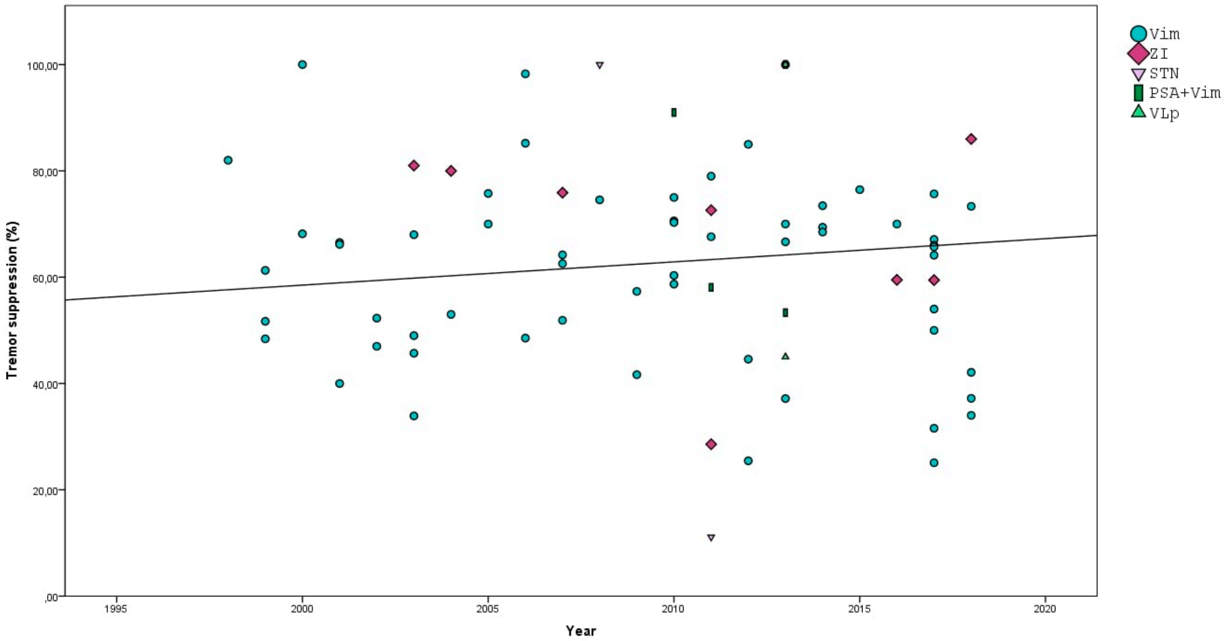
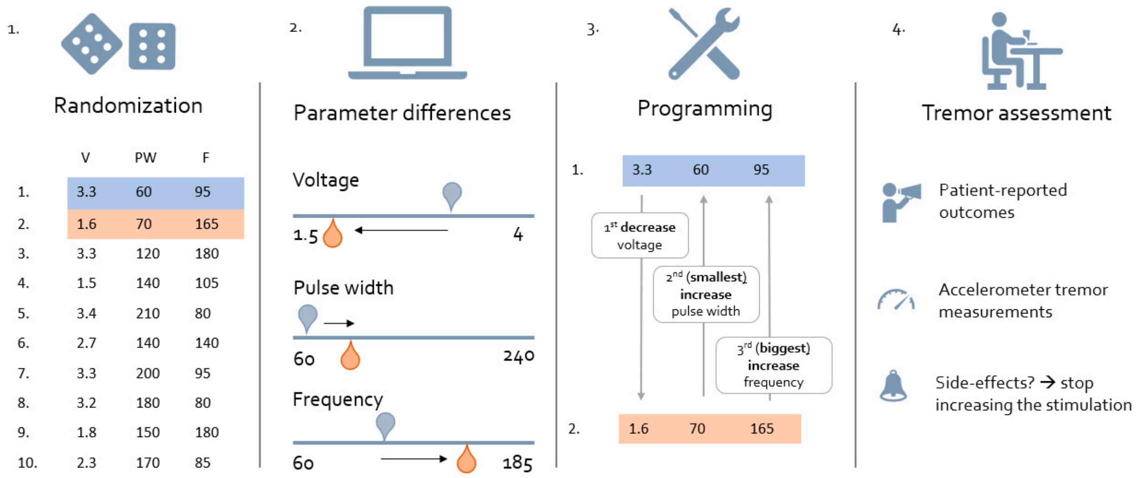


