	1	pulmonary embolus	1 <sup>§</sup>
			abulia (1 after initial cingulotomy and 3 others after the later limbic leukotomy)	days	4	suicide	2 <sup>¶</sup>
			intraop seizure	< 1min	3	ventriculostomy to rule out hydrocephalus	1 (Permanent sequela of postoperative brain edema)
			postoperative seizure	NR	1	ICH	0
Spatola	2018	10	no significant adverse event	NR		weight gain	1
Yang	2014	19	NR			NR	
Yin	2018	36	NR			NR	
Zhan	2014	53	impaired memory and confusion	7-10 d	12	impaired memory and confusion	1 (still in most recent FU)
			hiccuph	3-5 d	7	mild hypersexuality	1
			urinary incontinence	1-2 w	11	personality changes (apathy, inactive and lack of interest)	2
			mild hypersexuality	1 y	2		
			personality changes (apathy, inactive and lack of interest)	1 y	1		
Zhang	2013	7	urinary incontinence	NR	1		
			limb movement deficits	several days	1		
			small epidural hematoma	NR	1		

GK: Gamma knife; RF: radiofrequency; mos: months; ICH: intracerebral hematoma; NSAID: nonsteroidal anti-inflammatory drug; MDD: major depression disorder; AED: automated external defibrillator; FU: follow-up; NR: not reported.

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\*: still present at the time of follow-up examinations

†: a short course of steroids to cure, but followed development of cyst, this patient underwent GVC after a failed cingulotomy procedure. 2 isocenters with the Gamma Knife Model Perfexion (Elekta AB) with a maximum dose of 180 Gy.

‡: 2 asymptomatic, 1 neurological symptom, all from double shot group with model C, no model U.

§: In the setting of a long plane trip home.

¶: One patient: history of major depressive disorder (preoperative BDI 41, severe depression) and Y-BOCS score unchanged at 7 months' follow-up; suicide at 10 months postoperatively. Other patient: history bipolar and severe depression (preoperative BDI 39); stable on discharge at postoperative Day 2; committed suicide 8 days later.

\*\* : in the calculation of adverse events from this study, 'most' was assumed to be 75% of the population and 'some' was assumed to be 25% of the population.

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**Supplemental Digital Content 12. Table. Incidence of adverse events as a function of the extent of coverage of internal capsule areas.**

Severe or permanent event (%)	T group	D group	Mild and transient event (%)	T group	D group
<b>Surgery-related</b>					
brain edema or cyst	1.3	3.1	deep vein thrombosis	2	0
intracerebral hemorrhage	0.7	0.0	fever	2	0
			intracerebral hemorrhage	2	0
			brain edema or cyst	0.7	6.3
			pneumonia	0.7	0
			urinary infection	0.7	0
			asymptomatic lacunar infarct	0	6.3
			skin edema	0	4.2



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			sore throat	0	1
<b>Neurological</b>					
cognitive deficits	2.7	0.0	cognitive deficits	17.3	2.1
urinary incontinence	1.3	0.0	urinary incontinence	12.7	0
disturbances of consciousness	0.7	0.0	disturbances of consciousness	10	0
hemiplegia	0.7	0.0	hiccough	4.7	0
seizure	0.7	0.0	seizure	0.7	0
headache	0.0	1.0	headache	0	58.3
			vestibular symptoms	0	29.2
			paresthesia	0	9.4
			vertigo	0	4.2
			abdominal discomfort	0	3.1
			muscle pain	0	1
<b>Neurobehavioral</b>					
personality changes	6.0	0.0	behavior disorder <sup>†</sup>	10.7	11.5

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behavior disorder <sup>†</sup>	3.3	0.0	personality changes	4.0	0.0
			mood changes <sup>‡</sup>	1.3	8.3
			sialorrhea	0.0	1.0
<b>other</b>					
weight change	2.0	0.0	weight change	0.0	11.5
<b>Median incidence of</b>	1.3	0.0		0.7	1
<b>reported adverse</b>	(0.0–6.0)	(0.0–3.1)		(0.0–17.3)	(0.0–58.3)
<b>events (range)</b>					

150 patients in T group, 96 patients in D group and 5 patients in S group provided information about adverse events. No adverse event was found in S group.

<sup>†</sup>behavior disorder: including sexual disinhibition, insomnia, increased appetite, hypersomnia, somnolence, slurred speech and childish behavior.

<sup>‡</sup>mood changes: including depression, anxiety, and mania.