

Ultrasound neuromodulation; a review of results, mechanisms and safety: Supplementary Information

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This document contains the tabulated data extracted from the CNS and PNS ultrasonic neuromodulation studies, respectively. Where possible, parameters were directly taken from the literature and these are marked in the tables in black. If additional parameters could be calculated from the published parameters, this was done and these parameters are marked in red.

The majority of calculations were converting between intensities and pressures. We did this using the following equation assuming a plane time harmonic wave,

$$I = \frac{p^2}{2\rho_0 c_0}, \quad (1)$$

where p is the pressure amplitude, ρ_0 was taken to be 1046 kg/m^3 (Hasgall et al., 2015) and c_0 was 1562 m/s (Duck, 1990). We also converted between intensities over different time scales (temporal-averaged, burst-averaged and pulse-averaged) using the duty cycle information given in the reference.

Studies have been split into multiple rows where necessary in order to account for different experiments and ultrasound sequences.

If continuous wave ultrasound was used, the burst parameters are undefined and therefore marked with a dash.

References

Hasgall PA, Di Gennaro F, Baumgartner C, Neufeld E, Gosselin MC, Payne D, Klingensack A, Kuster N. ITIS Database for thermal and electromagnetic parameters of biological tissues. Version 3.0, www.itis.ethz.ch/database.

Duck, FA. Physical properties of tissue: A comprehensive reference book. 1990;73–124.

