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Enhancing Semantic Memory with Transcranial Focused Ultrasound Stimulation of the Anterior Temporal Lobe

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Introduction

- Converging evidence from neuropsychological and neuroscientific studies highlights the anterior temporal lobe (ATL) as a crucial hub for semantic memory (Lambon Ralph et al., 2017).
- Our previous work has demonstrated that GABAergic activity in the ATL plays a key role in shaping semantic memory (Jung et al., 2017). Additionally, non-invasive brain stimulation, such as TMS over the ATL, can modulate regional GABA levels and task-induced activity, leading to changes in semantic memory performance in healthy individuals (Jung & Lambon Ralph, 2016; Jung, Williams, & Lambon Ralph, 2023).
- Low-intensity transcranial focused ultrasound stimulation (FUS) is an emerging and highly promising method for treating brain disorders by applying acoustic energy to specific brain regions to transiently alter their neurochemistry and functioning (Yaakub et al., 2023).
- Our goal is to enhance semantic memory by using FUS to stimulate the ATL, thereby modulating regional neurochemicals and neural dynamics within the semantic network.

Methods & Results

Participants
- 23 healthy English speakers (6 males, mean age = 21 ± 3yrs)

MRI parameters
- **T1-weighted image** using a 3D MPRAGE sequence (voxel size = 1mm isotropic, field of view [FOV] = 256, matrix = 256, 256 sagittal slices, inverse time [TI] = 800ms, flip angle [FA] = 8°).
- **fMRI** using whole- brain 2D GE-EPI sequence (TR = 1400ms, TE =35ms, flip angle = 68°, in-plane FOV = 212 × 212mm, 57 slices, slice thickness = 2 mm, voxel size = 2mm isotropic, hyperband factor = 3, ARC factor =2, 330 volumes).
- **Single voxel H^1 MRS** using a GABA-edited MEGA-PRESS spectra with the application of the MEGA inversion pulse at 1.95ppm (TR = 2000ms, TE = 68ms)

Experimental design and procedures

Session 1
- FUS & MRI screening
- Informed consent
- T1 imaging

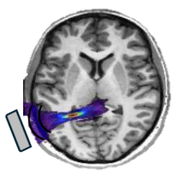
Participant assigned to two FUS orders with 5 days gap

Order of FUS	
Session 2	Session 3
Ventricle FUS	ATL FUS
ATL FUS	Ventricle FUS

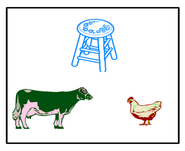
Behavioural tests → **Theta-burst FUS** → **Participant enters MRI scanner** → **MRS** (**T1** (~ 10mins post FUS), **OCC** (~ 15mins post FUS), **ATL** (~ 20mins post FUS)) → **fMRI** (**task-fMRI** (~ 35mins post FUS)) → **Behavioural tests & Questionnaires**

ATL: semantic hub

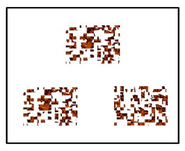
Ventricle: control site

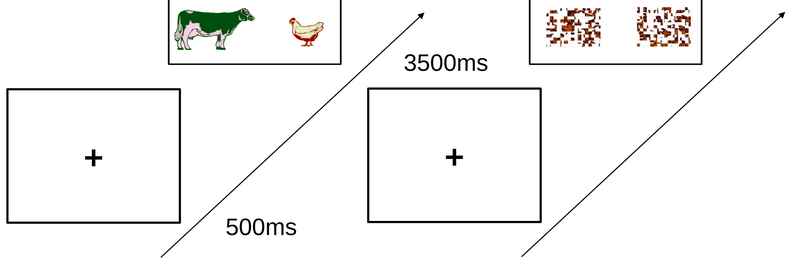


Semantic association task



Pattern matching task

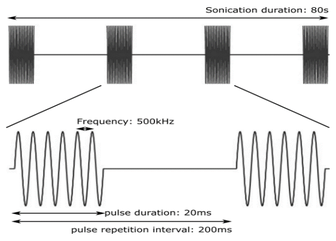




FUS parameters
- **Theta-burst FUS (tbFUS) parameters**

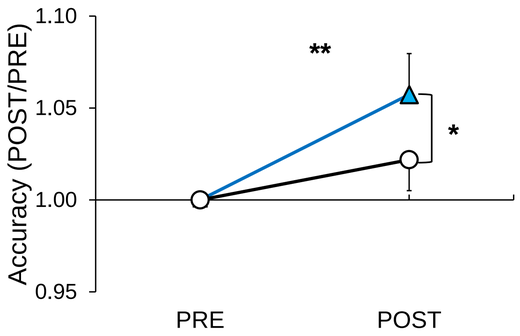
central frequency = 500 kHz, pulse duration = 20 ms, pulse repetition interval = 200 ms, duty cycle = 10%, ISPPA = 54.51 W/cm2, total duration = 80 sec (Zeng et al., 2022)

