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Executive Functioning at Baseline Prospectively Predicts Depression Treatment Response*

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Abstract

Objective.—Existing cognitive and clinical predictors of treatment response, to date, are not of sufficient strength to meaningfully impact treatment decision making, nor are they readily employed in clinical settings. The present study investigated whether clinical and cognitive markers used in a tertiary care clinic could predict response to usual treatment over a period of 4–6 months in a sample of 75 depressed adults.

Methods.—Patients (N=384) were sequentially tested in two half-day clinics as part of a quality improvement project at an outpatient tertiary care center between 8/2003 and 9/2007. Diagnosis was according to DSM-IV, completed by residents and attending faculty. Test scores obtained at intake visits on a computerized neuropsychological screening battery were the Parametric Go/No-Go task (PGNG) and Facial Emotion Perception Task (FEPT). Treatment outcome was assessed using Personal Health Questionnaire (PHQ) self-ratings at follow-up (N=75). Usual treatment included psychotropic medication and/or psychotherapy. Decline in PHQ scores was predicted based upon baseline PHQ and education, with neuropsychological variables entered in the second step.

Results.—PHQ scores declined by 46% at follow-up, 56% responders. Using two-step multiple regression, baseline PHQ and education were significant step one predictors of percent change in PHQ-9 follow-up scores. In step two of the model, faster Processing Speed with Interference Resolution (Go Reaction Time) independently explained a significant amount of variance over and above variables in step one (12% of variance), while other cognitive and affective skills did not. This two-step model accounted for 28% of the variance in treatment change in PHQ scores. PSIR also accounted for 12% variance in treatment/follow-up attrition.

Conclusions.—Use of executive functioning assessments in clinics may help identify individuals with cognitive weaknesses who are at risk for responding less well to standard treatments.

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Keywords

depression; executive functioning; attention; affect perception; cognitive screening

Introduction

Despite significant advances in the field of psychiatry, there is currently no empirically-derived method for the order or combination in which medications and/or therapies should be employed to treat depressive symptoms.^{1,2} Indeed, half of the adults hospitalized for a major depressive episode take at least a year to achieve symptom remission with standard treatments.³ Additionally, approximately 30% of individuals who respond well to cognitive behavioral therapy relapse within a 12-month period.⁴ Therefore, the identification of prognostic characteristics for treatment responsiveness and sustained wellness may help maximize the efficacy of health care delivery and improve the quality of life among individuals with depression. If patients can be identified earlier as having a low probability of response to usual treatment, alternative or augmented treatment plans might be developed in an effort to reduce short and longer term morbidity in this population.

Previous studies have identified a number of clinical characteristics that predict treatment outcomes in depressed adults e.g., age of depression onset, number of prior hospitalizations, psychiatric comorbidity, baseline depression severity;^{3,5,6} However, predictors in these models often account for only a small portion of the variance in treatment response (e.g., 5–20% cumulative variance accounted for), and these studies typically do not examine longer-term outcomes. Other studies support modest links between cognitive strengths and better treatment responsiveness, and the combination of clinical characteristics and cognition often yields a stronger predictive model.^{6–9} In one study that assessed cognition as a predictor of treatment responsiveness, poorer performance on measures of novel problem solving and verbal inhibition at baseline significantly predicted a lack of response to fluoxetine in a sample of 14 women experiencing a major depressive episode.¹⁰ Poorer divided attention has also been associated with less responsiveness to antidepressants six months following psychiatric hospitalization in a sample of 73 adults with major depressive disorder or bipolar disorder.¹¹ Additionally, for 32 adults experiencing a major depressive episode, poorer performance at baseline on measures of attentional shifting, working memory, and verbal fluency predicted an unfavorable response to selective serotonin reuptake inhibitors (SSRIs) within three months.⁸ Other studies, in contrast, have failed to support cognitive strengths as a predictor of improved treatment responsiveness among depressed adults e.g.,⁹. Of note, the sample sizes, measures used, and degrees of freedom available in each statistical model varied significantly across these studies, limiting the degree to which they can be compared. More recent studies and reviews completed after this trial started have solidified the importance of executive functioning measures in prediction of treatment response^{12,13}.

Accurate facial affect recognition is also frequently impacted by depression, but its relationship with treatment responsiveness is currently unknown. Depressed individuals typically exhibit difficulty recognizing subtle positive facial expressions¹⁴ and can have difficulty disengaging from the negative affect of others.¹⁵ These findings are even more

robust with greater depression severity and lower educational attainment.¹⁴ Given that affective signals of others represent important social cues, impaired facial affect recognition may have negative psychosocial implications. There do not appear to be treatment prediction studies in adults with major depressive disorder using facial affect recognition measures, although see a recent neuroimaging study related to response, and other studies related to outcome^{16–18}. In addition, at least one study that supports an association between higher Global Assessment of Functioning scores¹⁹ and more accurate recognition of happiness.²⁰

