Multiple perspectives in psychosocial functioning and cognition in bipolar disorder: Preliminary findings from the ELICE-BD trial.

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INTRODUCTION

The presence of cognitive and functional impairment in bipolar disorder (BD) is well-documented[1,2]. However, few studies have integrated multiple perspectives (i.e. subjective, clinician-rated, and performance-based) into the evaluation of associations between these crucial outcomes. Additionally, while recent research has suggested that BD subtype may influence cognition and functioning[1,3], this finding is not consistent across studies[4,5] and further exploration is warranted. We aim to (1) investigate the associations among various measures of cognition, mood, and functioning in BD and (2) compare BD I and II groups on the described outcomes.

METHODS

From 2017 to 2024, 100 euthymic BD I and II participants, aged 19 to 65 and meeting criteria for cognitive impairment, were recruited into ELICE-BD, a randomized controlled trial of adjunctive lurasidone. All participants were at a stable dose of mood stabilizer and/or atypical antipsychotic. The following analyses examine blinded data collected at the baseline visit.

Performance-Based Assessments

Neurocognitive testing followed the International Society for Bipolar Disorders (ISBD) recommendations. **Verbal memory** was assessed with the California Verbal Learning Test-II, **executive function** was assessed with the Trail-Making Test B and Stroop Test, and **processing speed** was assessed with the TMT-A, Animal Naming Fluency, and Symbol Coding tasks. The Brief UCSC Performance-based Skills Assessment (UPSA-B) was used to evaluate **functional capacity**.

Clinician-Rated Assessments

The Montgomery-Åsberg Depression Rating Scale (MADRS) and the Young Mania Rating Scale (YMRS) were used to assess **depressive and manic symptoms**, respectively. The Functioning Assessment Short Test (FAST) assessed **functional impairment** in six areas, such as interpersonal functioning.

Patient-Rated Questionnaires

Subjective cognition was measured using the Cognitive complaints in BD Rating Assessment (COBRA). The Sheehan Disability Scale (SDS) was used to assess **functional impairment** in three domains: work/school, social life, and family life/home responsibilities. The Brief Quality of Life in BD (Brief QoL.BD) measured **quality of life**.

KEY: Higher scores on the MADRS, YMRS, FAST, COBRA, and SDS indicate poorer outcomes; higher scores on the cognition measures, UPSA-B, and Brief-QoL.BD indicate better outcomes.

RESULTS

- See Table 1 for demographic and clinical characteristics.
- Aim 1 was assessed with bivariate correlations; Aim 2 was assessed with one-way ANCOVAs to control for age, education, and mood symptoms. Covariates were selected on the basis of between-group differences and known impact on outcome variables.
- Clinical and demographic variables were compared between groups using one-way ANOVA and chi-square or Fisher's exact test. BD type was not independent from education, country of recruitment, or medication group.
- **No significant differences were detected between groups**. Depression symptoms, as measured by MADRS scores, were significantly associated with many outcomes, including scores on the FAST (F[1, 94] = 15.50, p <.001), COBRA (F[1, 94] = 5.03, p = .033), SDS (F[1, 93] = 8.15, p = .005), and Brief-QoL.BD (F[1, 94] = 27.45, p <001).

