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http://psychophysiology.cpmc.columbia.edu/mmedia/SoBP2020/RS-Alpha-MDD_SoBP2020.pdf

Introduction

- **Greater posterior EEG alpha**, a putative biomarker of clinical outcomes in major depression (MDD)¹, may predict responsiveness to antidepressants²
- EEG alpha has been linked to **risk for** and **lifetime history of MDD**^{1,3,20}
- **Personal importance of religion/spirituality (R/S)** has separately demonstrated protective effects against MDD⁴
- In a longitudinal study of families at high-risk for depression^{5,6}, we found greater posterior EEG alpha in individuals with high R/S importance, particularly those with a lifetime history of MDD^{7,8}

Current Study:

- ❖ New and improved conceptualization and estimation of R/S importance
- ❖ Extant data were analyzed using new measures of current depression symptoms

Objectives:

1. Obtain virtual estimates of R/S importance at age 21 from all lifetime ratings
2. Explore the relationship of R/S importance and posterior EEG alpha to current depression symptoms

Method: Estimating R/S importance

We asked participants **5** times over a span of 25 years (in Year 10 [1992], Y20, Y25, Y30, Y35):

“How important is religion or spirituality to you?”

0 **1** **2** **3**
Not important at all Somewhat important Moderately important Highly important

- Mixed-effects model⁹ used to predict R/S importance based on **Age-Adjusted Time** (age of each person centered at age 21, representing early adulthood¹⁰).
- Model included a random slope and fixed effect slope, removing the random effect of participant.
- Participants' intercepts used as R/S estimates (**Fig. 1**)