Supplementary Figure 1. Overall tremor outcomes. The average tremor suppression achieved with ET-DBS from 1987 until present was 62.98% ± 16%, r = 0.16, $p < 0.001$. Abbreviations: PSA = posterior subthalamic area, STN = subthalamic nucleus, Vim = ventral intermediate nucleus of the thalamus, VLp = ventrolateral thalamic nucleus, ZI = zona incerta.



Supplementary Figure 2. Experimental Set-up. In this example, the successive steps for generating and testing the stimulation parameters for participant ET7 are depicted and described. 1. Randomization. The ranges for the 10 random values of voltage, pulse width and frequency were set, as following: voltage 1.5–4 V, pulse width 60–240 µs, and frequency 60–185 Hz. From here, 10 values for voltage, pulse width and frequency were generated at random, using a custom written MATLAB script. 2. Parameter differences. The transition between the 10 combinations was done systematically. Namely, (i) the parameters that needed to be lowered were identified and adjusted first; (ii) if the remaining parameters needed to be increased, the one requiring the smallest increase was adjusted next, followed by the one requiring the bigger increase. For example, let us consider the transition between the first combination, depicted in blue, and the second, in orange. The adjustments needed to transition from the blue to the orange combinations can be summarized as follows:

voltage needs to be lowered and both pulse width and frequency need to be increased. 3. Programming. Given that parameters needing to be lowered are the first to be adjusted, the voltage was changed first. Second, we considered the remaining parameters, which both needed to be increased (in this case, pulse width and frequency). Pulse width needed to be increased from 60 to 70 μs, which required one increment (1 × 10 μs). Frequency needed to be increased from 95 to 165 Hz, requiring 14 increments (14 × 5 Hz). Thus, the parameter requiring the smallest increase, in this case pulse width, was changed first followed by the bigger increase, in this case, the frequency. 4. Tremor assessment. For each combination, tremor was rated by patients, as well as objectively quantified with accelerometry. During the entire process, patients were requested to report the emergence of side effects, beyond which stimulation would not be further increased. This process was iterated 10 times in each patient. Abbreviations: V = voltage, PW = pulse width, F = frequency.

Supplementary Table 1. Characteristics of studies included in the meta-analysis.

