

Reconsidering Remission in Recurrent Late-Life Depression: Clinical Presentation and Phenotypic Predictors of Relapse Following Successful Antidepressant Treatment

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SUPPLEMENTAL MATERIALS:

Supplemental Table 1. Comparison of Cross-Validation Methods

| Group Comparison | Model | LASSO | Ridge Regression | Elastic Net | | |
|---------------------------------|-----------------------|------------------|------------------|-------------------|-------------------|-------------------|
| | | | | $\alpha = 0.1$ | $\alpha = 0.55$ | $\alpha = 1$ |
| LLD v Comparison | Clinical Predictors | 0.746 (0.179) | 0.704 (0.548) | 0.964 (0.058) | 0.966 (0.058) | 0.970 (0.058) |
| | Neuropsych Predictors | 0.68 (0.012) | 0.64 (0.095) | 0.571 (0.0001) | 0.572 (0.0001) | 0.572 (0.0001) |
| Relapsing v Sustained Remission | Clinical Predictors | 0.332 (0.484) | 0.3 (0.135) | 0.495 (0.035) | 0.496 (0.035) | 0.536 (0.035) |
| | Neuropsych Predictors | 0.610 (0.039) | 0.574 (0.043) | 0.336 (0.009) | 0.345 (0.009) | 0.358 (0.009) |

Table 1 displays the area under the curve (AUC) and lambda value, presented as AUC (lambda), from optimal LASSO and Ridge regression models (i.e., models with the lowest mean-squared error) identified during the 10-fold cross-validation. The elastic net compared examined three alpha levels ($\alpha = 1, .55, .1$) approximating a LASSO, mixed, and Ridge penalizations. Data presented from the optimal model (i.e., highest ROC) from the elastic net. Both comparisons support LASSO regression approach, showing improved or equal fit to similar approaches.

Supplemental Table 2. Clinical predictors retained in LASSO regression between comparison participants and LLD subgroups

| | Comparison vs. Sustained Remission | | | | Comparison vs Relapse | | | |
|---|------------------------------------|------------------|---------|--------------|-----------------------|------------------|---------|--------------|
| | OR (SE) | 95% CI | z-value | p-value | OR (SE) | 95% CI | z-value | p-value |
| • Age (y) | 0.76 (0.21) | 0.51, 1.15 | -1.30 | 0.195 | 0.90 (0.21) | 0.59, 1.37 | -0.48 | 0.630 |
| • Gender (% women) | 235.92 (2.52) | 1.68, 33114.87 | 2.17 | 0.030 | 139.01 (2.56) | 0.92, 20986.53 | 1.93 | 0.054 |
| • Education (y) | 2.73 (0.48) | 1.06, 7.01 | 2.09 | 0.037 | 2.69 (0.49) | 1.03, 7.03 | 2.02 | 0.044 |
| • Race (%URM) | 0.30 (2.84) | 0.00, 78.80 | -0.42 | 0.673 | 0.01 (3.26) | 0.00, 4.28 | -1.51 | 0.130 |
| Psychiatric Phenotypic Symptoms | | | | | | | | |
| • Depression (MADRS) | 796.92 (3.73) | 0.54, 1181615.13 | 1.79 | 0.073 | 2705.50 (3.75) | 1.75, 4172829.38 | 2.11 | 0.035 |
| • Apathy (AES) | 3.90 (1.18) | 0.39, 39.52 | 1.15 | 0.249 | 2.45 (1.20) | 0.23, 25.82 | 0.75 | 0.457 |
| • Fatigue Severity (FSS) | 0.52 (1.35) | 0.04, 7.30 | -0.49 | 0.626 | 0.83 (1.38) | 0.06, 12.53 | -0.13 | 0.894 |
| • Resilience (CD-RISC10) | 2.09 (1.13) | 0.23, 19.07 | 0.65 | 0.513 | 5.20 (1.17) | 0.52, 51.88 | 1.40 | 0.160 |
| • Rumination (RRS) | 279.34 (2.71) | 1.39, 56223.69 | 2.08 | 0.037 | 371.38 (2.71) | 1.84, 75020.86 | 2.19 | 0.029 |
| Personality Traits (FFI) | | | | | | | | |
| • Conscientiousness | 1.17 (1.10) | 0.14, 10.07 | 0.14 | 0.885 | 1.37 (1.11) | 0.16, 12.12 | 0.29 | 0.775 |
| • Neuroticism | 5.45 (1.24) | 0.48, 61.73 | 1.37 | 0.171 | 3.67 (1.29) | 0.29, 45.89 | 1.01 | 0.313 |
| Medical | | | | | | | | |
| • Medical Morbidity (CIRS-G) | 56.32 (1.70) | 2.03, 1566.43 | 2.38 | 0.018 | 34.25 (1.72) | 1.19, 988.60 | 2.06 | 0.039 |
| • Disability, Self-Care (WHODAS domain 3) | 234.08 (3.20) | 0.44, 124602.76 | 1.70 | 0.088 | 649.57 (3.24) | 1.14, 369570.53 | 2.00 | 0.045 |
| • Disability, Life Activities (WHODAS domain 5) | 1.00 (1.46) | 0.06, 17.58 | 0.00 | 0.999 | 0.90 (1.50) | 0.05, 16.61 | -0.07 | 0.941 |
| • Blood pressure, systolic | 4.34 (0.85) | 0.83, 22.84 | 1.73 | 0.083 | 6.99 (0.87) | 1.27, 38.33 | 2.24 | 0.025 |
| • BMI | 3.07 (1.03) | 0.41, 22.92 | 1.10 | 0.273 | 5.66 (1.05) | 0.72, 44.61 | 1.65 | 0.100 |
| Social | | | | | | | | |
| • Instrumental support | 2.27 (1.05) | 0.29, 17.92 | 0.78 | 0.437 | 1.19 (1.05) | 0.15, 9.31 | 0.17 | 0.868 |

