



# Excitatory-inhibitory modulation of transcranial focus ultrasound stimulation on human motor cortex

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## Introduction

We hypothesize that transcranial focus ultrasound stimulation (tFUS) regulates the cortical excitability patterns by affecting plasticity associated with the balance of GABAergic and glutamatergic excitation and inhibition. We evaluated the effect of tFUS on the excitability of the human motor cortex (M1) and explored its mechanism.

## Methods

Two sets of ultrasound stimulation program parameters were used.

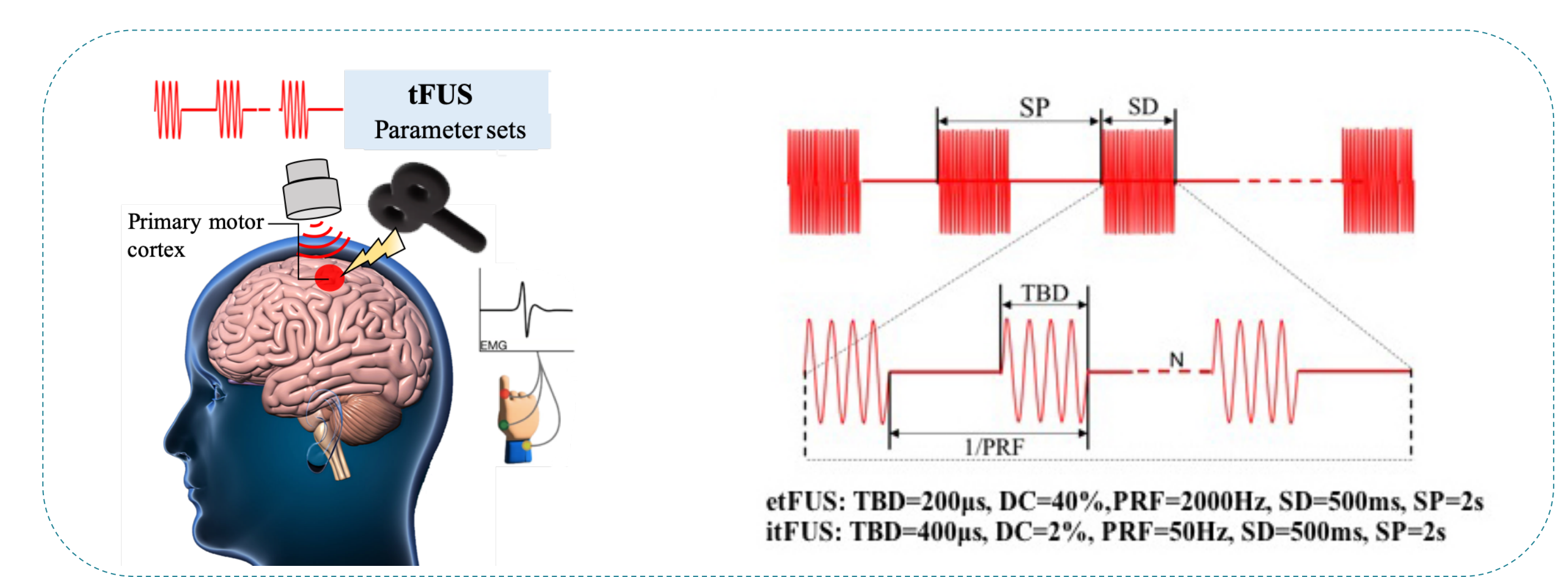


Fig1. Experimental paradigms. The transcranial ultrasound waveforms is generated by an Ultrasound Stimulation System that integrates ultrasound transducer (center frequency =500kHz) with image-guided localization software.

## results & discussion

MRI-guided tFUS with different parameter sets exert excitatory or inhibitory effects on human motor cortical activity.