References	*N*	DBS target	Voltage ± SD	Pulse width ± SD	Frequency ± SD	Follow up ± SD	Tremor reduction (%)
Benabid et al., 1987 [1]	6	Vim	n.a.	n.a.	130	n.a.	n.a.
Blond et al., 1992 [2]	4	Vim	n.a.	n.a.	130	11 ± 5	n.a.
Ondo et al., 1998 [3]	12	Vim	2.7 ± 0.9	256.4 ± 91.6	168.9 ± 16.4	3	82
Hariz et al., 1999 [4]	36	Vim	1.9 ± 0.74	73.3 ± 30	163.7 ± 17.6	3	48.4
Limousin et al., 1999 [5]	37	Vim	2.17 ± 0.81	92.73 ± 39.26	156.36 ± 24.72	3	51.7
Kumar et al., 1999 [6]	9	Vim	2 ± 1	195 ± 75	115 ± 15	14.9 ± 8.1	61.28
Obwegeser et al., 2000 [7]	27	Vim	n.a.	n.a.	n.a.	n.a.	68.17
Schuurman et al., 2000 [8]	7	Vim	n.a.	n.a.	n.a.	n.a.	100
Ceballos-Baumann et al., 2001 [9]	6	Vim	2.53 ± 0.76	115 ± 74.49	155.83 ± 25.18	min 4	66.53
Koller et al., 2001 [10]	25	Vim	3.4 ± 0.7	78.8 ± 37.3	157.5 ± 28.2	3	40
Ondo et al., 2001 [11]	11	Vim	2.6	212	149.5	3	66.17
Fields et al., 2002 [12]	40	Vim	3.32 ± 0.65	86.57 ± 24.33	150.07 ± 18.56	3	52.29
Hariz et al., 2002 [13]	27	Vim	n.a.	n.a.	n.a.	12.5 ± 4.7	47
Bryant et al., 2003 [14]	16	Vim	2.74 ± 0.99	119 ± 44	160 ± 28.2	13	33.9
Kumar et al., 2003 [15]	5	Vim	n.a.	n.a.	n.a.	12	68
Murata et al., 2003 [16]	8	Zi	1.99 ± 0.9	60	130	6	81
Rehncrona et al., 2003 [17]	19	Vim	2.4 ± 0.9	91.6 ± 33.9	171.6 ± 19.2	24	49
Sydow et al., 2003 [18]	19	Vim	2.3 ± 0.9	85.9 ± 28.2	163.2 ± 24.1	12	45.69
Vaillancourt et al., 2003 [19]	6	Vim	2.9 ± 1.5	80 ± 24.5	185	min 3	n.a.
Woods et al., 2003 [20]	49	Vim	3.34 ± 0.64	92.23 ± 32.26	148.05 ± 25.46	n.a.	n.a.
Papavassiliou et al., 2004 [21]	37	Vim	2.7 ± 0.9	98.5 ± 27	184 ± 7.5	26	53
Plaha et al., 2004 [22]	4	Zi	1.8 ± 0.2	108.8 ± 14.4	170 ± 11.5	12	80
Ushe et al., 2004 [23]	16	Vim	3.4 ± 0.5	67.5 ± 13.4	185	30.3 ± 17.8	n.a.
Capelle et al., 2005 [24]	2	Vim	2.8 ± 0.25	180 ± 51.96	146.66 ± 12.58	48	n.a.
Lee and Kondziolka, 2005 [25]	18	Vim	n.a.	n.a.	n.a.	27 ± 10	75.75
Putzke et al., 2005 [26]	22	Vim	2.8 ± 1.1	80.9 ± 33	158.3 ± 30.8	3	70
Chen et al., 2006 [27]	13	Vim	3.78 ± 1.13	110.76 ± 57.94	181.92 ± 11.09	20.48 ± 16.97	n.a.
Kronenbuerger et al., 2006 [28]	4	Vim	n.a.	n.a.	n.a.	3	48.54
Kuncel et al., 2006 [29]	9	Vim	2.9 ± 0.86	87.85 ± 21.9	150.35 ± 24.21	20.86 ± 17.62	98.26
Pahwa et al., 2006 [30]	22	Vim	3.26 ± 0.67	111	155	3	n.a.

