

1. Introduction

- Cognitive impairment (CI) is associated with worse clinical and functional outcomes in depression
- Typical cognitive performance is –0.5 to –1 SD below healthy controls across cognitive domains
- Estimates of CI in depression range from 30-60%, but prior studies have been limited by sample size or do not take premorbid cognitive function into consideration
- The purpose of the present study is to determine the prevalence of CI in depression as well as clinical and functional correlates of CI

2. Study Design

- Data was from the Dallas 2K (D2K) sub-study from the Texas Resilience Against Depression (T-RAD) study, a large prospective study of individuals with current or past depression or bipolar disorder
- Cognition was assessed with the NIH Toolbox Cognitive Battery (NIHTB-CB); patient- and clinician-rated measures of symptom severity and function were also assessed
- The first visit with cognition was used for this analysis
- Participants were included in analyses if they had a primary diagnosis of depression (per MINI) and were ≥ 18 years old at the time of the assessment

3. Data Analysis

- Participants were classified as having CI if they had ≥ 2 NIHTB-CB scores below their estimated premorbid function measured by the NIHTB-CB Crystallized Composite using demographically-corrected norms (Holdnack et al., 2017)
- Independent samples tests and Pearson chi-square was used to test differences between CI and non-CI on all characteristics; False Discovery Rate (FDR) used to protect against Type I Error

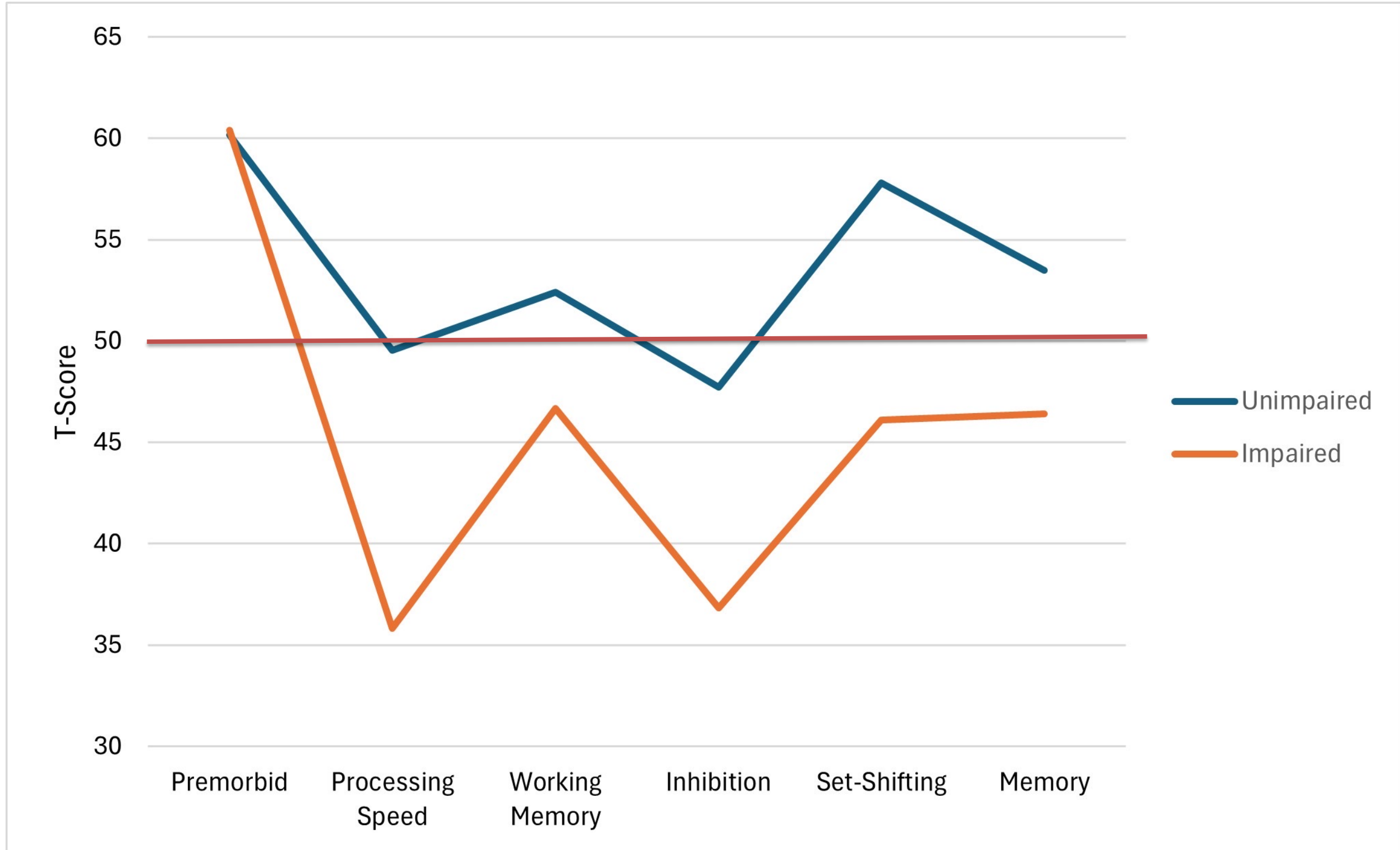
Premorbid Function Range	Cognitive Impairment Criteria
T ≥ 58	Two or more tests with T ≤ 43
T = 50 to 57	Two or more tests with T ≤ 40
T = 43-49	Two or more tests with T ≤ 37
T < 43	Two or more tests with T ≤ 34