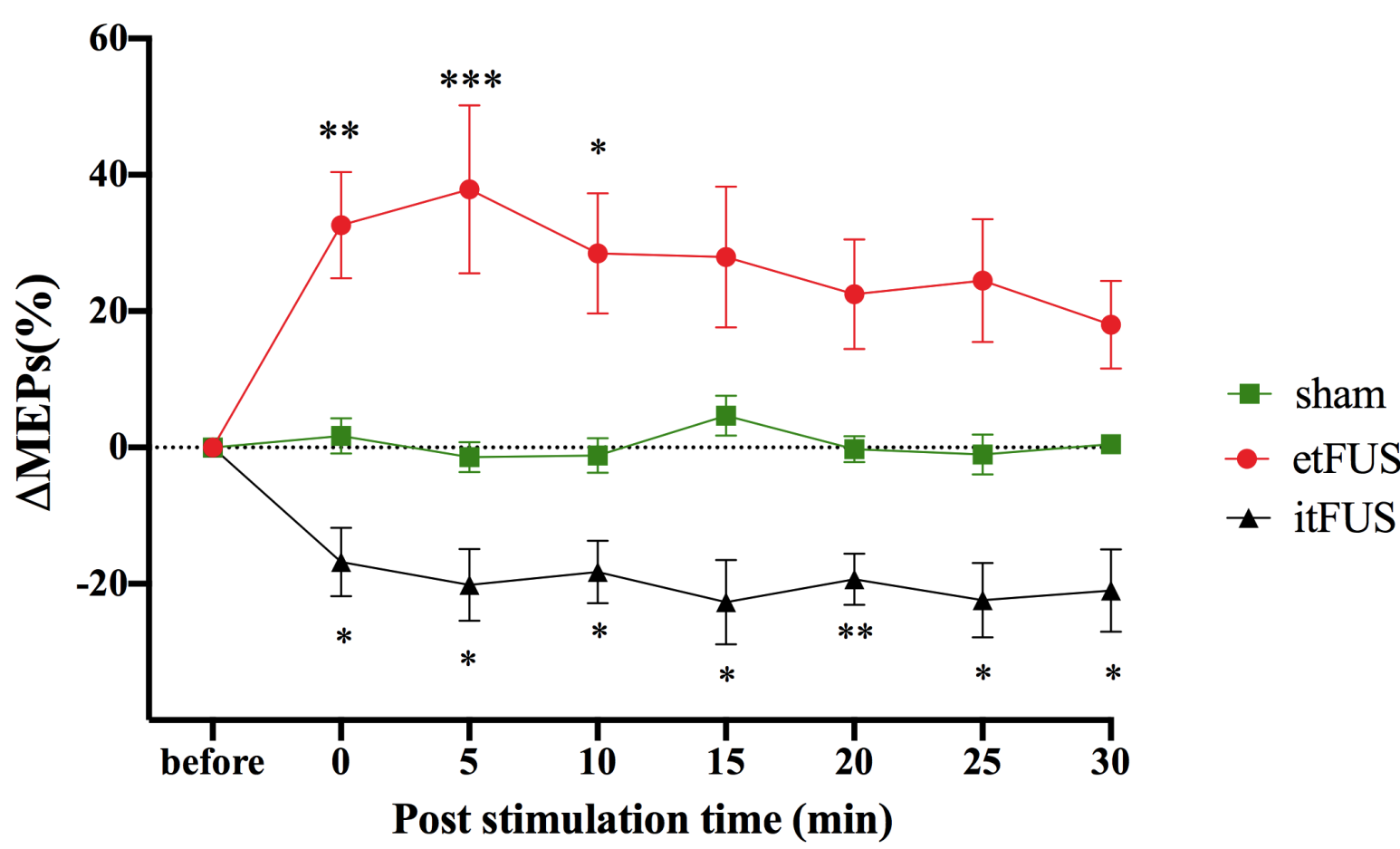


Fig2. The effect of tFUS on MEPs induced by single TMS. The figure shows mean ΔMEPs percentages ± SEM. (\* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , etFUS vs sham or itFUS vs sham at each time point,  $n = 10$ ).

## Conclusion

tFUS with different parameters can exert excitatory and inhibitory modulatory effects on the human motor cortex. tFUS change cortical excitability and plasticity by regulating excitatory-inhibition balance related to the GABAergic and glutamatergic receptor function and neurotransmitter metabolic level.

## results & discussion

The etFUS significantly decreased intracortical inhibition (SICI and LICI), suggesting possible inhibition of GABA receptor function. The itFUS significantly increased SICI, LICI, and decreased intracortical facilitation (ICF), suggesting possible excitation of GABA receptors and inhibition of glutamate NMDA receptor function.

