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Personality Measures and Antidepressant Response in Subcallosal Cingulate Deep Brain Stimulation Treatment

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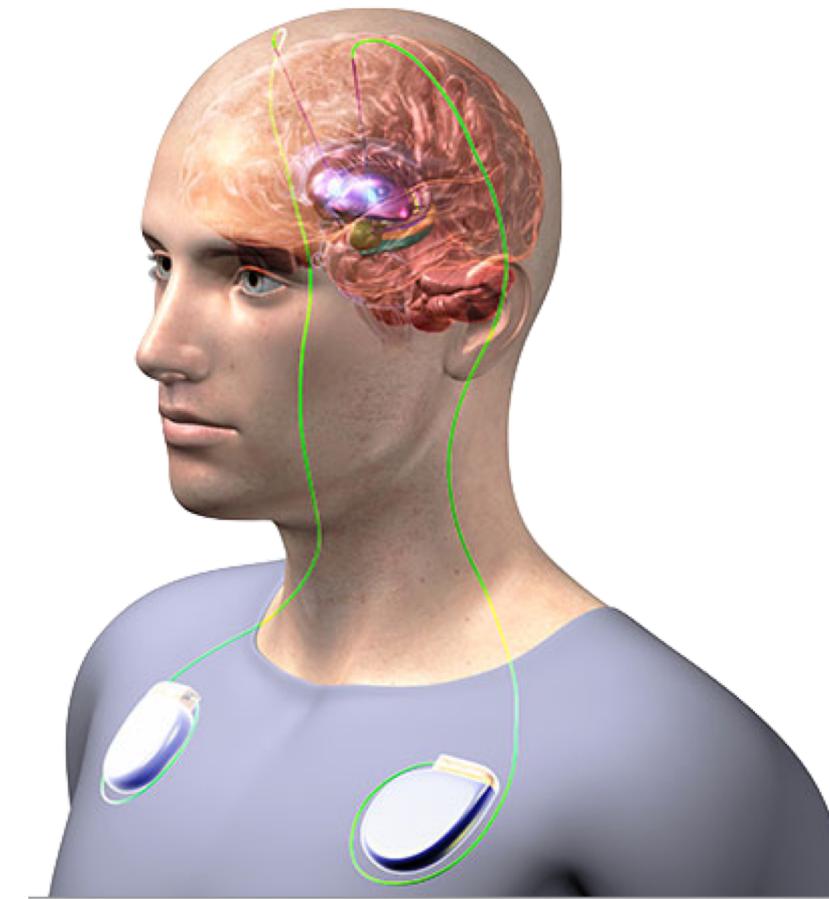


BACKGROUND

Depression prevalence is on a rise with an estimated 4.4%, or 332 million people, living with the condition. Ranking as the third most common health problem causing disability, various treatment opportunities are being explored for depression resistant to conventional treatments. Subcallosal cingulate (SCC) deep brain stimulation (DBS) is a promising investigational therapy for treatment resistant depression (TRD) with ~50% response rates. Previous reports suggest changes in social behavior in Parkinson's patients after administration of DBS targeted at the subthalamic nucleus. However, the impact of SCC-DBS on personality in TRD patients remains unknown.

What is DBS?

In DBS, electrodes are surgically implanted in a specific region of the brain (i.e. SCC) which deliver different frequency stimulation to the site. Lead wires from a pacemaker like device are placed under the skin of the chest delivering externally programmable signals to the target.



OBJECTIVES

The objectives of this study were: (i) to examine changes in personality profiles of individuals with TRD following SCC-DBS and (ii) identify personality measures as predictors of response to DBS.

MATERIALS / METHODS

Twenty two patients with TRD of both genders aged 20 to 70 years were enrolled in the study. Electrodes were implanted bilaterally in the SCC as guided by Diffusion Tension Imaging tractography. Depression severity was measured pre-DBS at baseline and post-DBS monthly for 15 months with Hamilton Depression Rating Scale (HDRS). Personality was measured pre-DBS at baseline and post-DBS every 3 months for 15 months with the NEO-Five-Factor Personality Inventory (neuroticism, extraversion, openness to experience, agreeableness, conscientiousness). Patients with 50% reduction in HAMD scores at 6 months from baseline were considered as responders.