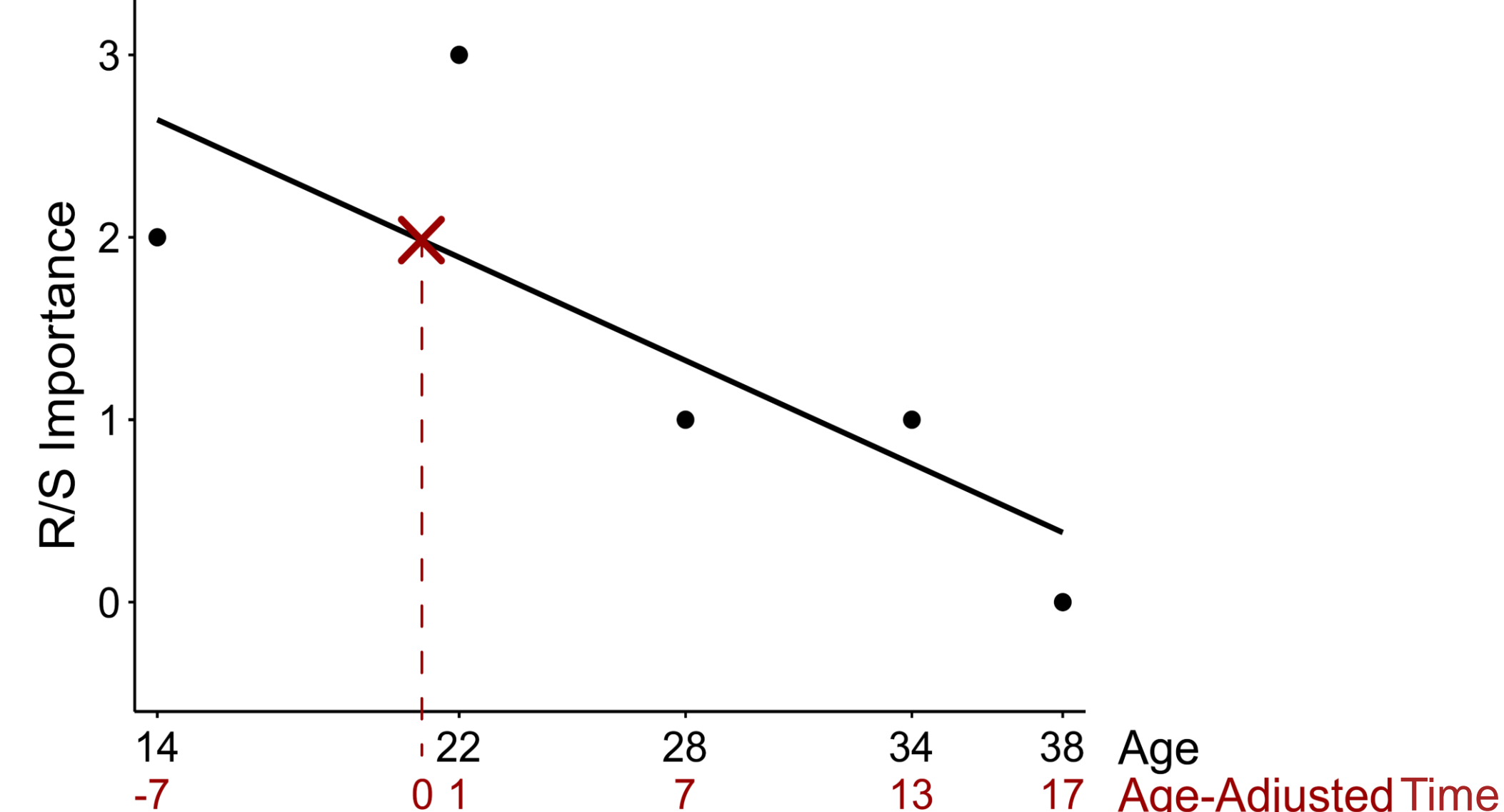


Fig 1. Representation of the mixed-effects model on a single participant. R/S importance ratings plotted by age (black points/best fit line). By using **Age-Adjusted Time**, the regression intercept (red cross) output was used as the R/S importance estimate when Age-Adjusted Time = 0, or when participant is aged 21.

Method: Variables for Predicting Depression Severity

- Obtained measures of depression symptoms: 1. **Personal Health Questionnaire (PHQ-9)**¹¹ at two most recently completed waves (Y35 and Y40), score range: 0 – 27; 2. **Inventory of Depression and Anxiety Symptoms II – General Depression (IDAS-II-GD)**¹² at Y40, score range: 20 – 100. Higher scores indicate greater severity.
- Depression measures were separately normalized¹³, transformed to Z-scores, and then averaged.
- **Posterior EEG Alpha:** 72-channel resting EEG epochs (2 s) transformed to scalp current source density (CSD)^{14,15}. Mean CSD amplitude spectra submitted to frequency PCA^{15,16}. Alpha factors (peak within 8-13 Hz) pooled across posterior sites.