Study	Category	Organism	f (MHz)	SPTA (mW/cm ²)	SPBA (W/cm ²)	ISPPA (W/cm ²)	p (MPa)	BD (ms)	BI (g)	PL (ms)	PRF (Hz)	BDC (%)	TDC (%)	N	TL (s)	MI	Histology	Damage	Notes
Lejon et al., 2018	H	Human (MI)	0.5			0.44	0.12	500	8-10	0.36	1000	36	300	300	100				
Lejon et al., 2018	H	Human (Thalamus)	0.5	2.15		0.44	0.12	500	8-10	0.36	1000	36	300	300	100				
Lee et al., 2016a	H	Human (VI)	0.27	0.85-5.8		1.7-11.6	0.24-0.62	300	2.5, 13	0.36	1000	36	50	50	50				Dual single-element transducers.
Lee et al., 2016b	H	Human (SI, S2)	0.21	3.5-4.4		7-8.8	0.48-0.54	500	7	1	500	50	50	50	50				
Al et al., 2016	H	Human (SI)	0.5	2.16		6	0.44	500	12.0-14	0.36	1000	36	90	90					
Lee et al., 2015	H	Human (SI)	0.86	3		6	0.44	500	10.0-14	0.36	1000	36	50	50					
Muehle et al., 2014	H	Human (SI)	0.25	0.25-1.25		0.5-2.5	0.13-0.29	300	3	1	500	50	50	50	50				
Lejon et al., 2014	H	Human (SI)	0.5	2.12		5.9	0.44	500	6	0.36	1000	36	120	120					
Hannaford et al., 2013	H	Human (Posterior Frontal Cortex)	8	152		8.00E-06	5.00E-04	500	6	0.36	1000	36	120	120	15	0.7			LOGiGe imaging probe p1, ISPPA estimated from MI value, denoting and accounting for skull.
Kubanek et al., 2017	L	Monkey (Frontal Eye Field)	0.27					300											
Wanzen et al., 2017	L	Monkey (Frontal Eye Field)	0.32			1.9156	0.24, 0.41	100						386, 400					
Delpeux et al., 2013	L	Monkey (Frontal Eye Field)	0.22			4	0.35												
Delpeux et al., 2016	L	Pigs (Thalamus)	0.32			30	0.99			43.7	10			40	40				Assuming ISPPA = ISA
Delpeux et al., 2016	L	Pigs (Thalamus)	0.71			30	0.99			43.7	10			40	40				Assuming ISPPA = ISA
Delpeux et al., 2016	L	Pigs (Thalamus)	1.145			30	0.99			43.7	10			40	40				Assuming ISPPA = ISA
Demélie et al., 2018	S	Rat	0.23			4.6	0.38		3	100				52	52				Quoted pressures do not correspond with intensities. Assumed quoted intensity correct.
Demélie et al., 2018	S	Rat	0.23			2.3-4.6	0.27-0.38		3	100				52	52				Quoted pressures do not correspond with intensities. Assumed quoted intensity correct.
Lee et al., 2016	L	Sheep (SM1)	0.25	1.7-5.9		3.4-11.6	0.34-0.62	300	5	1	500	50	50	100	100				Damage >500 times every second at moderate (ISPPA 0.6-1.0 W/cm ² , MI=0.9-1.2).
Fisher et al., 2018	S	Mouse (Cortex)	0.25	0.85-7.15		0.74-14.3	0.24-0.68	300	1	0.5	1500	30	50	100-600	100-600				
Han et al., 2017	S	Rat (Motor Cortex)	0.35	0.4-4.67		1.16-15.35	0.06-0.69	66.67	2	0.23	1500	34.5	1500	34.5	1500	34.5			
Han et al., 2017	S	Rat (Motor Cortex)	0.35	0.4-4.67		1.16-15.35	0.06-0.69	66.67	2	0.23	1500	34.5	1500	34.5	1500	34.5			
Han et al., 2017	S	Chimpanzee (Caudate)	0.35	0.02		0.02	0.04	66.67	2	0.23	1500	34.5	1500	34.5	1500	34.5			
Guo et al., 2017	S	Guinea Pig (A1, S1)	0.22			0.25	0.1	300		0.10									A1 activation.
Guo et al., 2017	S	Guinea Pig (A1, S1)	0.22			1.22	0.2	10		0.1-10	10-1500								First spike latency experiment.
Guo et al., 2017	S	Guinea Pig (A1, S1)	0.22			1.22	0.2	10		0.1-10	10-1500								Auditory nerve transection.
Guo et al., 2017	S	Guinea Pig (A1, S1)	0.22			1.22	0.2	10		0.1-10	10-1500								Indirect somatosensory activation.
Guo et al., 2017	S	Guinea Pig (A1, S1)	0.22			1.22	0.2	10		0.1-10	10-1500								Cochlear fluid removed.
Shao et al., 2017	S	Mouse (Visual Cortex)	0.5	0.039-4.2		1.81	0.68	80	0.2	0.2	1500	30	30	30	30				USIECS interaction, ISPPA calculated from quoted table.
Shao et al., 2017	S	Rat (Motor Cortex)	0.2	4500		30	60 (SPTP = 100)	1.81	3	10	0.5	1000	50	100	50	3.1			EMG latency, ISPPA calculated from quoted table.
Shao et al., 2017	S	Rat (Motor Cortex)	0.25	9		30	60 (SPTP = 100)	1.81	3	10	0.5	1000	50	100	50	3.1			EMG latency, ISPPA calculated from quoted table.
Lee et al., 2017	S	Rat	0.23			0.5-1.1	0.1-1.1												
Li et al., 2016	S	Mouse (Motor Cortex)	1	130-230		2.3	4.6	300	3	0.5	1000	50	5	60	60				
Li et al., 2016	S	Mouse (Motor Cortex)	5	130-230		2.3	4.6	300	3	0.5	1000	50	5	60	60				
Kamruza et al., 2016	S	Mouse (Motor Cortex & Cognitive Areas)	1.9	44-1-275.4		22-137.2	1.2-3	1000	2	1	1000	50	5	10	20				
Davies et al., 2016	S	Rat	1.4	1.4		6.8	0.42	1000	2	0.2	1050	21	100	200	200				
Yu et al., 2016	S	Rat	0.5	0.1-0.6 mW/cm ²		0.7-4.6 mW/cm ²	18.3-45.9 Hz	5-200	3	0.07	2000	14	14	100	200				
Moore et al., 2015	S	Mouse	0.35			0.07-0.23	0.08	10	0.14	0.214	2000	42.8		10 min					
Moore et al., 2015	S	Mouse (Motor Cortex)	0.3	0.3		0.1-0.5	0.06-0.34			66.7-133.3									
Moore et al., 2015	S	Mouse (Motor Cortex)	0.6	0.6		0.1-0.5	0.06-0.34			66.7-133.3									
Moore et al., 2015	S	Mouse (Motor Cortex)	1.4	1.4		0.02-9.4	0.02-9.4			80									
Moore et al., 2015	S	Mouse (Motor Cortex)	1.4	1.4		0.02-9.4	0.02-9.4			80									
Moore et al., 2015	S	Mouse (Motor Cortex)	2.9	2.9		0.04-3.1	0.04-3.1			80									
Moore et al., 2015	S	Mouse (Motor Cortex)	2.9	2.9		0.04-3.1	0.04-3.1			80									
Moore et al., 2015	S	Mouse (Motor Cortex)	2.9	2.9		0.04-3.1	0.04-3.1			80									
Kim et al., 2015	S	Rat (Visual Cortex)	0.35	50-250		1-5	0.4			0.5	20-166		1-8.3	150					
Kim et al., 2014	S	Mouse (Motor Cortex)	0.35			2.45-11.2	4.91-22.4	0.40-81	200-400	2	0.25-5	60-2800	30-70		1.38				
Kim et al., 2014	S	Rat (Motor Cortex)	0.35			7.73	0.5	150		150									
Kim et al., 2014	S	Rat (Motor Cortex)	0.65			3.5-5	7-10	0.48-0.57	300	0.5-5	100-1000	50	50						
Kim et al., 2014	S	Rat (Thalamus)	0.35	3.5-4.5		7-9	0.48-0.54	300	2	0.5	1000	50	50	40 min	40 min				PL and PDC variation.
Kim et al., 2014	S	Rat (Motor Cortex)	0.5	0.15-5.25		0.5-17.5	0.19-0.76	58.7	1	0.2	1500	30	10	10	10				Planar transducer.
Kim et al., 2014	S	Rat (Motor Cortex)	1.75 & 2.25	1-8		3.3-26.7	0.18-0.93	14.7-58.7	1	0.1-0.2	1500	15-30	10	10	10				Planar transducer.
Younan et al., 2013	S	Rat (Motor Cortex)	0.32			17.5	1.2	250	0.23	0.23	2000	50	50	2.2	2.2				mFU: two frequencies separated by 500 kHz.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Incorporates correction factor for standing waves.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Acoustic intensity sweep.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Sonication duration.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Frequency sweep.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Pulsed v. CW.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Pulsed.
Younan et al., 2013	S	Mouse (Motor Cortex)	0.5			0.16-8	0.4-0.51		>5	80									Full CW parameter sweep.
Yang et al., 2012	S	Rat (Thalamus)	0.65	175		3.5	0.35			0.5	100			20 min					
Yang et al., 2012	S	Rat (Thalamus)	0.65	175		3.5	0.35			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Somatomotor & Visual Areas)	0.69			1.8-6.3	3.3-12.6	0.5-2		0.65-50	10-1000	50							
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat (Thalamus)	0.69			2.6	0.27			0.5	100			20 min					
Yoo et al., 2011a	S	Rat																	