Figure 1. Cognitive performance by diagnosis

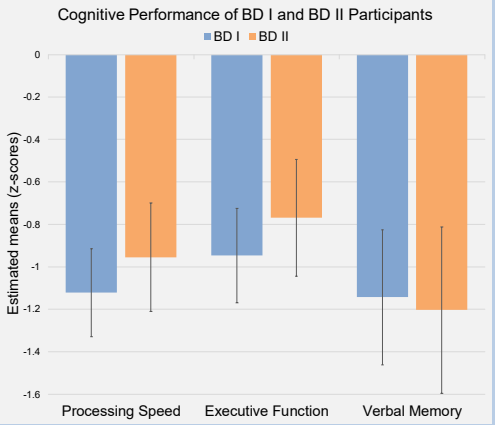


Table 1. Means, standard deviations, and bivariate Spearman's correlations

Variable	M	SD	Correlations								
			1.	2.	3.	4.	5.	6.	7.	8.	9.
1. Processing Speed	-1.05	.80	—								
2. Executive Function	-.88	.87	**.716****	—							
3. Verbal Memory	-1.17	1.20	**.320****	.149	—						
4. MADRS	3.42	2.69	-.148	-.180	0.45	—					
5. YMRS	.73	1.43	.079	**.210***	.021	.135	—				
6. FAST	15.64	12.31	**-.332****	**-.309****	**-.202***	**.386****	-.050	—			
7. UPSA-B	79.71	10.61	.032	.099	**.202***	.158	.001	.026	—		
8. COBRA	18.64	7.68	.162	-.056	.091	**.205***	-.192	.189	.057	—	
9. SDS	12.45	8.63	-.012	-.079	-.096	**.268****	-.081	**.525****	-.170	**.397****	—
10. Brief-QoL.BD	26.19	9.02	.089	.089	.140	**-.450****	.018	**-.352****	.041	**-.422****	**-.586****

Note. N = 100. *p < .05. **p < .01.

Figure 2. QoL by diagnosis

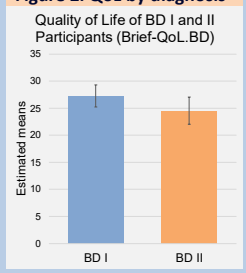
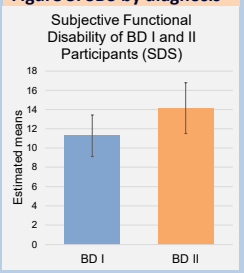


Figure 3. SDS by diagnosis



RESULTS (CONTINUED)

In a simpler model, patients with BD II had significantly more impaired QoL and subjective functional disability scores than patients with BD I; however, these differences did not remain once education and MADRS score were entered as model covariates. Figures 2 and 3 show the estimated means by group from the ANCOVAs.

Table 2. Characteristics of participants

	All N = 100	BD-I N = 60 (%)	BD-II N = 40 (%)
Female	49	26 (43.3)	23 (57.5)
Age (years): Mean ± SD	44.86 ± 12.86	45.12 ± 12.85	44.48 ± 13.02
Education (years): Mean ± SD			
	14.52 ± 2.09	14.93 ± 2.16	13.90 ± 1.82
Country			
Canada	17	13 (21.7)	4 (10.0)
USA	3	3 (5.0)	0
UK	9	8 (13.3)	1 (2.5)
Japan	71	36 (60.0)	35 (87.5)
Employment Status			
Full-time	28	17 (28.3)	11 (27.5)
Part-time	27	14 (23.3)	13 (32.5)
Student	31	19 (31.7)	12 (30.0)
Disability	7	4 (6.7)	3 (7.5)
Unemployed	7	6 (10.0)	1 (2.5)
Number of previous episodes of depression: Mean ± SD			
	8.88 ± 10.52	9.22 ± 11.51	8.38 ± 8.97
Medication Group			
Mood Stabilizer (MS)	36	26 (43.0)	10 (25.0)
Antipsychotic (AA)	27	17 (28.0)	10 (25.0)
Combination (MS + AA)	21	17 (28.0)	4 (10.0)
Lamotrigine (BD-II only)	16	0	16 (40.0)

DISCUSSION

- Multiple perspectives of psychosocial functioning and cognition likely capture different, inconsistently related constructs.
- Subthreshold depression symptoms are a major driver of subjective cognition, quality of life, and patient- and clinician-rated functioning during euthymia.
- In a sample where all participants met criteria for cognitive impairment, there were no significant differences between diagnostic groups in cognitive domains salient to BD or any functional measures.
  - This finding is in contrast with the conclusions of a recent meta-analysis[1], which found BD type I to be associated with more severe and widespread impairments than BD II.

LIMITATIONS & FUTURE DIRECTIONS

- The analyses herein are cross-sectional, were not pre-specified and no a-priori power analysis was conducted; results should be interpreted with caution.
- No adjustments were made for country of recruitment or medication group given the size of the sample and the unbalanced nature of the data. Future research may employ hierarchical models to account for nested data.

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