T-Scores have a Mean of 50 and Standard Deviation (SD) of 10. Impairment is therefore classified using roughly 1-1.5 SD from an individual's estimated premorbid function. Criteria used was developed by Holdnack et al. (2017)

4. Prevalence of Cognitive Impairment (N=378)

Age	N	Impaired %
18-29	77	60%
30-39	67	42%
40-49	68	59%
50-59	87	51%
60-85	79	47%
Total	378	52%

5. Profile of Performance on NIHTB-CB



Red line represents average performance; although performance on non-premorbid tests are around the average range, they reflect 1-2 standard deviations below their premorbid estimate.

6. Group Comparisons

Variable	Unimpaired	Impaired	SMD	P-Value
Demographics				
Age	46.12 (15.41)	44.55 (15.24)	0.10	0.320
Sex (Female)	73.8%	67.7%	0.13	0.195
Race - White	80.3%	75.4%	0.12	0.248
Clinical				
Age of Onset	20.19 (11.89)	18.85 (10.54)	0.12	0.258
PHQ-9 (Depression)	9.97 (5.94)	11.32 (6.50)	0.22	0.056
GAD-7 (Anxiety)	7.25 (5.50)	8.27 (5.61)	0.18	0.103
DARS (Anhedonia) [†]	16.50 (12.60)	20.64 (12.87)	0.33	0.003*
CHRT (Suicidality)	18.27 (11.38)	20.90 (12.61)	0.22	0.042
BASC (Cognition)	68.54 (16.81)	66.52 (22.02)	0.10	0.320
Functioning				
WHOQOL Overall	56.29 (22.81)	48.78 (24.03)	0.32	0.003*
WHOQOL Physical	57.85 (19.08)	52.06 (20.32)	0.29	0.006*
WHOQOL Psychological	47.33 (18.93)	42.42 (19.19)	0.26	0.016*
WHOQOL Environmental	65.96 (17.62)	61.90 (18.81)	0.22	0.038
WHOQOL Social	46.50 (22.90)	43.47 (24.04)	0.13	0.222
WPAI Employment	65.54%	47.19%	0.38	< 0.001*
WPAI Activity Impairment	35.06 (32.39)	46.34 (33.19)	0.34	0.002*
WSAS	17.66 (10.77)	18.19 (11.98)	0.05	0.653

