Neuron, Volume *108*

Supplemental Information

Ultrasound Technologies for Imaging and Modulating Neural Activity

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Supplementary Table 1 – Studies of Ultrasonic Neuromodulation

Study/ Exp. model	Target/ Readout	Neuromodulation effect	Parameters			
			Freq. (Mhz)	ISPPA (W/cm^2)	SD (ms)	PRF (kHz)
(Tyler et al., 2008)/ Brain slice and ex vivo mouse brain	CA1/ Optical imaging	Direct Calcium and sodium responses	0.44, 0.67	2.9	0.25 ms -15 sec	0.01
(Tufail et al., 2010)/ mouse	M1, hippocampus/ Electrode, EMG	Increase in M1 MUA, EMG and LFPs,	0.25-0,5	0.075-0.229	26-333	1.2-3
(Yoo et al., 2011)/ Rabbit	V1, M1/ EEG, BOLD	Increase in M1 BOLD signal, decrease VEP	0.69	3.3-12.6	500 ms - 18 sec	0.1-1
(Min et al., 2011)/ Rat	thalamic area/ EEG	Suppression of induced epileptic EEG signals	0.69	2.6	3 min	0.1
(Kim et al., 2012)/ rat	abducens/ video recording	Ipsilateral eyeball movement	0.35, 0.65	0.5-20	200	1.5
(King et al., 2013)/ mouse	Basal ganglia, motor cortex/ EMG	EMG responses after 55-170 ms latency	0.25-0.6	0.1-100	20-320	0.01-3
(Younan et al., 2013)/ rat	cortex/ video recording, EMG	Motor responses of tail, whisker and eyeball	0.32	7.5	250	2
(Deffieux et al., 2013)/ monkey	FEF/ antisaccade task	Increase in antisaccade latency	0.32	4	100	Cw
(Kim et al., 2014)/ rat	Somatomotor area/motor sensor	Motor response of tail	0.35 ,0.65	4.9-5.6	300	0.25
(Mueller et al., 2014)/ human	S1/ EEG	Change in phase distribution of EEG recorded from SEP	0.5	23.87	500	1
(Legon et al., 2014)/ human	S1/ EEG, sensory discrimination task	Suppression of SEP and enhanced performance on the task	0.5	23.87	500	1
(Lee et al., 2015)/ human	S1/ EEG, survey	Increase in SEP and tactile sensations on hands	0.25	3	300	0.5
(Lee et al., 2016a)/ Sheep	SM1, V1/ EMG, EEG	Contralateral EMG responses, increase in VEP	0.25	14.3	300	0.5
(Ye et al., 2016)/ Mouse	motor cortex/ EMG	Decrease EMG response rate with higher freq.	0.3-2.9	0.1-127	80	Cw