Theta-burst FUS protocol

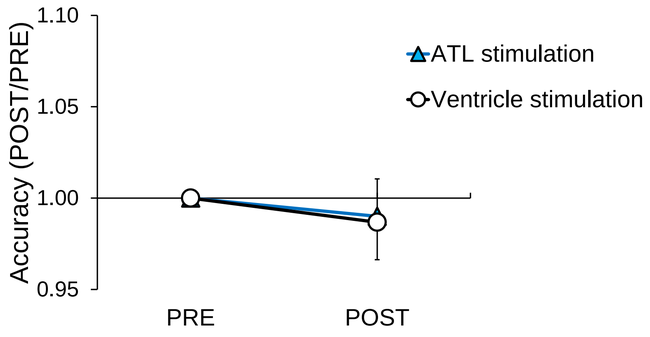


The effects of tbFUS on behaviour

Semantic association task

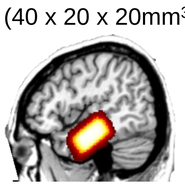


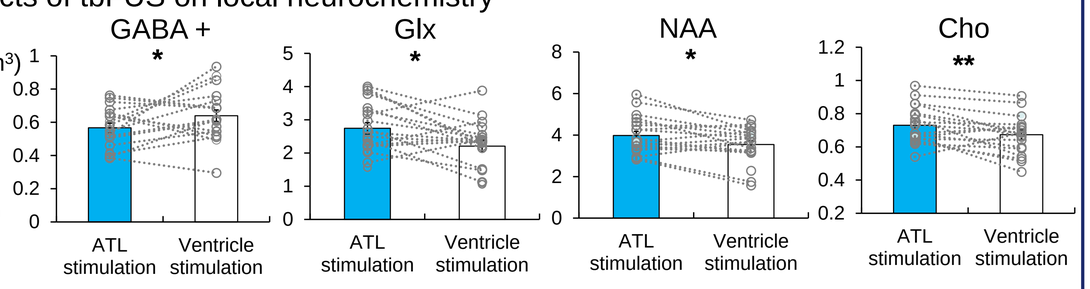
Control task



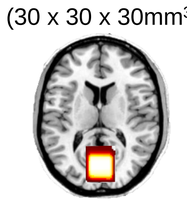
The effects of tbFUS on local neurochemistry

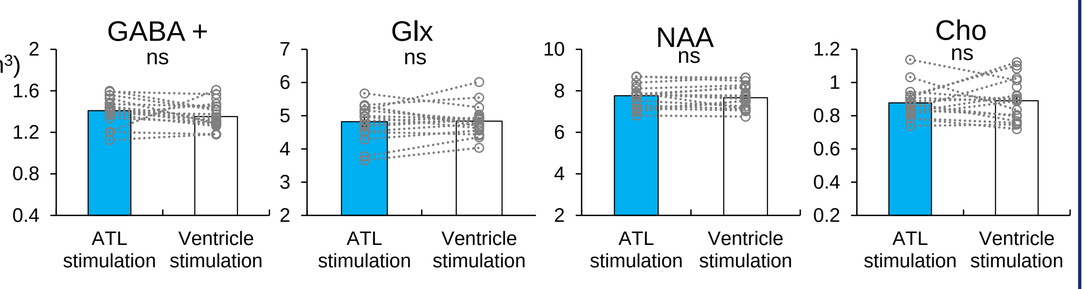
ATL (40 x 20 x 20mm³)



