

Supplementary Material

Article Title: Exploratory Analysis of the Effects of Celecoxib on Cognitive Function in Vortioxetine-Treated Patients With Major Depressive Disorder in the PREDDICT Study: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

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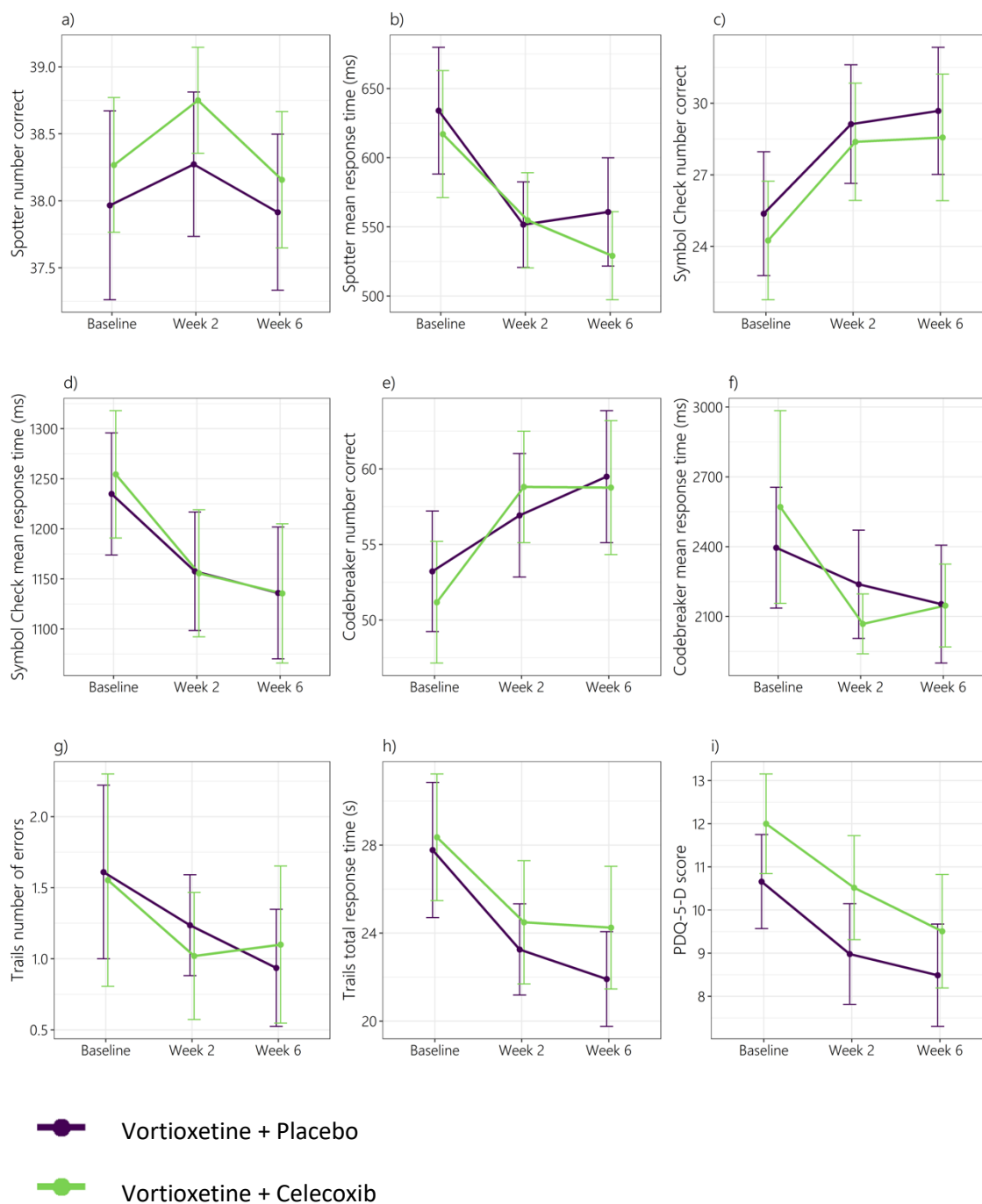
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Supplementary Figure 1: Graphs of change of individual cognitive outcome measures over time for vortioxetine + placebo and vortioxetine + celecoxib participants