(Lee et al., 2016b)/ human	V1/ BOLD, EEG, survey	Increase in VEP and others and phosphene perception	0.27	16.6	300	0.5
(Wattiez et al., 2017)/ monkey	FEE/ electrode	Increase in SEF	0.32	1.9, 5.6	100	Cw
(Leo Ai, 2018)/ human	M1/ BOLD	Increase in volume of the M1 thumb	0.5	16.95	500	1
(Yang et al., 2018)/ monkey	3a,3b/ BOLD	Increase in BOLD at target and others	0.25	29.5	300	2
(Legon et al., 2018a)/ human	thalamus/ EEG, discrimination task	Suppression of SEP and worse discrimination task	0.5	7.03	500	1
(Legon et al., 2018b)/ human	M1/ EMG, stimulus task	Decrease EMG amplitude and faster reaction time	0.5	17.12	500	1
(Dallapiazza et al., 2018)/ swine	thalamus/ EEG	Suppression of SEP	0.22-1.14	20	40 sec	0.01
(Lee et al., 2018)/ rat	motor cortex/ video recording	Motor responses of tail, limb, whiskers and head from awake rats	0.6	2.3-14.9	300	0.1
(Sharabi et al., 2018)/ rat	olivo cerebellar/ EMG,	Reduction of essential tremor, motor responses of tail and limbs	0.23	27.2	52 sec (100 ms on 2.9 sec off)	Cw
(Sato et al., 2018)/ mouse	visual cortex/ wide-field calcium imaging, EMG	Calcium response at auditory cortex followed by brain-wide response, startle motor response	0.5	0.11-4.2 spta	80	1.5
(Guo et al., 2018)/ guinea pig	SC1, A1, visual cortex/ electrode	Responses from auditory cortex (off-target) results in brain-wide activation	0.22	0.02-133.33	1-20 ms	cw-16
(Yoon et al., 2019)/ sheep	S1, thalamus/ EMG, EE	Contralateral EMG responses, suppression of SEP	0.25	15.8, 18.2	60-200	cw-1.4
(Mohammadjavadi et al., 2019)/ mouse	motor cortex/ EMG	EMG responses from genetically deaf mouse	0.5	1-3.78	80-640	cw-8
(Folloni et al., 2019)/ monkey	amygdala, ACC/ BOLD	Functional connectivity changes with targets after sonication	0.25	17, 51	40 sec (30 ms bursts every 100 ms)	Cw
(Verhagen et al., 2019)/ monkey	SMA, FPC/ BOLD	Functional connectivity changes with targets after sonication	0.25	24.1, 31.7	40 sec (30 ms bursts every 100 ms	Cw
(Wang et al., 2020)/ mouse	STN/ electrode	Decrease in oscillatory activity after sonication	0.5	5.1	5 min (50 ms burst every 1 sec)	1
(Braun et al., 2020)/ human	V1/ EEG, survey	Subjects hear sound during stimulation, phosphene perception	0.5	0.6 Mpa	300	1
(Sanguinetti et al., 2020)/ human	rIFG/ survey, BOLD	Positive shift in mood after sonication, functional connectivity changes	0.5	16.2	30 sec, 2 min	0.04
(Kubanek et al., 2020)/ monkey	FEF/ choice task	Change in success rate of collect choice	0.27	11.6	300	0.5

Supplementary Table 2 – Summary of Ultrasonic Neuromodulation Studies

		In vitro and Small animal (mouse, rat, guinea pig)	Large animal (rabbit, swine, sheep, monkey)	Human
Parameter	Frequency (MHz)	0.22-2.9	0.22-1.14	0.25-0.5
	Isppa (W/cm^2)	0.02-133.33	3.3-31.7	3-23.87
	SD	0.25 ms-5 min	60 ms-40 sec	300-500 ms
	PRF (kHz)	CW or 0.01-16	CW or 0.01-8	CW or 0.04-1
Target		hippocampus, motor or visual or auditory cortex, thalamic area, somatosensory area, STN	V1, M1, SM1, FEF, thalamus, amygdala, ACC, SMA, FPC	S1, V1, M1, thalamus, rIFG
Neuromodulation effects		- Direct optical response - Excitation effect recorded by electrode or BOLD - Motor responses including tail, whisker, eyeball, limb and head - Suppressed motor responses from tremor, epilepsy and PD model - Indirect auditory excitation	- Excitation effect recorded by BOLD or EMG - Suppression effects recorded by EEG - Change in behavioral responses - Functional connectivity changes after sonication	- Increase BOLD signals at target - Excitation or suppression effects recorded by EEG - Tactile sensation, phosphene perception - Change in behavioral responses - Positive shift in mood after sonication - Functional connectivity changes after sonication - Hearing of audible sound during sonication
References		(Tyler et al., 2008), (Tufail et al., 2010), (Min et al., 2011), (Kim et al., 2012), (King et al., 2013), (Younan et al., 2013), (Kim et al., 2014), (Ye et al., 2016), (Lee et al., 2018), (Sharabi et al., 2018), (Sato et al., 2018), (Guo et al., 2018), (Mohammadjavadi et al., 2019)	(Yoo et al., 2011), (Deffieux et al., 2013), (Lee et al., 2016a), (Wattiez et al., 2017), (Yang et al., 2018), (Dallapiazza et al., 2018), (Yoon et al., 2019), (Folloni et al., 2019), (Verhagen et al., 2019), (Kubanek et al., 2020)	(Mueller et al., 2014), (Legon et al., 2014), (Lee et al., 2015), (Lee et al., 2016b), (Leo Ai, 2018), (Legon et al., 2018a), (Legon et al., 2018b), (Braun et al., 2020), (Sanguinetti et al., 2020)

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