S	Cell (LGN)	43	50-90	1.71	200	20-120	√	x	No histologically observed legions.
Fry et al., 1998	Cat LGN	43	50-90	1.71	200	20-120	√	x	No histologically observed legions.
Prato et al., 2018	Cell cultures	10	11-30.6	0.641.0	200	50			
Kubarek et al., 2017	C. Elegans	5.5-15.4	11-30.6	0.641.0	200	50			
Menz et al., 2017	Isolated Salamander Retina	43	0-120	0-1.98	1-1000				
	Isolated Salamander Retina	15	0-120	0-1.98	1-1000				
	Isolated Salamander Retina	0.5	1.6	0.23	100				
Kim et al., 2017	Hippocampal slice		780 uW/cm2	11.52 kPa	2	2.087 us	1.16 KHz	3 min	Preliminary tests with additional high frequency modulation.
Menz et al., 2013	Isolated salamander retina	43	30	1000	2	1000	10 Hz - 1 MHz		
	Isolated salamander retina	0.5	0.05-60	0.04-1.4	2	1000	0.5	745 min	
Choi et al., 2013	Hippocampal neurons	0.5	16.1-62.8	0.8-2.0	5000	6	0.02	10-100	0.02-0.2
	Hippocampal slice	0.44	0.023	0.31	22.7 us	0-100 (sweep)	5		LILFU-1.
	Hippocampal slice	0.44	0.023	0.31	22.7 us	10	0.5		Patch clamp recordings
	Hippocampal slice, ex-vivo mouse brain	0.44	0.023	0.31	0.18	10	0.3		Transients.
	Hippocampal slice	0.44	0.023	0.31	22.7 us	0.002	36-48 h		Membrane integrity test, LILFU-1 every 8 min for 36-48 h.
	Hippocampal slice	0.67			74.5	10	0.57		Synaptic vesicle release.
Khrachche et al., 2008	Hippocampal slice	7.75	50-150 (1.1P)	1.28-2.21	2	2	0.55		
Bachold et al., 1998	Hippocampal slice	0.5	140-110	1.89	100 ns	200 KHz	5 min		Assuming quoted ISFTA = ISPPA
Finnald et al., 1991	Hippocampal slice	0.75	80	1.62	6 us	150 KHz	2-15 min		Assuming quoted ISFTA = ISPPA