	22	Vim	3.55 ± 1.09	111	155	60	50.42
Ushe et al., 2006 [31]	11	Vim	3.3 ± 0.5	70 ± 15	185	min 4	85.2
Blomstedt et al., 2007 [32]	19	Vim	1.8 ± 0.7	68 ± 14	164 ± 15	13 ± 4.9	51.89
Earheart et al., 2007 [33]	11	Vim	3.7 ± 0.62	81.8 ± 23.6	185	47.6 ± 26.4	62.55
Herzog et al., 2007 [34]	10	Vim	2.4 ± 0.76	67 ± 13.11	141.76 ± 20.07	14.14 ± 10	64.2
Plaha et al., 2007 [35]	6	Zi	2.48 ± 1.04	120 ± 42.42	147.14 ± 25.63	57.6	75.9
Lind et al., 2008 [36]	3	STN	1.76 ± 0.7	90	131.6 ± 2.88	104	100
Pilitsis et al., 2008 [37]	28	Vim	3.21 ± 1.78	61.6 ± 9.43	177.3 ± 18.55	40 ± 17	74.55
Earheart et al., 2009 [38]	13	Vim	3.6 ± 0.9	87.8 ± 31.1	181 ± 13.9	50.8 ± 30.6	41.66
Kronenbuerger et al., 2009 [39]	12	Vim	2.7 ± 0.9	98.2 ± 55.5	145.9 ± 16.7	n.a.	57.33
De Los Reyes et al., 2010 [40]	1	Vim	2.6	90	185	24	75
DiLorenzo et al., 2010 [41]	1	Vim	2.8	60	130	144	n.a.
Fasano et al., 2010 [42]	11	Vim	n.a.	n.a.	n.a.	24.7 ± 20.3	70.6
Fytagoridis et al., 2010 [43]	27	PSA	2.2 ± 0.9	65 ± 11	164 ± 21	12	91
Graff-Radford et al., 2010 [44]	31	Vim	2.8	91	151	6	60.33
Sitburana et al., 2010 [45]	11	Vim	3 ± 0.8	60	170	6	58.7
Zhang et al., 2010 [46]	35	Vim	2.89 ± 0.74	93.4 ± 20.3	173.7 ± 21.2	24 ± 12	n.a.
Barbe et al., 2011 [47]	23	Vim	2.4 ± 1.01	66.97 ± 21.55	133.72 ± 14.6	49 ± 39	67.61
Blomstedt[1] et al., 2011 [48]	1	Zi	0.9	60	185	3	28.57
	2	STN	2.45 ± 0.05	60	165 ± 28.28	3	11.11
Blomstedt[2] et al., 2011 [49]	15	Vim	n.a.	n.a.	n.a.	28 ± 24	55.33
	34	PSA	n.a.	n.a.	n.a.	12	58.09
Mandat et al., 2011 [50]	18	Vim	1.75 ± 1.06	80	130	3	79
Plaha et al., 2011 [51]	15	Zi	2.65 ± 1.2	105 ± 16	150 ± 22.9	48	72.6
de Oliveira et al., 2012 [52]	26	Vim	n.a.	n.a.	n.a.	57.14 ± 30	25.45
Favilla et al., 2012 [53]	28	Vim	n.a.	n.a.	n.a.	6	44.58
Nazzaro et al., 2012 [54]	78	Vim	n.a.	n.a.	n.a.	12	85
Chang et al., 2013 [55]	1	Vim	n.a.	n.a.	n.a.	6	100
	1	PSA	n.a.	n.a.	n.a.	6	100
	2	PSA + Vim	n.a.	n.a.	n.a.	6	100
Shih et al., 2013 [56]	12	Vim	2.7 ± 0.8	78 ± 28.9	155.5 ± 26.9	55.9 ± 34.4	n.a.
	33	Vim	3.1 ± 0.7	112 ± 47.8	184 ± 1.9	55.9 ± 34.4	n.a.
Baizabal-Carvallo et al., 2013 [57]	13	Vim	3.25 ± 0.81	114 ± 41.9	161.7 ± 23.9	132.54 ± 15.3	37.16
Cagnan et al., 2013 [58]	10	Vim	2.43 ± 0.67	78 ± 15.49	145 ± 24.15	6	70

