Brain Stimulation Effects on Negative Thought Disorder: A MRI and BERT Analysis

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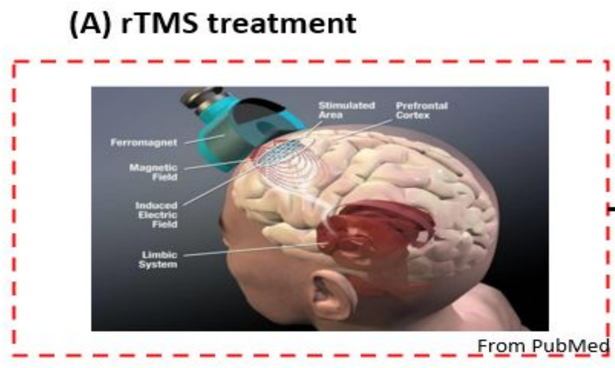
Background

- **Negative formal thought disorder (impoverishment)** is a **core symptom** of schizophrenia, commonly assessed using clinical scales like TLI
- Speech derived **BERT sentence similarity** may reflect the same construct, but provide an automated, objective index of impoverishment.
- **Repetitive Transcranial magnetic stimulation (rTMS)** of the left dorsolateral prefrontal cortex (DLPFC) improves other negative symptoms, though the effect on impoverishment is unknown.
- **Hurst Exponent** of fMRI signals reflects local excitation/inhibition balance; this can be used to measure the biological effect of rTMS application

Questions: 1. Does impoverishment improve with negative symptoms when using 10Hz left DLPFC rTMS [110% MT,1000 stim/day] in schizophrenia?
2. Do patients that show changes in BERT sentence similarity and in local E/I balance (Hurst exponent) also show changes in impoverishment ratings?
3. Is there a role for brain's semantic network in the rTMS induced improvements seen in schizophrenia?

Methods & participants



N=32	M	SD
Age (years)	41.52	13.23
Sex (M/F)	(26, 6)	
Education (years)	11.67	2.7
PANSS total	85.52	18.36
PANSS positive	16.1	6.25
PANSS negative	30.55	7.1
TLI total	1,00	0.68

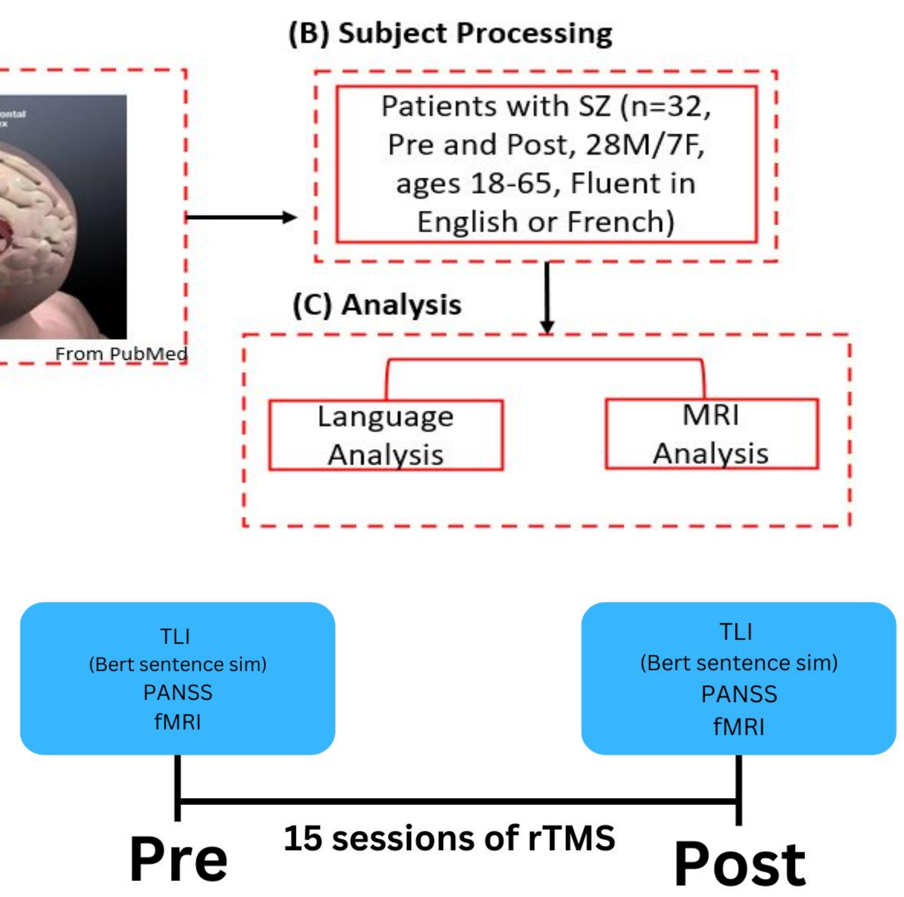
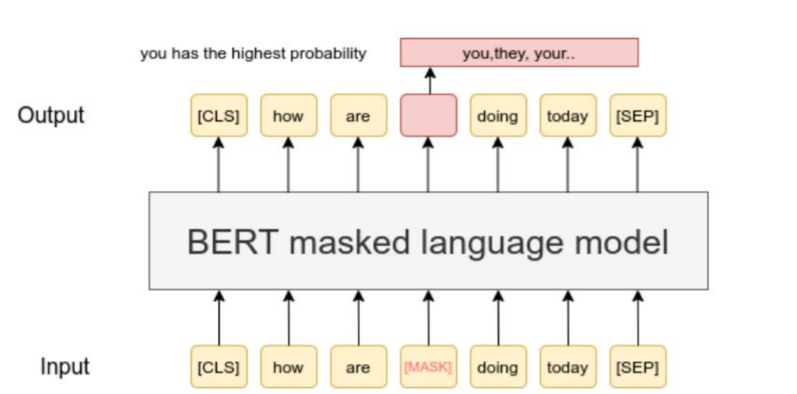