Study	Category	Organism	f (MHz)	I_SPTA (mW/cm2)	I_SFBA (W/cm2)	I_SPPA (W/cm2)	p (MPa)	BD (ms)	BI (s)	PL (ms)	PRF (Hz)	BDC (%)	TDC (%)	N	TL (s)	MI	Histology	Damage	Notes	
Lee et al., 2014	H	Human (Finger tip)	0.35	3-100	0.003-0.1	0.3-10	0.118-1.148	10 s	0.1-1	10-100	10-100	1	0.13-0.71	1	0.1-1	0.1-0.97	x		Pain thresholds	
Legon et al., 2012	H	Human (Finger tip)	0.35	3-100	0.003-0.1	0.3-10	0.21-1.145	10 s	0.1-1	10-100	10-100	1		1	0.1-1	0.13-0.71	x		Pain thresholds	
Dickey et al., 2012	H	Human (Finger tip)	1.117	-	11.8	84.3	1.66	500	12	2	70	14		3x50						
Gavrilov et al., 1977a	H	Human (Hand, forearm)	0.48	-	54.8	54.8	1.34	1000	12	10	100	100		3x50						
Downs et al., 2018	S	Mouse (Sciatic Nerve)	3.57	348-994	207-994	2.6-5.7	0.8-10.5	1000	35-100	1000	1000	35-100								Successful parameters for EMG activity
Casella et al., 2017	S	Mouse (Sciatic Nerve)	3.57	42.7-155	122-442	2-3.8	1	1000	95	1000	1000	90								Positive control
Ni et al., 2016	S	Rat (Micturition Reflex)	0.25	2.1	28	0.95	300	2	0.252	2000	2000			5-15 min						
Juan et al., 2014	S	Rat (Vagus Nerve)	1.1	0.2	13.6-93.4	74.8-102.8	1.83	15 s	-	200-1000	18.2-90.9			1	1 min/dsly	1.43-1.67				
Tych et al., 2013	S	Rat (Sciatic Nerve)	1.15	-	50-283	3.04	-	200	-	200	200									
Kim et al., 2012	S	Rat (Abducens Nerve)	0.35	4.6	8.6	0.53	200	1	0.36	1500	1500	54		10					8.6W/cm2 min for response. No responses.	
Foley et al., 2008	S	Rat (Sciatic Nerve)	5.7	0.27-10.8	0.5-20	0.8	200	1	0.36	1500	1500	54		10						
Ellisman et al., 1987	S	Rat (Sciatic Nerve)	5.7	-	2255-7890	16.1	-	5 s	-	5 s	5 s									
Gavrilov et al., 1977b	S	Rat (Dorsal Nerve Root)	2.4	-	1.9 (ISPTP=8.7)	0.53	-	0.1	-	0.1	-	-							Nerves in developing myelination stage	
Lele et al., 1963	S	Earthworm (Giant Axon)	0.6	-	41	1.16	-	1	500	1	500									
Young & Henneman, 1961	S	Earthworm (Giant Axon)	0.9	-	139.2	2.13	-	3	1400-2000	3	1400-2000									
Wahab et al., 2012	S	Cat (Saphenous Nerve)	2.7	-	420	3.7	-	100-2000	-	100-2000	-									
Wright et al., 2017	I	Crab Leg Nerve Axon	0.67	10-84.5	20-169	1.8-2.4	8	15-75	50 us	100	100	0.5								
Colucci et al., 2009	I	Bullfrog (Sciatic Nerve)	1.986	115-281	230-562	2.9-4.7	8	30 s	1.5	1-10	10-20									
Tsui et al., 2005	I	Bullfrog (Sciatic Nerve)	3.5	84.5	17-475	0.7-4.2	300	1.5	1-10	10-20	10-20									
Mihran et al., 1990	I	Frog (Sciatic Nerve)	4	-	1-3 W	0-1.14	-	5 min	-	5 min	-									
Fry et al., 1950	I	Crayfish (Ventral Nerve)	0.98	35	1.07	2.8-43.5	0.5	0.5	0.5	0.5	0.5								Damage at higher intensities	