The present study is an extension of our previous cross-sectional work,²¹ which evaluated executive functioning and affective processing in a naturalistic sample of adults presenting to outpatient mental health clinics for initiation of treatment for mood and/or anxiety disorders. The present study used a longitudinal design to evaluate whether psychomotor speed, attention/executive functioning, and emotion perception at baseline would predict treatment responsiveness in a sample of depressed adults receiving usual, “open-label” treatment. Our hypothesis was that participants who demonstrated better executive functioning and emotion perception at baseline would respond more robustly to usual psychiatric and/or psychological treatments at follow-up. The naturalistic approach to participant recruitment was intended to promote generalizability to real-world applications, and the duration of 4–6 months was intended to evaluate more sustained remission. A secondary goal of this study was to evaluate the potential utility of administering a computerized cognitive screening battery in outpatient mental health clinics as part of the intake process by identifying cognitive limitations early in the treatment process, which might inform subsequent treatment plans. The ultimate goal of this study, while not directly assessed, was to identify whether the process of cognitive screening at intake could inform empirically-based treatment choices. We are unaware of any existing study that has analyzed the potential value of such clinical screening as a standard procedure.

Methods

Participants

Participants represented a portion of the larger sample of adults with various psychiatric conditions ($N = 384$) that is described in an earlier paper,²² including additional subjects evaluated in the clinic between 2007 and 2009. Inclusion criteria for the current sample were a current or lifetime diagnosis of major depressive disorder or mood disorder NOS, an estimated verbal IQ of at least 75, mild to severe depression (defined by baseline scores on the Patient Health Questionnaire (PHQ-9) of 5 or greater), and completion of a follow-up PHQ-9 within four to six months after intake. The sample was restricted to adults up to age 65 to reduce the potential effects of age-related cognitive changes. Exclusion criteria were a current alcohol or substance abuse disorder or a history of a medical condition likely to negatively impact cognition or the ability to complete computerized testing (e.g., developmental disability, cerebrovascular accident). Because this study aimed to capture a representative sample of individuals initiating care for depression, participants were not excluded for other comorbid conditions.

The final sample included 75 adults diagnosed with major depressive disorder ($n = 67$) or mood disorder NOS ($n = 8$; see Table 1). The sample was largely female ($n = 60$) and

Caucasian ($n = 56$). Most participants had completed some college ($n = 69$; range = 9 to 22 years), typical of the setting from which they were recruited. There was wide variability in age at disease onset (ranging from 5 to 54). IQs were estimated using the Shipley Institute of Living Scale see description below;²³ with 67% ($n = 50$) falling within the average range (score range = 82 to 121). Most participants endorsed experiencing moderately severe depression at the point of treatment initiation at the clinic (range = 5 to 24).

Design and Procedure

Institutional Review Board approval was obtained from the University of Michigan, as was permission to waive written informed consent and acquire verbal assent for use of clinical data for research purposes. Testing occurred prior to intake evaluations at University of Michigan, Department of Psychiatry tertiary care treatment facilities, in two afternoon (one women's mental health) and one morning clinic. Diagnoses were made using DSM-IV¹⁹ criteria by board-certified psychiatrists or psychologists.²⁴ Research assistants administered the cognitive screening battery described below. A brief, automated report describing the patient's strengths and weaknesses in comparison to normative data was provided to the treating physician, psychologist, or social worker, typically prior to or during the visit. Additional measures not described here were administered as part of a broader clinical care improvement initiative. The PHQ-9 was completed at baseline and at variable follow-up intervals. We analyzed changes from baseline to follow-up at four to six months to assess sustained improvement.

Due to the naturalistic, observational nature of this study, treatments ranged from psychotropic medication only, psychotherapy only, or a combination of medication and therapy (see Figure 1 for participants in the treatment cells). Due to the range of treatments employed, we monitored treatments following intake primarily for descriptive purposes. Of note, several participants were transferring care from different organizations and were therefore already receiving treatment(s). Since most participants' depressive symptoms were in the moderate to severe range despite the presence or absence of a prior treatment regimen, we identified participants who completed a new trial of psychotherapy and/or a change in psychotropic medication (e.g., increased dosage, typically of SSRI, substitution of new SSRI, often followed later by augmentation) following intake as a means of assessing response to intervention. A *completed treatment trial* was defined as (1) participation in eight or more individual psychotherapy sessions following intake, (2) at least eight weeks of treatment with an increased dosage of at least one psychotropic medication after intake, and/or (3) a minimum eight-week trial of one or more new psychotropic medications within the four to six month treatment window.

Sixty-six participants completed eight-week trials of at least one psychotropic medication. Of the 71 patients with psychotherapy data, 52 were referred to individual psychotherapy but only 23 of those patients (44%) completed at least eight sessions within six months, with 14 (60%) receiving an evidence-based treatment (i.e., cognitive-behavioral, interpersonal, or dialectical behavioral therapies, <https://www.div12.org/psychological-treatments/>) and 9 receiving supportive therapy. Of note, the final sample included two patients who failed to meet criteria for a completed treatment trial due to medication non-compliance, four patients

who had imprecise medical records due to ongoing treatment at outside facilities, and one patient whose treatment information was missing. We chose to retain participants with missing or incomplete data in the current sample for better representativeness given the naturalistic recruitment method. The exclusion of these subjects did not change the treatment prediction estimates.