Figure 1: **Demographics & study overview**

Computed variables



Sentence- similarity using BERT:
distiluse-base-multilingual-cased-v1

fig 2; we calculated sentence-to-sentence predictability using the **BERT** architecture to assess semantic content of transcribed interviews (French and English; no significant differences across languages)

the **Hurst exponent** assesses the autocorrelation of an fMRI timeseries, and reflects the **excitatory/inhibitory** balance of activity in the ROI. Here, we use as timeseries 10-minute resting-state fMRI using a 6mm sphere in the DLPFC with TR = 1000ms; TE = 30ms, flip angle = 45°; 48 slices; slice thickness = 3mm, FOV = 210 x 210mm; voxel dimensions = 3 x 3 x 3mm) using the DPARSF processing pipeline. Higher Hurst exponents indicate more anticorrelation, while lower exponents denote over-time autocorrelation.

Results

Effect of rTMS on PANSS, impoverishment and BERT similarity

	pre	post	change pre-post	T value	P value
PANSS-Positive	16.0(6.2)	13.0(6.3)	3.0(3.6)	4.655	**0.0001**
PANSS-Negative	30.1(7.4)	23.2(7.2	7.0(5.7)	6.896	**>0.0001**
PANSS-General	38.4(9.7)	31.3(10.1	7.1(7.3)	5.483	**>0.0001**
PANSS-Total	84.5 (19.0)	67.4 (20.2)	17.1(10.7)	8.987	**>0.0001**
TLI impoverishment	0.61 (0.49)	0.49 (0.51)	0.11 (0.36)	0.888	0.378
Mean sentence similarity	0.11 (0.10)	0.12 (0.10)	-0.015 (0.14)	-0.61	0.55
Hurst exponent in DLPFC	0.03 (0.01)	0.05 (0,04)	-0.01 (0.02)	-3.362	**0.002**