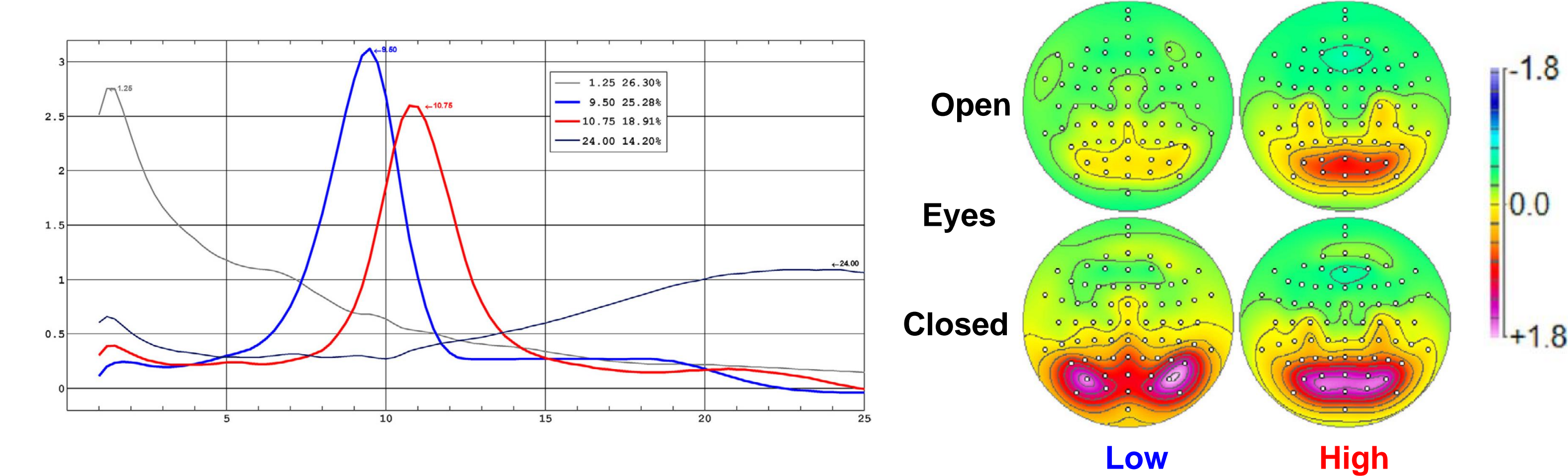


Fig 2. CSD-fPCA factor loadings for low and high frequency alpha (left). Factor score topographies (right) show greater alpha for Eyes Closed (EC), thus alpha operationalized as estimates in EC condition only

- Obtained **Sex, Age, Family Risk for MDD:** High Risk = offspring (children, grandchildren) of original probands (Generation 1) with MDD; Low Risk = offspring of healthy controls recruited from same community at same time

Measure collected	T0	T10	T20	T25	T30	T35	T40
Family Risk for MDD	x						
R/S Importance		x	x	x	x	x	
Resting EEG					x		
Age					x		
PHQ-9						x	x
IDAS-II-GD							x

Fig 3. Schematic for when each measure was collected. T0 refers to the start of the longitudinal study^{5,6}.

Statistical Model and Results

Aggregate depression severity (mean across three instruments) was the outcome, with R/S Intercept and Alpha as predictors within an interaction term, and Sex, Age, and MDD Family Risk as fixed covariates. The overall regression was highly significant, $F(5, 88) = 13.27$, $p < .001$, $R^2_{adjusted} = 0.397$. Sensitivity analysis¹⁷ determined that medium effect sizes¹⁸ could be detected.