*Plots of the mean of vortioxetine + placebo and vortioxetine + celecoxib scores at baseline, week 2, and week 6 time points for THINC-it tasks **a** Spotter number correct, **b** Spotter mean response time, **c** Symbol Check number correct, **d** Symbol Check mean response time, **e** Codebreaker number correct, **f** Codebreaker mean response time, **g** Trails number of errors, **h** Trails total response time, **i** PDQ-5-D score. Error bars represent 95% confidence interval.*

Supplementary Table 1: Change in THINC-it individual cognition objective measure estimates over time (adjusted model) for Vortioxetine + Placebo and Vortioxetine + Celecoxib treatment groups in the PREDDICT study

			SMD (95% CI)	Estimate (95% CI) change (baseline to week 6)	p value
THINC-it Spotter Choice reaction time (CRT)	number correct ^a	Time by treatment group interaction			0.875 [^]
		Vortioxetine + Placebo	-0.020 (-0.403, 0.363)	0.03 (-0.64, 0.69)	0.935
		Vortioxetine + Celecoxib	-0.057 (-0.436, 0.322)	-0.12 (-0.77, 0.54)	0.727
	mean response time	Time by treatment group interaction			0.137 [^]
		Vortioxetine + Placebo	-0.440 (-0.827, -0.052)	-67.36 (-98.49, -36.23)	<0.001
		Vortioxetine + Celecoxib	-0.576 (-0.961, -0.187)	-83.48 (-114.16, -52.79)	<0.001
THINC-it Symbol Check N-back	number correct ^a	Time by treatment group interaction			0.937 [^]
		Vortioxetine + Placebo	0.424 (0.035, 0.810)	3.85 (1.87, 5.83)	<0.001
		Vortioxetine + Celecoxib	0.438 (0.053, 0.821)	4.34 (2.39, 6.29)	<0.001
	mean response time	Time by treatment group interaction			0.721 [^]
		Vortioxetine + Placebo	-0.405 (-0.791, -0.017)	-84.70 (-129.40, -40.01)	<0.001
		Vortioxetine + Celecoxib	-0.466 (-0.850, -0.080)	-110.46 (-154.50, -66.42)	<0.001
THINC-it Codebreaker Digit Symbol Substitution Test (DSST)	number correct ^a	Time by treatment group interaction			0.322 [^]
		Vortioxetine + Placebo	0.389 (0.002, 0.775)	5.82 (2.89, 8.76)	<0.001
		Vortioxetine + Celecoxib	0.468 (0.082, 0.851)	7.46 (4.57, 10.35)	<0.001
	mean response time	Time by treatment group interaction			0.221 [^]
		Vortioxetine + Placebo	-0.244 (-0.628, 0.142)	-226.32 (-479.34, 26.71)	0.079
		Vortioxetine + Celecoxib	-0.341 (-0.722, 0.042)	-418.67 (-668.16, -169.18)	0.001
THINC-it Trails Trail making test part B (TMT-B)	number of errors	Time by treatment group interaction			0.755 [^]
		Vortioxetine + Placebo	-0.327 (-0.712, 0.059)	-0.70 (-1.41, 0.00)	0.050
		Vortioxetine + Celecoxib	-0.178 (-0.560, 0.204)	-0.47 (-1.17, 0.23)	0.187
	total response time	Time by treatment group interaction			0.679 [^]
		Vortioxetine + Placebo	-0.560 (-0.949, -0.168)	-5.54 (-8.27, -2.81)	<0.001
		Vortioxetine + Celecoxib	-0.377 (-0.761, 0.008)	-3.95 (-6.65, -1.25)	0.004

^a "number correct" measures have opposite directionality to all others, where a higher score indicates better performance. "Time" variable includes baseline, week 2 and week 6 observations for composite scores. Estimates are differences in means. P values refer to the difference between baseline and week 6. Covariates include participant age, sex, and education level. SMD calculated using package MBESS³³ where Group 1 = week 6 and Group 2 = baseline. Abbreviations: CI = confidence interval, SMD = standard mean difference.

Appendix 1: Summary of supplementary results

The majority of the individual THINC-it cognition measures showed a significant change between baseline and week 6. The directionality of each significant change indicates improvement in performance. Magnitudes of the significant changes over the RCT ranged from small (smallest SMD = -0.341 [DSST mean response time, vortioxetine + celecoxib group]) to medium (largest SMD = -0.576 [CRT mean response time, vortioxetine + celecoxib group]).