

# Novel TMS Strategies for Negative Symptoms in Schizophrenia Spectrum Disorders (SSD)

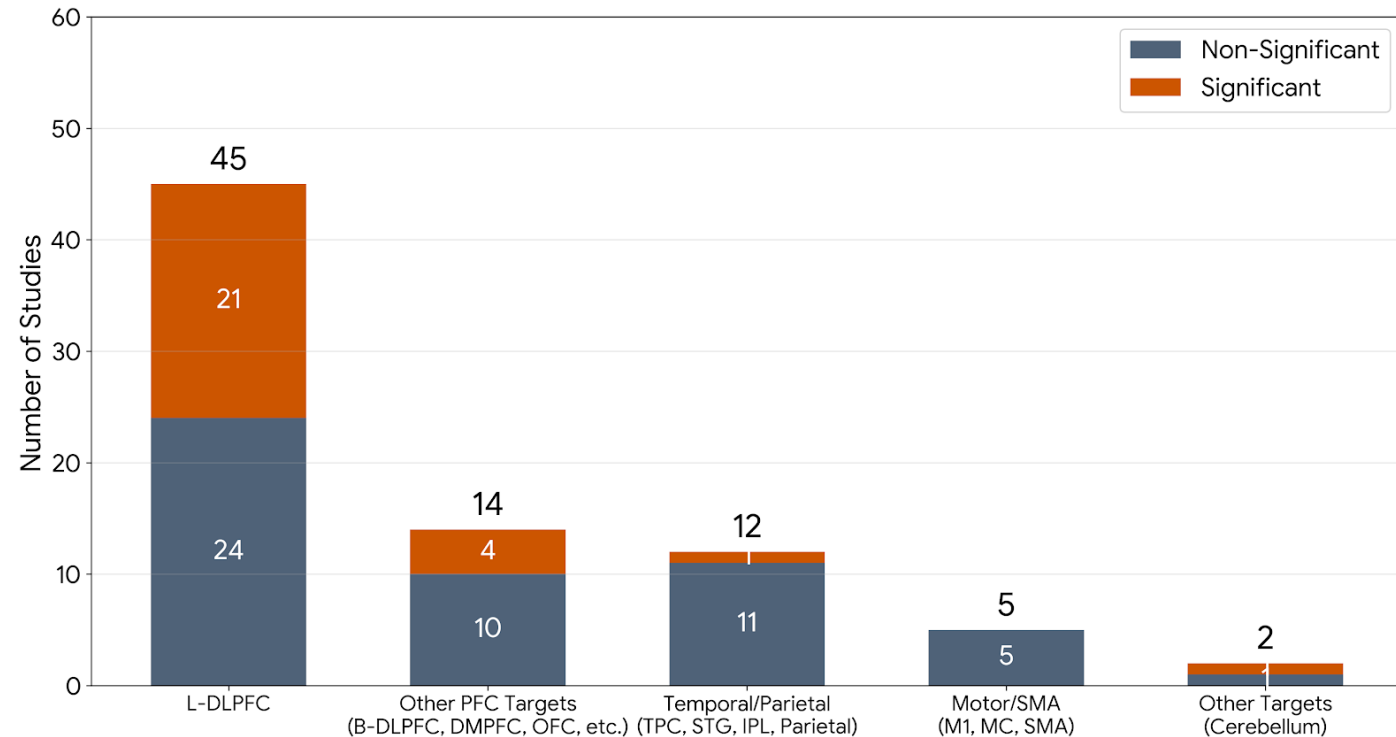
## Unmet Need

- Negative symptoms (diminished emotional expression, avolition) correlate with functional decline in schizophrenia.
- Negative symptoms often respond poorly to antipsychotic medications.

## Current Strategy

- Non-invasive brain stimulation (TMS) is a leading therapeutic modality.
- Left Dorsolateral Prefrontal Cortex (L-DLPFC) has been the most widely tested target, however, the efficacy results are mixed.

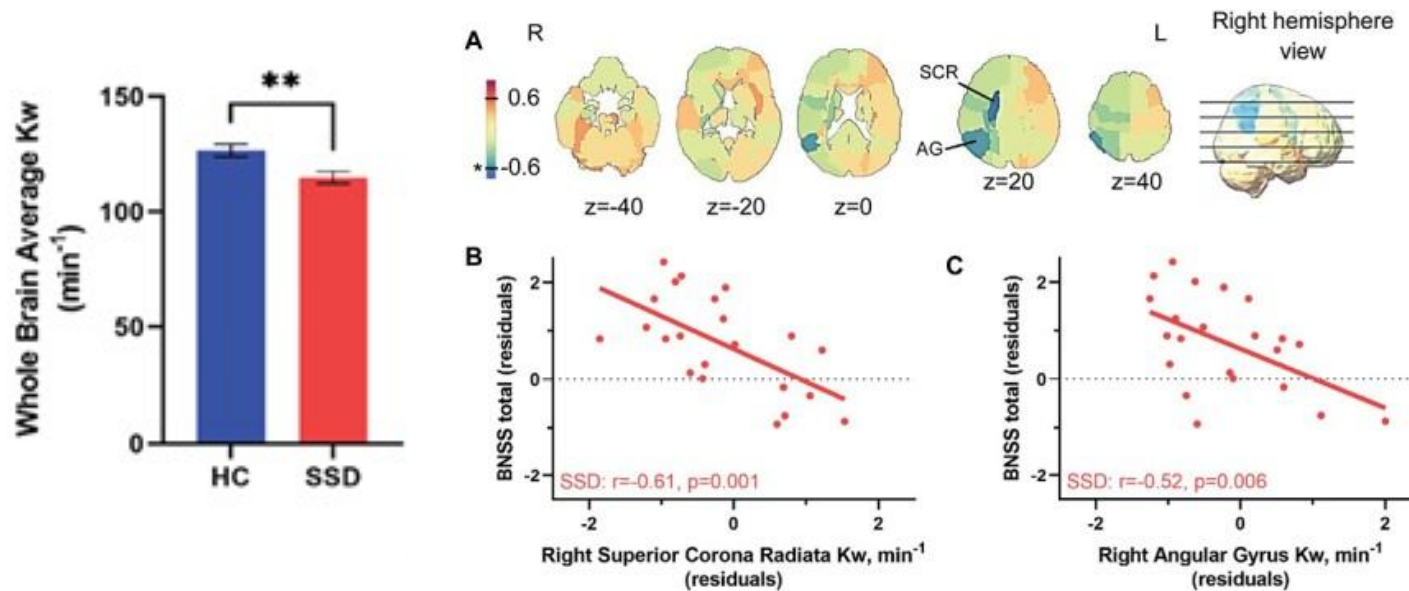
TMS Efficacy by Brain Target (N=78 Studies)



Exploring novel neural mechanisms and alternative circuits may lead to more optimal approaches.

# Targeting Blood Brain Barrier Dysfunction

- Patients with SSD exhibit reduced whole-brain water exchange rate (Kw) and peripheral endothelial function compared to healthy control.
- Lower Kw in the right angular gyrus and the superior corona radiata is significantly associated with more severe negative symptoms. (Goldwaser et al, 2023)



# Digital Behavioral Phenotyping

**Problem:** Clinical scales (e.g., BNSS) are subjective and prone to recall bias, obscuring trial signals.

**Solution:** Integrating clinical interviews with continuous, objective digital metrics.



*Capturing real-world mobility and social metrics objectively*

Future trials may benefit from incorporating novel mechanistic biomarkers and objective endpoints to help move the field forward.