R syntax: Depression Severity ~ R/S intercept*EEG alpha + Sex + Age + MDD Risk

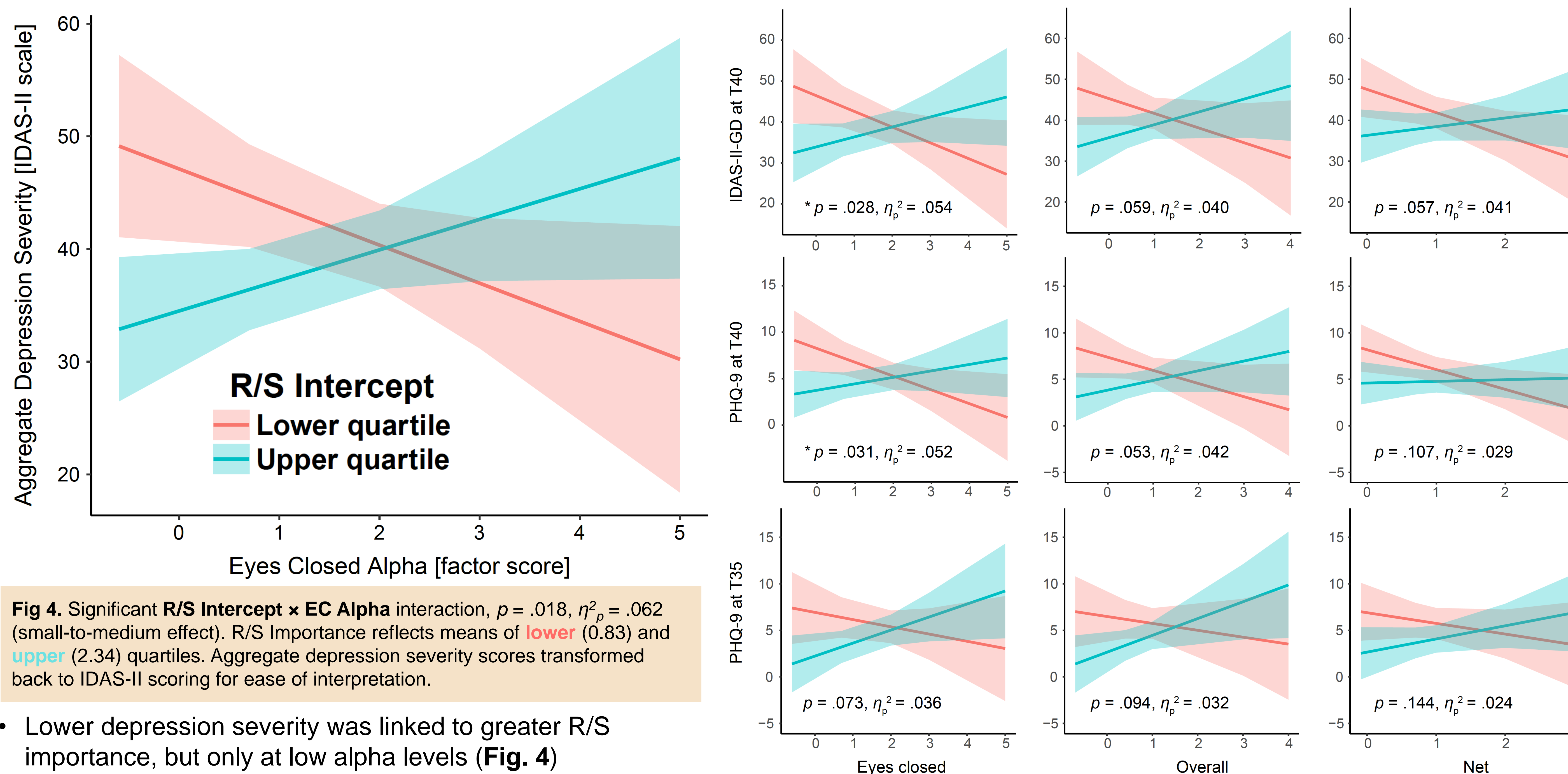


Fig 4. Significant **R/S Intercept x EC Alpha** interaction, $p = .018$, $\eta^2_p = .062$ (small-to-medium effect). R/S Importance reflects means of **lower** (0.83) and **upper** (2.34) quartiles. Aggregate depression severity scores transformed back to IDAS-II scoring for ease of interpretation.

- Lower depression severity was linked to greater R/S importance, but only at low alpha levels (**Fig. 4**)
- At high alpha levels, lower depression severity was instead linked with lower R/S importance (**Fig. 4**)
- Interaction effectively present in all follow-up models (**Fig. 5**)
- Main effects of **R/S**, $p = .008$, $\eta^2_p = .076$, **Alpha**, $p = .024$, $\eta^2_p = .056$, **Risk**, $p < .001$, $\eta^2_p = .213$, and **Age**, $p < .001$, $\eta^2_p = .199$