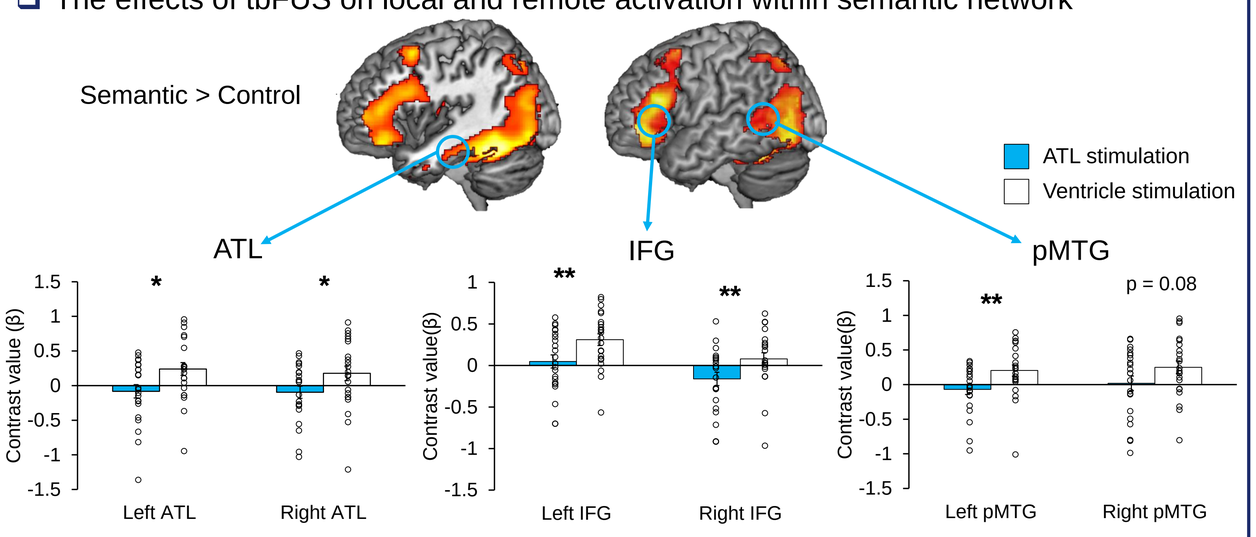


OCC (30 x 30 x 30mm³)



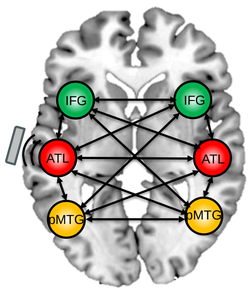


The effects of tbFUS on local and remote activation within semantic network



The effects of tbFUS on semantic network: Dynamic Causal Modelling

Semantic network



Intrinsic connectivity

Ventricle stimulation

	ATL	IFG	pMTG	r.ATL	r.IFG	r.pMTG
ATL		0.014	0.015	0.015	0.014	0.016
IFG	0.015		0.015	0.015	0.014	0.016
pMTG	0.016	0.015		0.016	0.015	0.017
r.ATL	0.015	0.014	0.016		0.014	0.016
r.IFG	0.014	0.014	0.015	0.014		0.016
r.pMTG	0.016	0.016	0.017	0.016	0.016	

ATL stimulation

	ATL	IFG	pMTG	r.ATL	r.IFG	r.pMTG
ATL		0.104	0.062	0.088	0.102	0.041
IFG	0.132		0.093	0.07	0.095	0.1
pMTG	0.135	0.1		0.09	0.083	0.096
r.ATL	0.122	0.081	0.093		0.091	0.086
r.IFG	0.139	0.094	0.084	0.083		0.077
r.pMTG	0.123	0.113	0.103	0.086	0.077	

Ten-fold increase in semantic network intrinsic connectivity following ATL stimulation compared to control stimulation

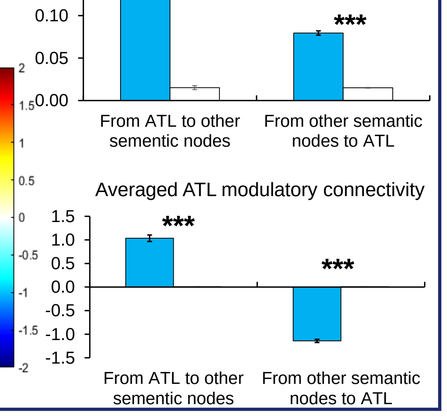
Modulatory connectivity: Semantic association task

Ventricle stimulation

	ATL	IFG	pMTG	r.ATL	r.IFG	r.pMTG
ATL		0.004	0.006	0.006	0.004	0.006
IFG	0.004		0.005	0.004	0.004	0.006
pMTG	0.006	0.006		0.006	0.005	0.009
r.ATL	0.007	0.004	0.006		0.004	0.007
r.IFG	0.004	0.004	0.005	0.004		0.006
r.pMTG	0.008	0.007	0.009	0.008	0.007	

ATL stimulation

	ATL	IFG	pMTG	r.ATL	r.IFG	r.pMTG
ATL		-0.488	-1.707	-0.677	-0.473	-2.389
IFG	1.329		-0.323	-0.22	-0.186	-0.393
pMTG	0.836	0.014		-0.074	-0.134	-0.489
r.ATL	1.159	-0.134	-0.309		-0.124	-0.382
r.IFG	1.264	-0.206	-0.304	-0.226		-0.337
r.pMTG	0.533	0.133	-0.282	-0.082	-0.179	



Conclusion

- FUS can enhance semantic memory by revealing ***task- and region-specific effects.***
- Specifically, FUS enhances semantic memory performance by modulating neurochemicals and neural dynamics of semantic network
- FUS is emerging as a promising therapeutic tool to enhance memory in patients with dementia with minimal side effects.
- Ventricle FUS can be a golden standard control site for FUS studies.

References

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