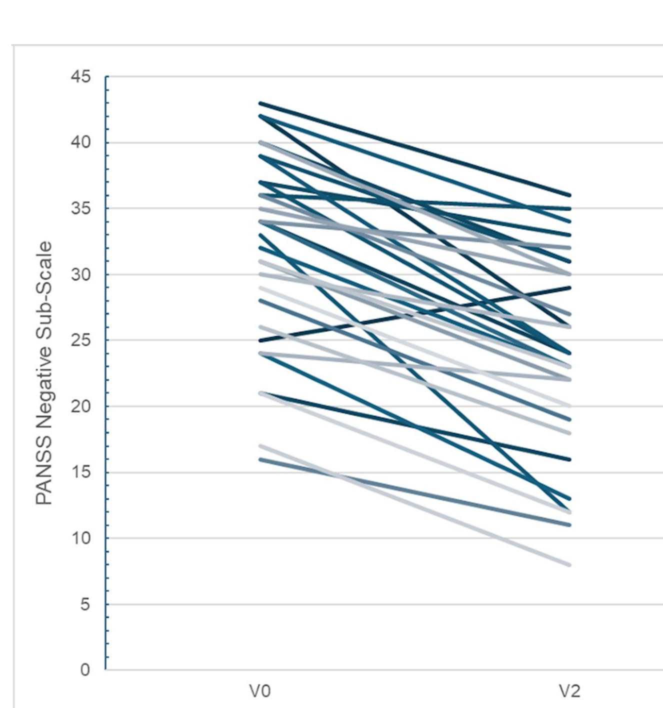


Figure 3, left; pre and post-rTMS PANSS, TLI, sentence similarity and Hurst exponent student's t-test. Bold denotes significance at alpha = 0.05. **Right**, main treatment effect of rTMS on PANSS-negative

Results (continued)