Table 1. Demographics and Clinical Characteristics of Recruited Participants					
	Outcome at 6 months		Outcome at 12 months		
	All patients (N=22)	Responder (N = 10)	Non Responder (N = 11)	Responder (N = 10)	Non Responder (N = 11)
Age	46.4 (14.35)	39.6 (12.92)	51.9 (14.03)*	40.8 (15.21)	50.8 (12.88)
Female	9 (45.45%)	6 (60.00%)	3 (27.27%)	5 (50.00%)	4 (36.36%)
MDD	17 (77.27%)	8 (80.0%)	8 (72.73%)	7 (70.00%)	9 (81.82%)
BP	5 (22.73%)	2 (20.0%)	3 (27.27%)	3 (30.00%)	2 (18.18%)
TRD Stage (IV&V)	18 (81.82%)	8 (80.0%)	9 (81.82%)	9 (90.00%)	9 (81.82%)
TRD Severity	12.7 (1.57)	12.9 (0.99)	12.7 (2.00)	13 (0.82)	12.7 (2.06)
Age of Onset in years	22.5 (12.28)	17.5 (10.42)	26 (12.88)	17.9 (8.79)	25.6 (14.17)
Duration since onset in years	24 (16.54)	22.1 (15.74)	25.9 (17.80)	22.9 (15.08)	25.2 (18.44)
Duration of Current Episode in Months	24 (17.63)	22.9 (20.42)	21.6 (15.67)	17.4 (19.80)	26.6 (14.97)
Past ECT	19 (86.36%)	8 (80.00%)	10 (90.91%)	9 (90.00%)	9 (81.82%)
Past tTMS	5 (22.73%)	2 (20.00%)	3 (27.27%)	2 (20.00%)	3 (27.27%)
Past Ketamine	4 (18.18%)	0 (0.00%)	4 (36.36%)	0 (0.00%)	4 (36.36%)
No. of Current Medications	3.4 (2.08)	3.2 (2.35)	3.5 (1.92)	3.4 (2.41)	3.3 (1.85)
No. of Past Medications	22.8 (11.94)	17.7 (6.13)	28.5 (13.81)	18.9 (5.55)	27.4 (14.83)

Data is given in mean (SD) or (%) ; MDD- Major Depressive Disorder; BP-Bipolar type II disorder; ECT-Electroconvulsive therapy; tTMS-repetitive Transcranial magnetic stimulation. * p=0.051

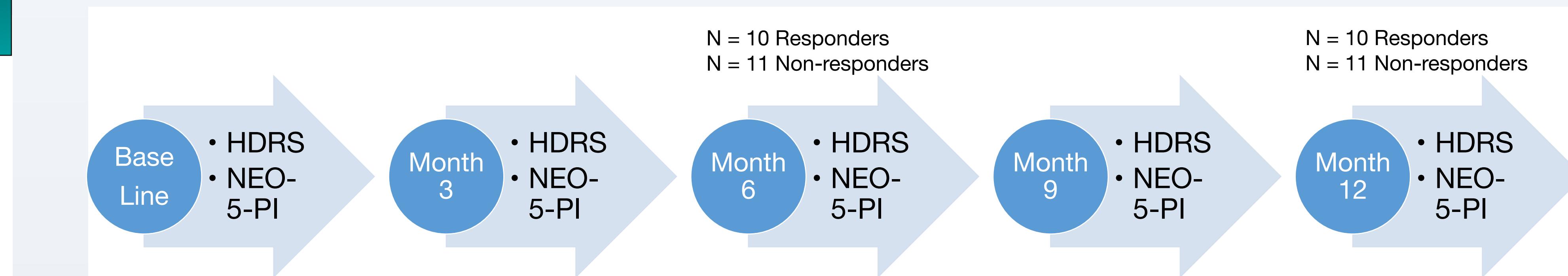


Figure 1. Timeline and procedure used for collecting scores used for study. NEO-5-PI, Neuroticism Extroversion, Openness Five-Factor personality inventory; HDRS, Hamilton Depression Rating Scale

Linear Mixed Model Analysis (LMM)

- An LMM (unstructured covariance matrix) was used to analyze if any change in personality dimensions was present from baseline to 15 months
- The fixed factor main effect was given as the different time points and random effect as the patient