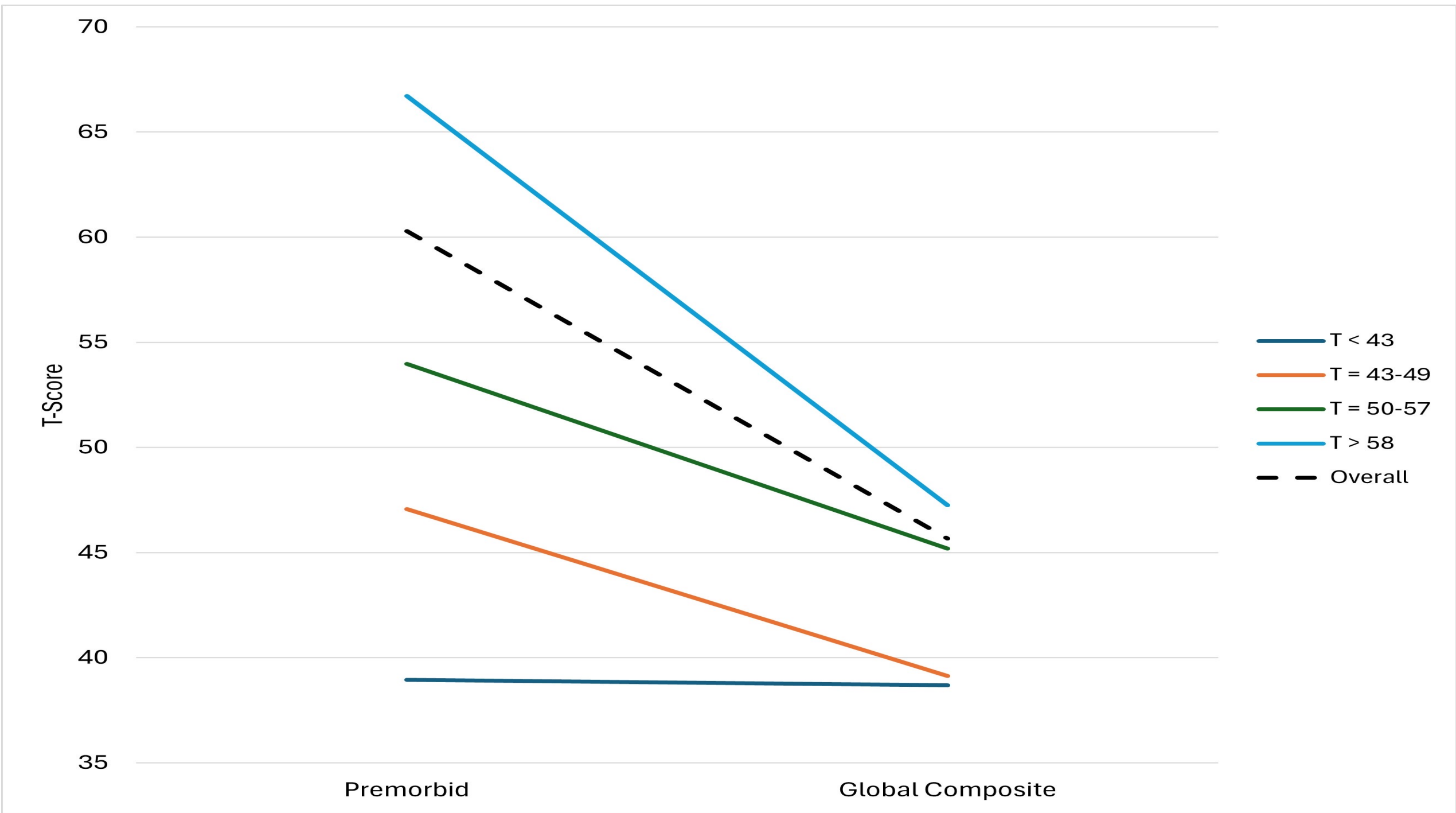
*P-Value statistically significant after FDR correction. [†]Higher scores represent more severe anhedonia.

7. Cognitive Impairment by Premorbid Cognition

Premorbid Function	Unimpaired	Impaired
T ≥ 58	100 (54.64%)	129 (66.15%)
T = 50 to 57	52 (28.42%)	39 (20.00%)
T = 43-49	21 (11.48%)	21 (10.77%)
T < 43	10 (5.46%)	6 (3.08%)
Total	183 (48.41%)	195 (51.59%)

Fisher's Exact P = 0.105

8. Global Cognition by Premorbid Function



Plot shows the average difference between premorbid cognitive function and current cognitive functioning.

9. Conclusions

- CI is present in approximately 50% of the depressed population
- CI in depression does not vary based on age or premorbid cognitive function
- Given that 16% of the healthy population meet criteria for CI as defined in this study, individuals with depression are 3x more likely to have CI
- Without taking premorbid cognition into consideration (as is the case for most studies), cognitive performance appears to be in the mildly impaired range, but is actually more profoundly impaired vs. their premorbid
- Individuals with CI and depression are:
 - No more depressed or anxious than non-CI depressed
 - Less likely to be employed
 - More likely to report impairments in activities
 - More likely to report worse quality of life

10. Acknowledgments

- We thank all participants who took part in this study
- JTJ, LS, AJS and AE receive salary and equity compensation from Alto Neuroscience. AE holds equity in Akili Interactive. AS holds equity in J&J.