Relationship between TLI-Imp, BERT & HE

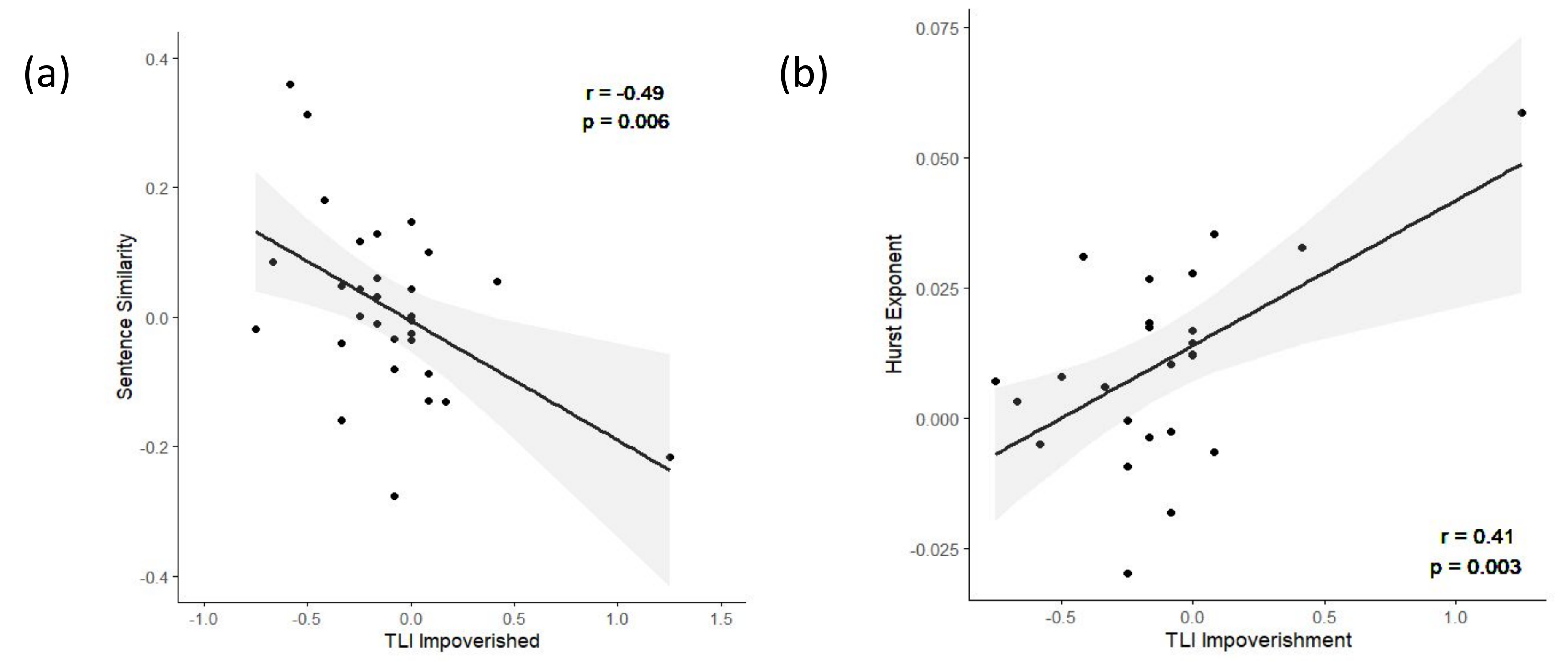
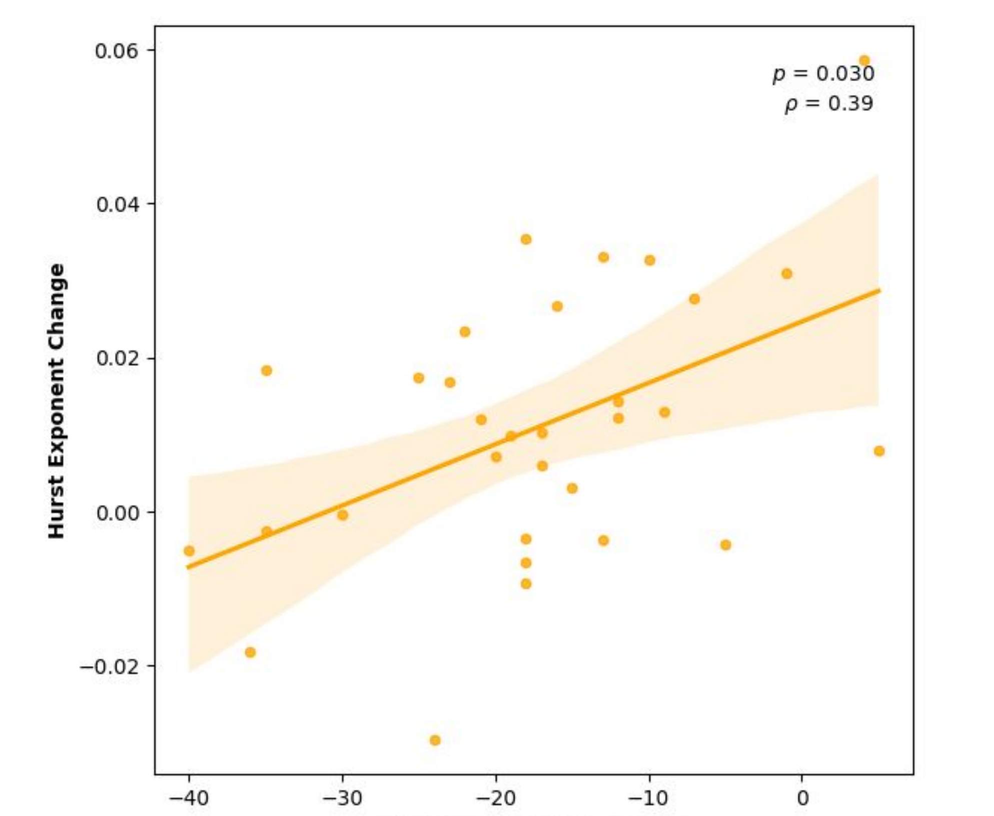


Figure 4: Scatterplot of Pearson correlation coefficient (r) change scores. **(a)** Average BERT sentence similarity & TLI impoverishment; with decreasing TLI impov severity, sentence similarity increases. **(b)** Hurst Exponent change score & TLI Impov change score. A decrease in TLI is associated with more prominent post-TMS changes in Hurst Exponent, though most patients show very small changes in TLI scores

Overall improvement, HE and language network

As the rTMS intervention improved PANSS total more than TLI impoverishment, we searched for **neural correlates of total symptom change**, first using **Hurst Exponent** in the DLPFC (right, figure 5), as well as using a 6 mm mask as a seed region to investigate whole-brain connectivity (figure 6, below)

Figure 5: **DLPFC** timeseries Hurst Exponent and PANSS total change score. Symptom decrease is associated with more prominent changes in Hurst Exponent.