RESULTS

Personality Changes

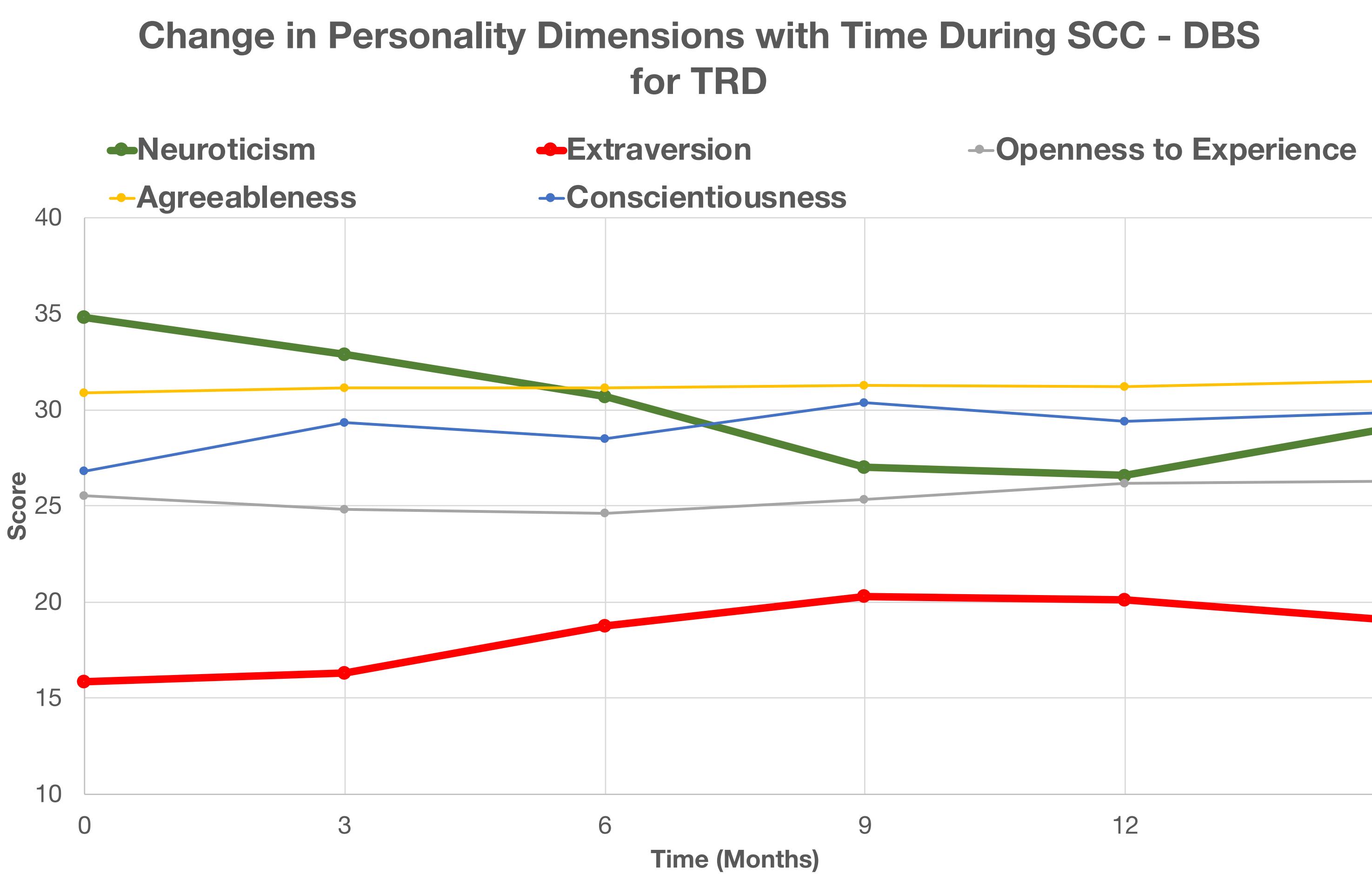


Figure 2. NEO 5 factors as a function of time. Bold lines indicate significant change from baseline scores.

Neuroticism significantly decreased over time ($F_{5, 18.47} = 5.88, p = 0.002$). Post-hoc test indicated a significant change from baseline to 9 months ($p = 0.002$) and baseline to 12 months ($p = 0.002$). A significant increase in **extraversion** was observed ($F_{5, 13.38} = 11.65, p < 0.001$) over time but post-hoc tests were insignificant. Responders influenced significant change in extraversion at 6 months ($F_{1, 19.18} = 13.85, p = 0.001$), and agreeableness at 12 months ($F_{1, 19.25} = 14.14, p = 0.001$) compared to non-responders. Change in neuroticism was correlated with change in HDRS at 6 months ($r = -0.71, p < 0.001$) and 12 months ($r = -0.734, p < 0.001$). Change in extraversion was correlated with change in HDRS at 12 months ($r = 0.576, p = 0.01$).

Personality Predictors

Pre-DBS agreeableness scores were positively correlated with decrease in depression severity ($r = 0.655, p = 0.002$) at 12 months. Refer to Figure 3.