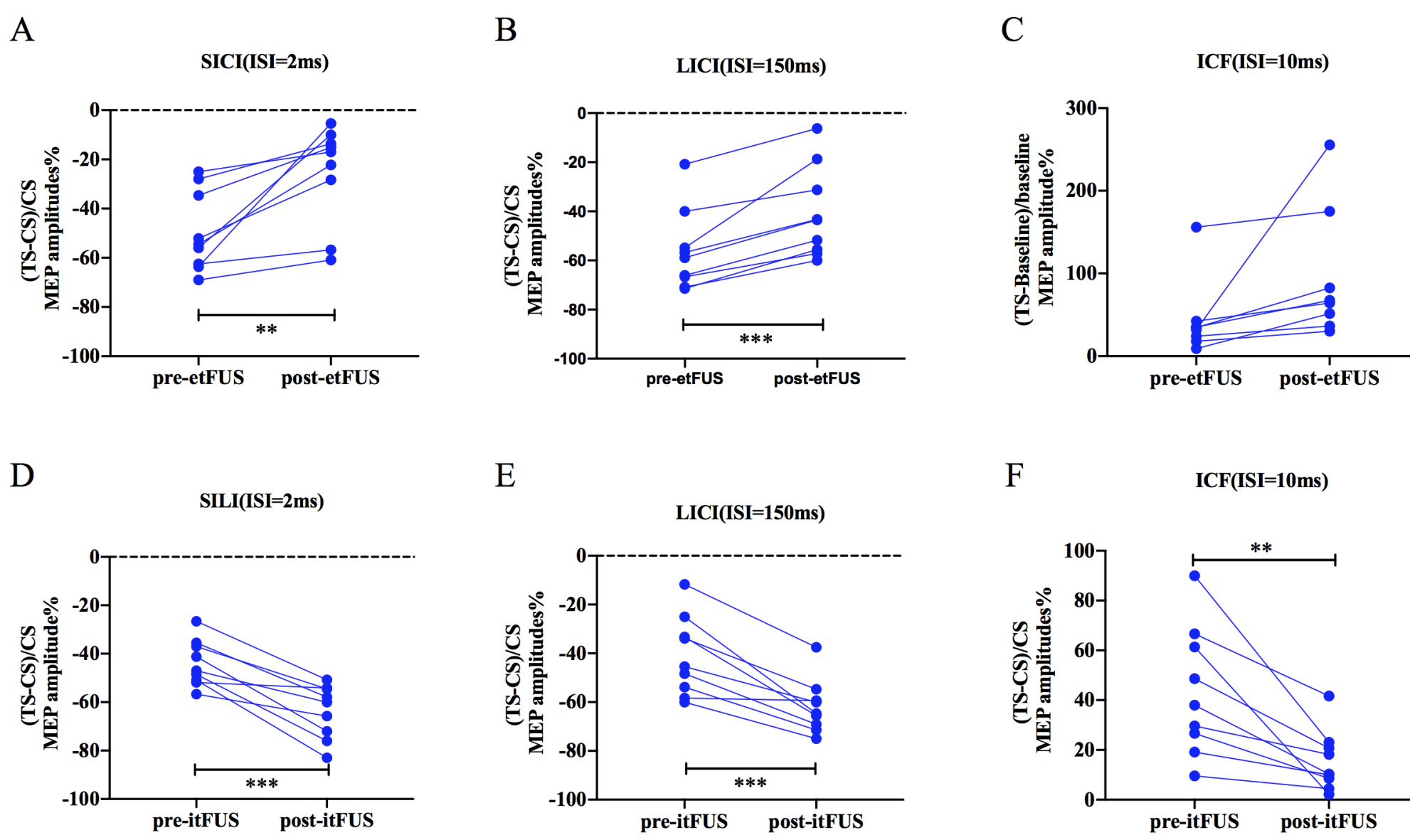
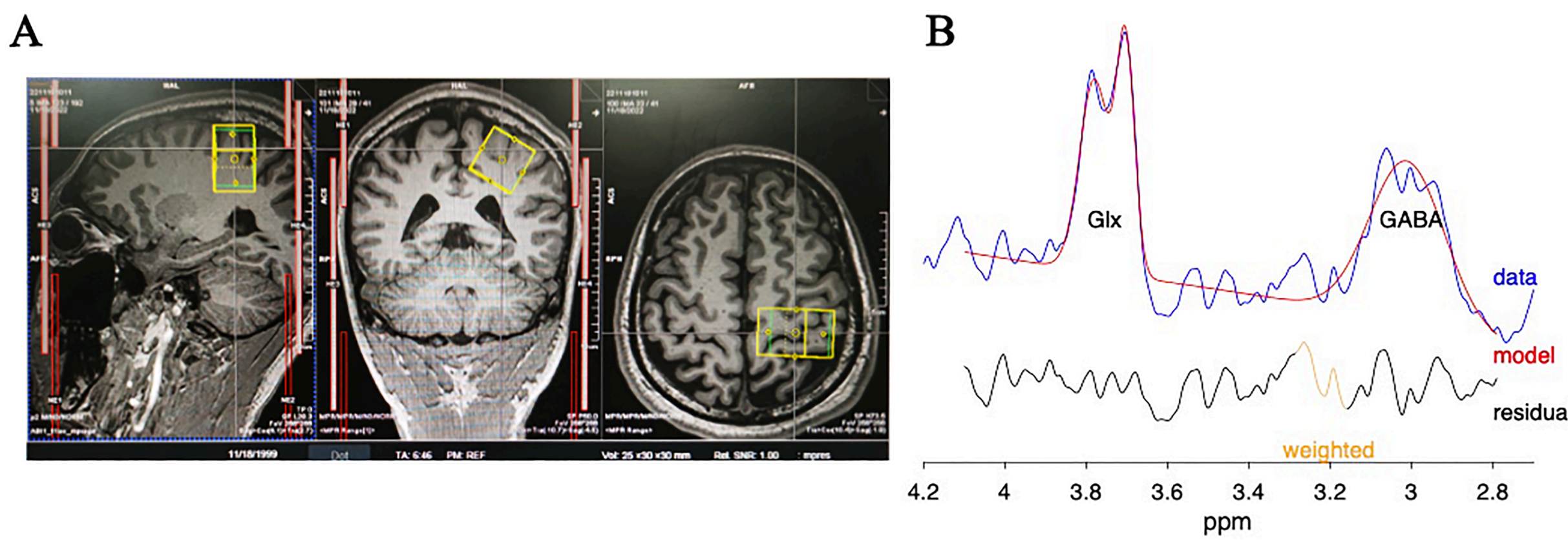


