

Mood symptoms related cognitive function is reflected through DLPFC TMS-EEG Interhemispheric Signal Propagation

Rafi Hadad^{1, 2}, Noa Zifman³, Rachel Ben-Hayun^{1, 4}, Hilla Fogel³, Natalya Yarovsky^{1, 4} Rawan Ayoub-Agbaria¹, David Tanne^{1, 3, 4}

¹Stroke and Cognition Institute, Rambam Health Care Campus, Haifa, Israel · ²Global Brain Health Institute, Dept. of Neurology, UCSF, USA · ³QuantalX Neuroscience Ltd., Kfar-Saba, Israel ·

⁴Rappaport Faculty of Medicine, Technion, Haifa, Israel

BACKGROUND

Cognitive complaints are common in aging and neurodegenerative disease, yet mood (anxiety and depression) symptoms frequently confound cognitive assessment and may independently alter underlying brain network function.

Transcranial magnetic stimulation combined with electroencephalography (TMS–EEG) provides a direct measure of interhemispheric signal transmission within prefrontal circuits, potentially capable of **disentangling mood-related effects from global cognitive performance**

Reduced left-to-right prefrontal connectivity has been associated with impaired cognitive control, slowed information integration, and poorer cognitive performance → rationale for targeting left DLPFC.

METHODS

We examined the relationship between LDLPFC interhemispheric signal propagation (ISP), HADS subscales, and cognitive performance (MoCA) among volunteers at the Rambam Stroke and Cognition Institute (N=61, mean age 70.3±11, 49% females).



Delphi-MD™
(QuantalX Neuroscience Ltd.)

- TMS–EEG integrated system**
- Single-pulse TMS to L-DLPFC
 - 64-channel EEG acquisition
 - Automated ISP computation
 - Standardised signal processing

LDLPFC ISP

Dependent variable — TMS-EEG interhemispheric signal propagation

HADS-D | HADS-A

Hospital Anxiety & Depression Scale — depressive and anxiety severity

MoCA Total Score

Montreal Cognitive Assessment — global cognitive performance

Univariate GLM (UNIANOVA WITH syntax): ISP as dependent variable; mood symptom severity + MoCA total score + their interaction as continuous predictors. Type III SS · $\alpha = 0.05$.

HYPOTHESIS

LDLPFC interhemispheric propagation is linked to mood symptom burden and captures mood-dependent modulation of cognitive performance, rather than global cognitive impairment per se.

RESULTS — MODEL FIT

Depression model

F(3,57) = 5.87

p = 0.001

R² = 23.6%

Adj. R² = 0.196

Both models significant, explaining ~24% of ISP variance

Anxiety model

F(3,57) = 6.95

p < 0.001

R² = 23.8%

Adj. R² = 0.23

Both models significant, explaining ~24% of ISP variance

ANOVA — DEPRESSION MODEL (HADS-D)

Source	SS	df	F	p	η ² p
Corrected Model	3.100	3	5.873	.001	.236
Intercept	.068	1	.389	.535	.007
Depression (HADS-D)	1.232	1	7.002	.011	.109
MoCA total score	.059	1	.335	.565	.006
Depression × MoCA	.999	1	5.680	.021	.091
Error	10.028	57			

Type III SS · Dependent variable: LDLPFC ISP · R² = .236 (Adj. R² = .196) · N = 61

ANOVA — ANXIETY MODEL (HADS-A)

Source	SS	df	F	p	η ² p
Corrected Model	3.124	3	6.95	<.001	.238
Intercept	0.07	1	0.39	.535	.007
Anxiety (HADS-A)	2.053	1	11.7	.001	.171
MoCA total score	0.198	1	1.12	.293	.021
Anxiety × MoCA	1.685	1	9.6	.003	.145
Error	10.004	57			