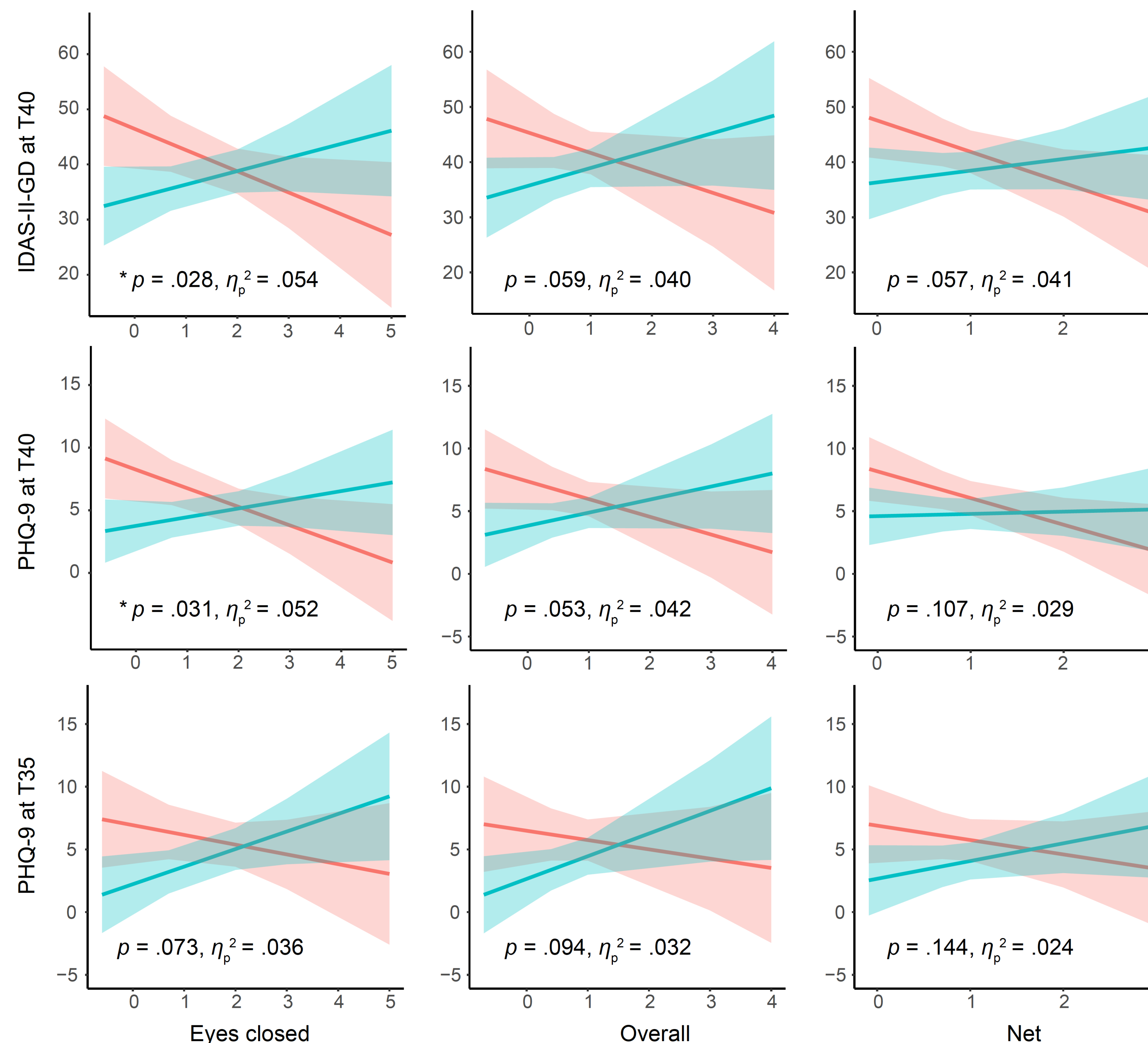


Fig 5. Follow-up models. In addition to EC condition, we also ran models with **Overall** (mean of EC and EO) and **Net** (EC – EO) alpha because these estimates have been used in previous analyses^{8,19} (columns). Individual depression measures were also substituted for the aggregate outcome (rows). Most **R/S Intercept x EC Alpha** interactions (8 out of 9 models) reached or approached at least marginal significance.

SUMMARY AND CONCLUSIONS

To predict LOWER depression severity:

Main effects consistent with prior research^{7,8}

- ❖ High R/S importance
- ❖ Greater posterior EC EEG alpha
- ❖ Familial risk for MDD
- ❖ Advanced age

R/S x Alpha constitutes new finding

- ❖ High R/S importance + low EEG alpha
- ❖ Low R/S importance + high EEG alpha

Findings show a complex relationship between R/S importance and EEG alpha in predicting depression severity.

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