Agreeableness Baseline Scores as a Function of Change in Depression Severity

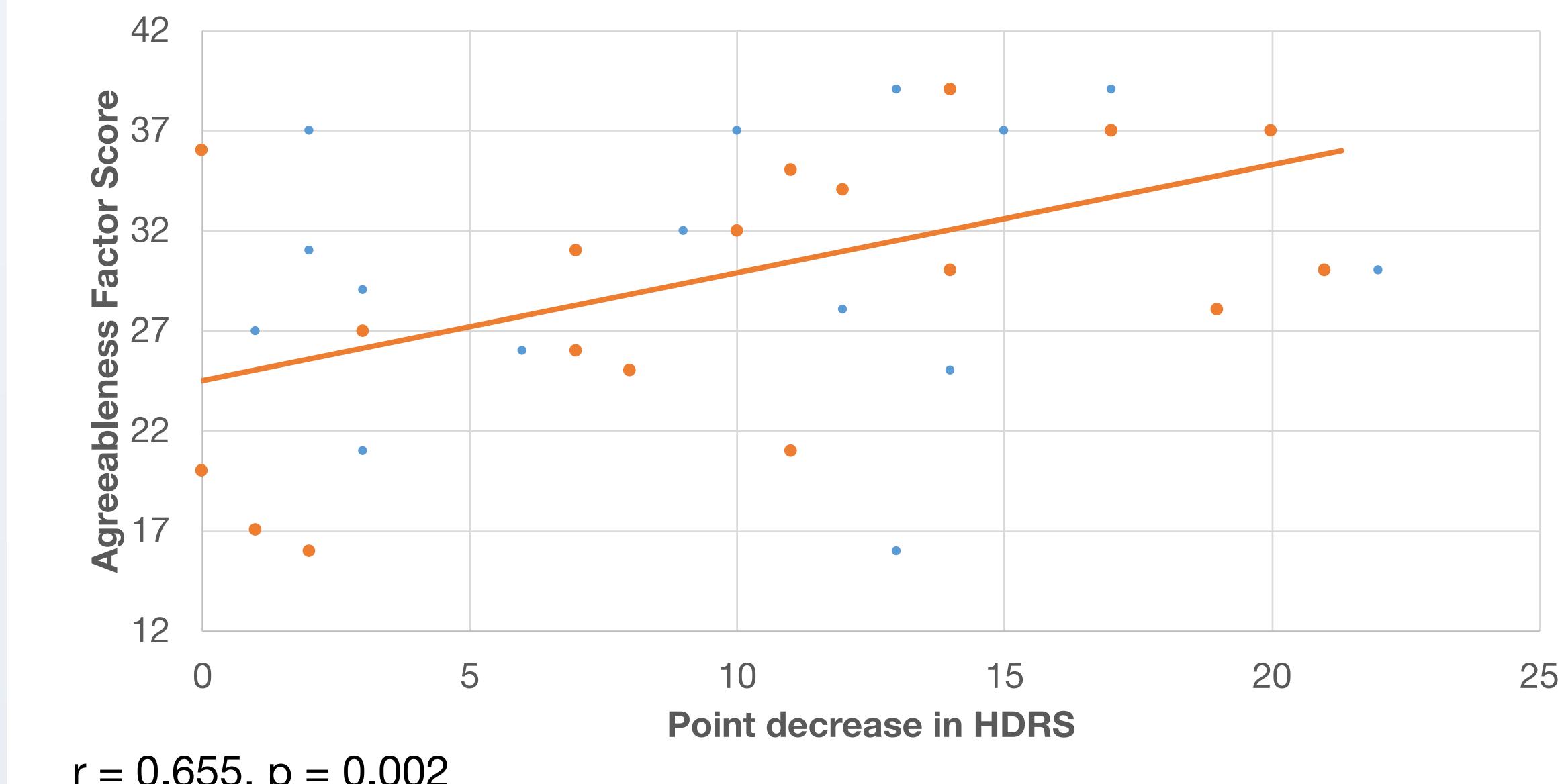


Figure 3. Graphical illustration of the correlation between baseline agreeableness scores and reduction of depression severity. Orange, 12 months; Blue, 6 months.

DISCUSSION

Our results indicate positive personality changes following SCC-DBS in terms of reduction in neuroticism and increase in extraversion over 15 months, which was in direct correlation with clinical improvement of depression. The change of extraversion and agreeableness scores was influenced by responders at 6 months and 12 months respectively. Baseline agreeableness scores predicted reduction in depression severity at 12 months suggesting that sociability in TRD patients may predict successful SCC-DBS treatment.

FUTURE DIRECTIONS

The use of personality measurement in subject selection for DBS and as one of the outcome measures of DBS treatment is a viable approach however, this needs to be examined in a larger study cohort.

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