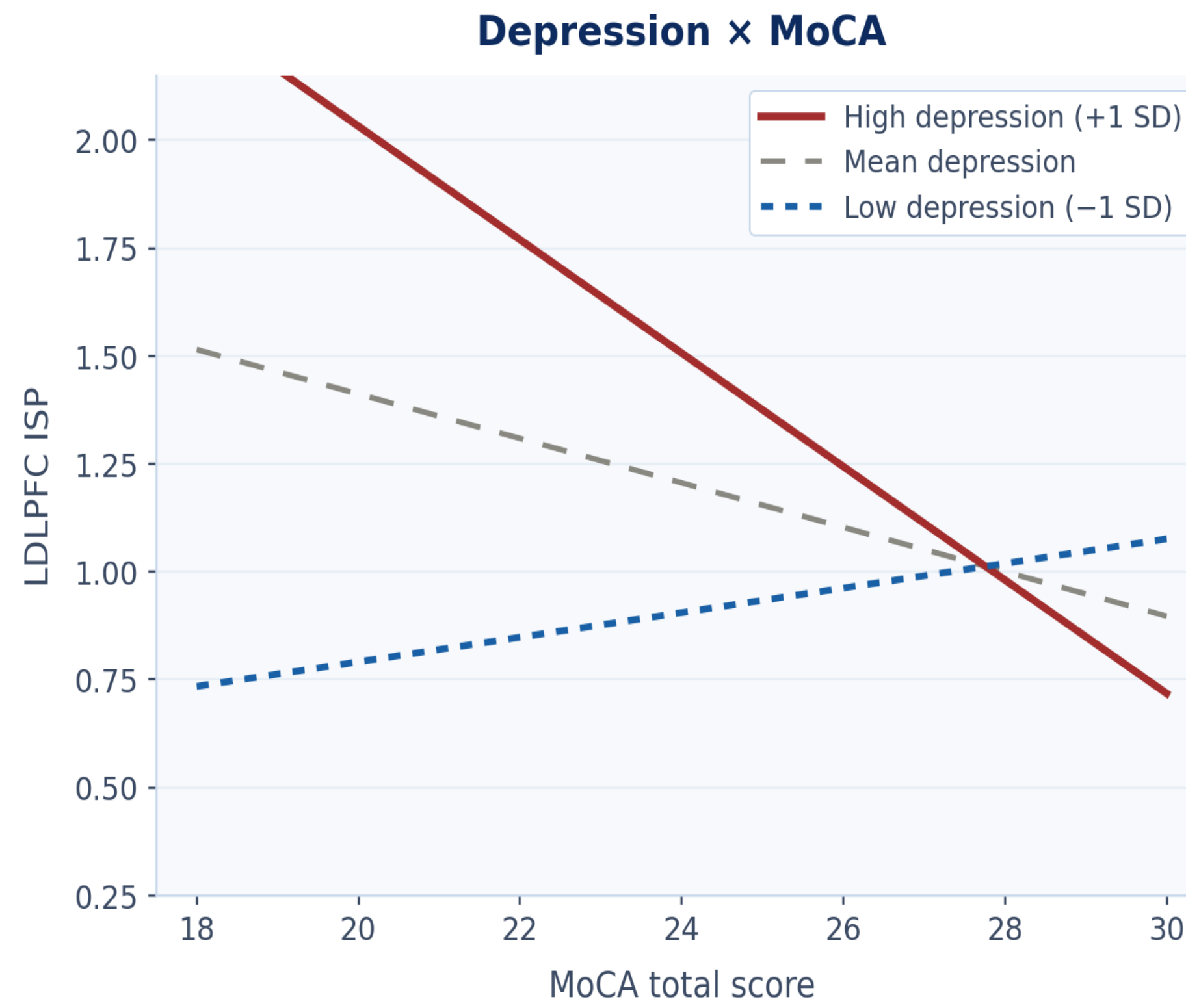
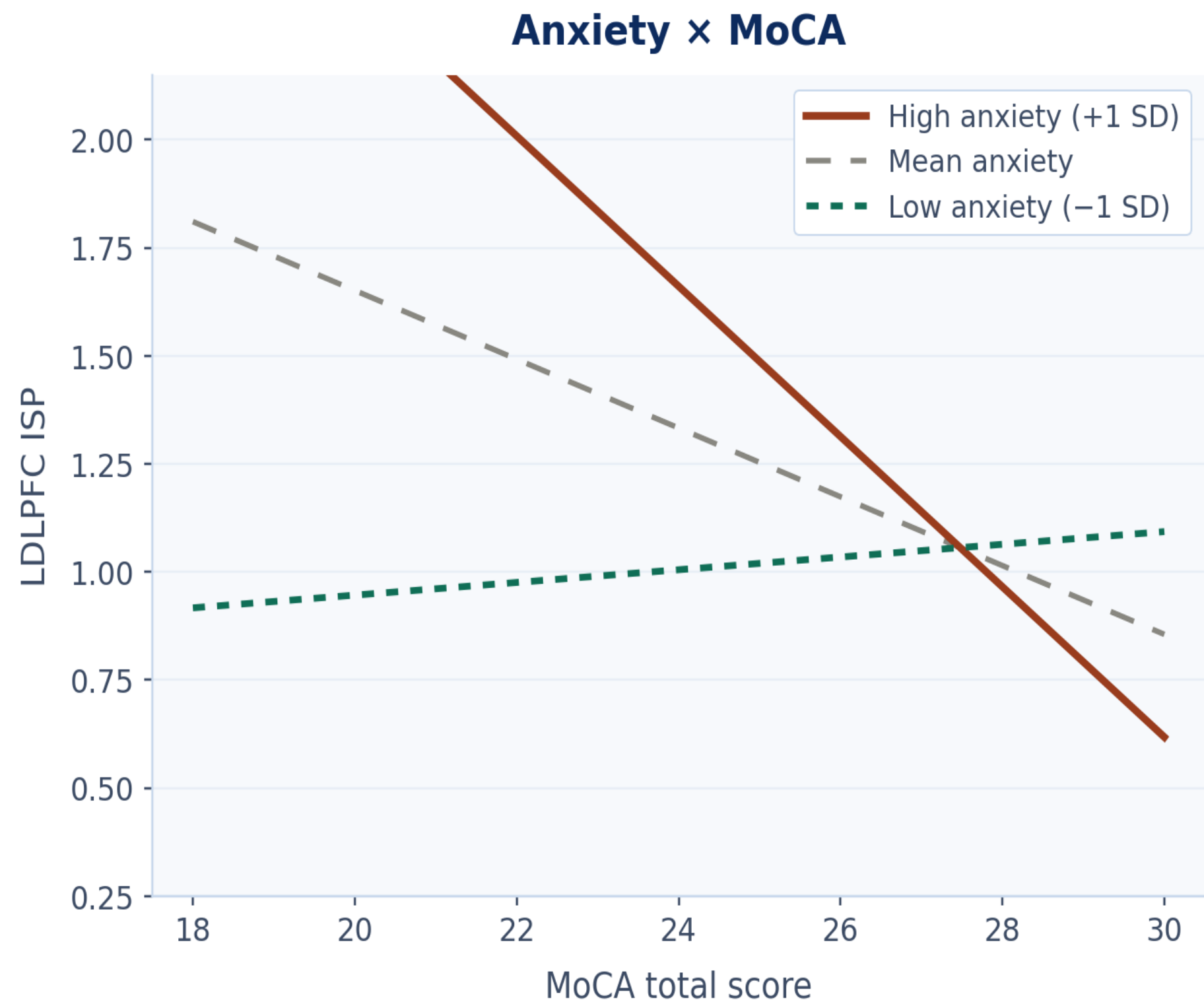
Type III SS · Dependent variable: LDLPFC ISP · R² = .238 (Adj. R² = .23) · N = 61

KEY FINDING

MoCA total score alone was **not** independently associated with ISP (p=0.565 and p=0.293, respectively), whereas **depressive and anxiety symptom severity showed a significant main effect** on LDLPFC ISP (F(1,57)=7.00, p=0.011, η²=0.109 and F(1,57)=11.7, p=0.001, η²=0.171, respectively).

A significant depression-by-cognition and anxiety-by-cognition interaction was observed (F(1,57)=5.68, p=0.021, η²=0.091 and F(1,57)=9.6, p=0.003, η²=0.145, respectively), indicating that the association between cognitive performance and prefrontal interhemispheric propagation **varied as a function of mood symptom burden**.

INTERACTION PLOTS — Mood Burden × MoCA → LDLPFC ISP



Lines computed from regression parameter estimates (B coefficients). Mood levels stratified at ±1 SD from mean. MoCA range 18–30.

CONCLUSIONS

LDLPFC interhemispheric propagation is linked to depressive and anxiety symptom severity and captures **mood-dependent modulation of cognitive performance** rather than global cognitive impairment per se.

This suggests that prefrontal TMS–EEG measures may provide an **objective marker of mood-associated cognitive vulnerability**, with potential relevance for improving **phenotypic stratification** in aging and neurodegenerative populations.