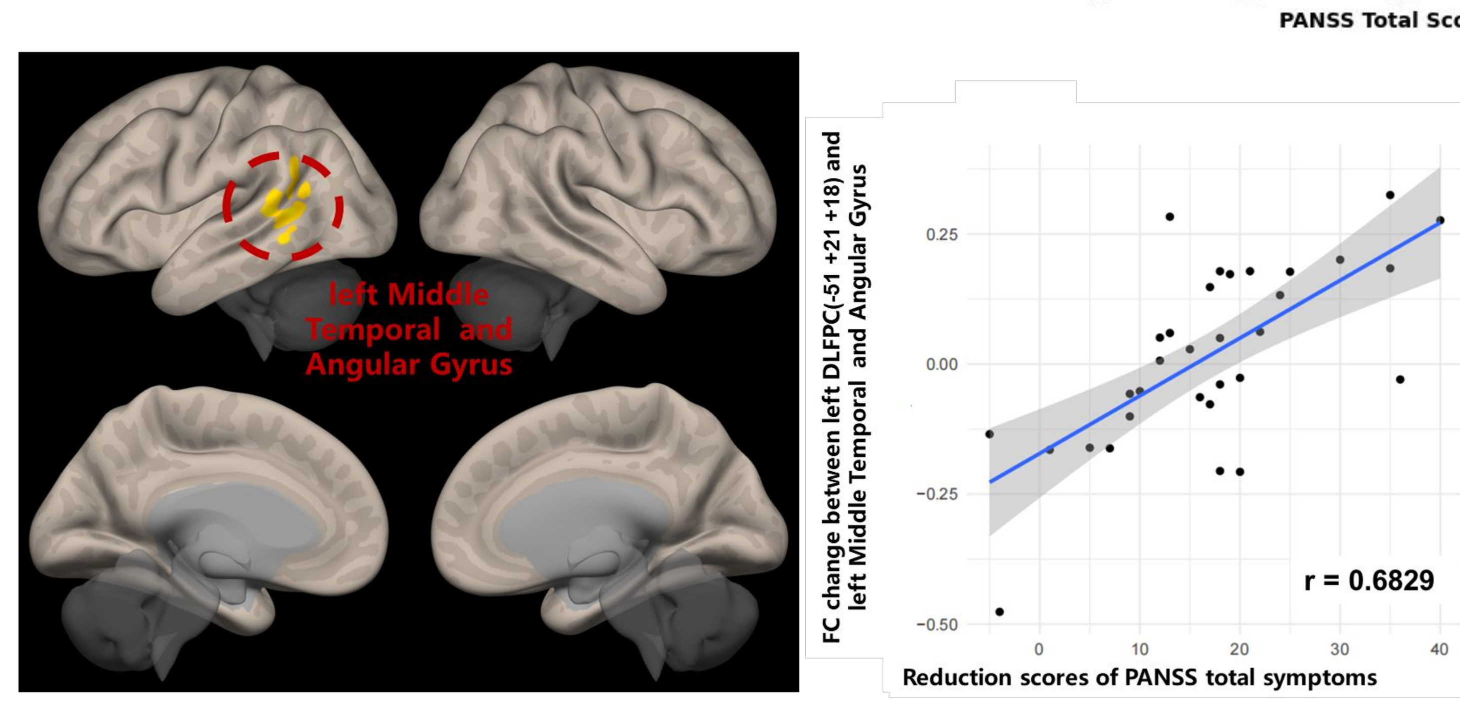


Figure 6: whole-brain seed based connectivity analysis using F3 (DLPFC) as seed area; (*corr.p<0.05, TFCE n.perm=5000*); pre-post rTMS shows significant functional connectivity effect on left posterior superior, middle temporal and Angular Gyrus. Symptom score reduction is associated with higher functional connectivity between DLPFC and temporal & angular gyrus.

Discussion

- The **effect of left DLPFC rTMS per se is small and nonsignificant on TLI-imp** despite the improvement in other symptoms
- BERT sentence predictability varies with changes in TLI-Imp in schizophrenia, indicating that **this computational measure captures negative FTD.**
- The relationship between **rTMS induced change in the Hurst Exponent** (towards higher autocorrelation in the time series reflecting reduced synaptic E/I ratio) and **negative FTD burden** provides evidence that **left DLPFC is a potential target for addressing negative FTD**.
- Whole-brain analysis shows that language network engagement is key for overall benefits of left DLPFC rTMS intervention in schizophrenia.
- Our approach of employing speech-NLP for tracking response holds promise for designing future neuromodulation trials targeting FTD.

References

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