Pedrosa et al., 2013 [59]	16	Vim	2.47 ± 1.11	76.88 ± 23.8	128.13 ± 8.54	50.4 ± 37.2	n.a.
Ramirez-Zamora et al., 2013 [60]	1	Vim	3.5	90	185	3	n.a.
Børretzen et al., 2014 [61]	30	Vim	3.5 ± 1.2	90 ± 30	181 ± 50	66 ± 30	n.a.
Coenen et al., 2014 [62]	11	Vim	3 ± 1.4	76 ± 16	173 ± 12	9 ± 6	69.4
Ehlen et al., 2014 [63]	13	Vim	3.1 ± 1.43	70.75 ± 14.98	149.74 ± 32.75	36.24 ± 33.96	68.5
Groppa et al., 2014 [64]	7	Vim	2.4 ± 0.6	62.5 ± 8.6	134.2 ± 14.4	19.7 ± 14.4	73.45
Mücke et al., 2014 [65]	16	PSA + Vim	2.39 ± 0.96	64.01 ± 10.61	130.25 ± 7.9	3	n.a.
Pedrosa et al., 2014 [66]	17	VLp	2.46 ± 0.96	75.5 ± 26	129 ± 8.61	55.2 ± 38.4	n.a.
Huss et al., 2015 [67]	70	Vim	n.a.	n.a.	n.a.	13 ± 10	76.47
Becker et al., 2016 [68]	16	PSA + Vim	2.6 ± 1.8	75 ± 15.5	130.6 ± 19.56	35.4 ± 15.5	n.a.
Ehlen et al., 2016 [69]	13	Vim	3.16 ± 1.47	60	157.5 ± 55.63	42 ± 38.28	n.a.
Fytagoridis et al., 2016 [70]	50	Zi	2.1 ± 0.8	64.6 ± 15.6	160.6 ± 21.6	12	59.5
Gibson et al., 2016 [71]	10	Vim	1.74 ± 0.6	60	135 ± 15.81	3	70.3
Ramirez-Zamora et al., 2016 [60]	4	Vim	2.35 ± 0.35	82.5 ± 15	181.25 ± 7.5	12 ± 5.71	n.a.
Reich et al., 2016 [72]	10	Vim	2.27 ± 0.76	61.65 ± 7.99	157.5 ± 21.68	24 ± 7	70
Allert et al., 2017 [73]	1	Vim	5.25 ± 0.25	90	130	12	n.a.
Cagnan et al., 2017 [74]	6	Vim	2.15 ± 0.65	84.28 ± 52.23	152.14 ± 27.66	6	n.a.
Chen et al., 2017 [75]	44	Vim	2.2 ± 0.7	72.45 ± 17.65	170.55 ± 21.3	12	67.1
Chockalingam et al., 2017 [76]	13	Vim	n.a.	n.a.	n.a.	min 3	25.09
Cury et al., 2017 [77]	35	Vim	n.a.	n.a.	n.a.	12	66
Ehlen et al., 2017 [78]	13	Vim	3.1 ± 1.39	60	146.92 ± 31.66	34.08 ± 28.08	64.13
Fiechter et al., 2017 [79]	7	Vim	3 ± 0.7	180 ± 40	141.5 ± 19.7	13.5 ± 8.5	54
Haddad et al., 2017 [80]	16	Vim	2.41 ± 0.48	67.6 ± 10.96	133 ± 12.64	57 ± 21	65.7
Holslag et al., 2017 [81]	19	Vim	2.4 ± 1	73 ± 15	184 ± 1.6	127.2 ± 54	31.57
	25	Zi	2.4 ± 0.9	70 ± 17	177 ± 19	69.6 ± 36	59.45
King et al., 2017 [82]	20	Vim	2.6 ± 0.9	66 ± 13	155 ± 27	12	min 50
Wharen et al., 2017 [83]	127	Vim	2.58 ± 1.73	96	164 ± 44	12	75.68
Akram et al., 2018 [84]	5	Vim	2.2	60	154 ± 25	23.6 ± 12	34
De Jesus et al., 2018 [85]	11	Vim	2.74 ± 0.76	100 ± 25	156.81 ± 24.31	41.54 ± 41.71	42.1
Mücke et al., 2018 [86]	12	Vim	2.3 ± 1.3	66.25 ± 12.44	128.75 ± 10.45	60.92 ± 12.31	73.33

Abbreviations: n.a. = not available; PSA = posterior subthalamic area; STN = subthalamic nucleus; Vim = ventral intermediate thalamic nucleus; VLp = ventrolateral thalamic nucleus.

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