Fig3. The effect of tFUS on intracortical facilitation and inhibition. The figure shows the MEP change of TS relative to CS. Values of  $>0$  indicate intracortical facilitation, and values of  $<0$  indicate intracortical inhibition. (paired  $t$  test, \* $p < 0.05$ , \*\* $p < 0.01$ , before vs after stimulation,  $n = 9$ ). SICI, short interval intracortical inhibition; LICI, long interval intracortical inhibition; ICF, intracortical facilitation.

The etFUS decreased GABA (6.32%), increased Glx (12.40%), and decreased the GABA/Glx ratio. While itFUS increased GABA (18.59%), decreased Glx (0.35%), and significantly increased the GABA/Glx ratio, suggesting that tFUS modulated the inhibitory and excitatory.



(A) Representative brain images of a subject showing the voxel ( $25 \times 30 \times 30$  mm) within the primary hand motor cortex. (B) Curve-fitting of the GABA and Glx peak using Gannet.

	GABA IU (SNR)		Glx IU (SNR)		GABA/Glx	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
etFUS						
Subject 1	2.440 (11.60)	2.496 (10.35)	5.229 (11.74)	6.849 (11.39)	0.467	0.364
Subject 2	3.272 (12.23)	2.778 (14.76)	7.203 (10.08)	6.820 (11.62)	0.454	0.407
Subject 3	2.702 (12.91)	2.210 (15.45)	6.168 (12.54)	7.279 (13.48)	0.438	0.304
Subject 4	2.725 (14.75)	2.881 (10.13)	6.780 (10.11)	7.181 (12.31)	0.402	0.401
Mean ± SEM	2.785 ± 0.175	2.591 ± 0.151	6.345 ± 0.428	7.032 ± 0.116	0.440 ± 0.014	0.369 ± 0.024 ( $p = 0.095$ )
itFUS						
Subject 5	2.911 (12.32)	4.931 (11.60)	7.578 (12.08)	8.457 (9.92)	0.384	0.583
Subject 6	2.084 (13.70)	2.266 (11.94)	6.313 (13.92)	6.190 (11.94)	0.330	0.366
Subject 7	2.135 (12.83)	2.395 (10.19)	5.103 (12.62)	5.135 (11.90)	0.419	0.466
Subject 8	2.622 (10.92)	3.216 (12.40)	6.818 (10.28)	6.633 (11.10)	0.385	0.485
Subject 9	2.907 (9.85)	2.502 (12.20)	6.658 (8.70)	5.169 (10.20)	0.437	0.384
Mean ± SEM	2.532 ± 0.180	3.062 ± 0.495	6.494 ± 0.405	6.317 ± 0.609	0.391 ± 0.018	0.477 ± 0.034*

Table1. MRS data analysis of GABA and Glx levels. Paired  $t$  test, \* $p < 0.05$ .

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