| | | | | | | | | |
|-------------------------|----------------|------------|------|-------|----------------|-------------|------|-------|
| • Life Stress Inventory | 1.12 (0.96) | 0.17, 7.29 | 0.12 | 0.906 | 3.79 (0.98) | 0.56, 25.65 | 1.37 | 0.171 |
|-------------------------|----------------|------------|------|-------|----------------|-------------|------|-------|

Estimates presented from final logistic regression model including all remaining LASSO predictors and demographic covariates. Psychiatric history variables not measured in comparison groups were excluded Variables with a dash (-) were not retained in that specific model. Final models included 145 participants.

AES = Apathy Evaluation Scale; BMI = body mass index; CD-RISC10 = Connor-Davidson Resilience Scale, 10 item; CI = confidence interval; CIRS-G = cumulative illness rating scale =geriatric; FFI = Five Factor Inventory; FSS = fatigue severity scale; MADRS = Montgomery-Asberg Depression Rating Scale; OR = odds ratio; RRS = ruminative response scale; URM = under-represented minority population; VAS = visual analogue 10-point scale; WHODAS = World Health Organization Disability Assessment Schedule

Supplemental Table 3. Differences in neuropsychological test performance between patients with LLD who do and do not subsequently experience a recurrent episode.

| | Relapse (N=60) | Sustained Remission (N=75) | <i>b</i> (SE) | t-value (residual df) | Unadjusted p value | Adjusted p value |
|--------------------------------|-------------------|----------------------------------|-----------------|-----------------------------|-----------------------|---------------------|
| MoCA | 26.43 (2.21) | 25.33 (2.08) | -0.63 (0.26) | -2.41 (133) | 0.019 | 0.263 |
| Learning (RBANS) | | | | | | |
| • List Learning | 27.67 (5.02) | 28.41 (4.19) | 0.07 (0.17) | 0.42 (185) | 0.678 | 0.917 |
| • Story Memory | 18.72 (3.16) | 18.26 (3.67) | -0.27 (0.20) | -1.33 (186) | 0.187 | 0.873 |
| Memory / Delayed Recall | | | | | | |
| • List recall | 6.39 (2.47) | 6.61 (1.87) | 0.05 (0.17) | 0.29 (185) | 0.773 | 0.917 |
| • Story recall | 9.88 (2.04) | 9.49 (1.95) | -0.29 (0.21) | -1.37 (186) | 0.174 | 0.873 |
| • Figure Recall | 13.80 (3.88) | 13.82 (3.43) | -0.03 (0.20) | -0.13 (181) | 0.901 | 0.917 |
| Processing speed | | | | | | |
| • RBANS Coding | 45.18 (9.04) | 46.03 (8.24) | -0.02 (0.19) | -0.12 (182) | 0.904 | 0.917 |
| • TMT, A | 33.27 (9.59) | 34 (10.69) | 0.00 (0.01) | 0.30 (181) | 0.762 | 0.917 |
| • Stroop Word Reading | 84.26 (14.42) | 83.46 (14.14) | -0.07 (0.17) | -0.41 (185) | 0.685 | 0.917 |
| • Stroop Color Naming | 59.83 (10.23) | 60.57 (9.07) | -0.01 (0.13) | -0.11 (185) | 0.917 | 0.917 |
| Executive Functions | | | | | | |
| • Verbal Fluency (COWA FAS) | 44.63 (10.97) | 45.39 (10.82) | 0.06 (0.15) | 0.44 (184) | 0.658 | 0.917 |
| • Letter-Number Sequencing | 19.07 (1.96) | 18.86 (2.97) | -0.17 (0.16) | -1.08 (185) | 0.283 | 0.917 |
| • TMT, B | 83.47 (38.22) | 77.61 (31.69) | -0.03 (0.04) | -0.76 (177) | 0.448 | 0.917 |
| • Stroop Color-Word | 33.59 (9.39) | 34.71 (8.71) | 0.07 (0.17) | 0.42 (185) | 0.675 | 0.917 |

Values presented as mean (standard deviation). Parameter estimates from binary group assignment presented. Models were controlling for age, gender, and estimated premorbid cognitive function measured with the Wide Range Achievement Test, 5th edition (WRAT5) word reading subtest. Adjusted p-values represent values after FDR (false discovery rate) correction.

MoCA = Montreal Cognitive Assessment; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; SE = standard error; TMT = Trails Making Test; COWA = Controlled Oral Word Association Test.