Measures

The following cognitive screening battery used in this study was selected to rapidly evaluate frequently impacted cognitive abilities among depressed adults, including psychomotor speed, attention and executive functioning (EF), and affect perception (AP). This specific combination of tests was chosen in 2002 at the start of this project, because both tests are easily administered via computer in under 25-minutes, enhancing accessibility to outpatient treatment providers.

The Parametric Go/No-Go task (PGNG; ^{25,26} was used to assess inhibitory control, attention, and set-shifting abilities. The task is well-described in previous literature and an overview is presented here. The PGNG consists of a rapid (interstimulus interval = 500ms) serial presentation of letters, with target letters of “x”, “y”, and “z.” Subjects follow a “respond to all targets” rule in the easiest level of the test (Level 1), and a “do not repeat” rule in the two No-Go levels (levels 2 and 3) of the test. The task is a specialized measure of *contextual inhibition*, as Go and No-Go response sets change with each response. Contextual inhibition is thought to reflect the same neural regions that support emotion regulation.²² Two aspects of inhibitory control are measured as parts of contextual inhibition:²⁷ behavioral response inhibition (e.g., impulsivity) and removal inhibition (e.g., updating working memory rules or set-shifting).²⁷ Psychomotor speed is also assessed during each level of the task. Outcome measures include reaction time across Levels 1–3, percentage of correct hits across Levels 1–3, and percentage of correct inhibited responses during Levels 2–3.

The Facial Emotion Perception Task (FEPT; ^{22,26,28,29} assesses emotion perception and processing, both of which can be impaired in depressed adults.^{30–32} Participants are asked to rapidly categorize a series of faces exhibiting happiness, sadness, anger, and fearfulness;³³ Categorization of animals (dogs, cats, primates, and birds) is included as a control task. The visual stimulus is presented for 300ms, followed by a mask (i.e., a gray checkerboard mask) for 100ms, and then 2600ms are provided as a response window. Trials are separated by the presentation of a fixation cross for 500ms. Outcome variables include reaction time across all trials and the percentage of correctly identified emotional expressions and animal categories.

A modified version of the vocabulary subtest of the Shipley-2²³ was used to estimate verbal intelligence. Participants are presented with a word and then asked to choose a synonym among four options. There is no penalty for guessing, and we did not impose a time limit for responding. Raw scores were prorated and converted to IQ estimates based upon age norms.

The Patient Health Questionnaire (PHQ-9; ³⁴ is a self-report measure of depression symptoms. This measure categorizes four degrees of depression severity based on the

individual's total score i.e., 5–9 = mild, 10–14 = moderate, 15–19 = moderately severe, and 20–27 = severe;³⁴ This measure does not require specialized training to administer or score and is therefore easily incorporated into clinic intake and follow-up procedures.

Analyses

As described in our previous cross-sectional study, a principal axis factor analysis with oblique rotation was computed using the FEPT and PGNG raw scores in the sample from the larger study (see Langenecker et al., 2007; $n = 73$ healthy adults and $n = 367$ adult psychiatric outpatients) to consolidate the number of variables to be used in subsequent analyses. The resulting factors included: 1. *Visual-Perceptual Processing Speed* (reaction time during all trials of the FEPT), 2. *Inhibitory Processing Speed* (reaction time during all levels of the PGNG, hereafter described as *Processing Speed with Interference Resolution*, PSIR, to reflect changes in the way the variable has been conceptualized and described following publication of the initial study:²¹ 3. *Attention Accuracy* (the percentage of hits during Levels 1–3 of the PGNG), 4. *Inhibitory Control Accuracy* (the percentage of correctly inhibited responses to lures during Levels 2–3 of the PGNG), and 5. *Visual-Perceptual Accuracy* (the percentage of correct identifications of different human expressions and animal categories). These factor scores were used in all subsequent analyses as key predictor variables (see Supplemental Table 1). Correlations between cognitive/affective variables and initial PHQ scores were not significant (all r s $< .17$, p s $> .13$).

Cognitive factor scores were assessed for invalid or out-of-range data. Outliers underwent a Winsor truncation procedure.³⁵ To address the primary aim of determining whether executive functioning (EF) and affect perception (AP) predict treatment responsiveness, a two-step, full model multiple regression analysis was computed. Given the significant association between baseline depression severity and the percent change in follow-up depression scores (two-tailed Pearson $r = .34$, $df = 73$, $p < .05$), baseline PHQ-9 scores were included in the first step of the model as a covariate. Age and education were also included as covariates as these are known to be related to these cognitive and affective measures. In addition, as there was substantial variability in baseline PHQ and follow-up PHQ scores, we used percent change in PHQ scores as an outcome measure. The EF and AP variables were entered in a second step, with the goal of determining whether cognition contributed significantly in predicting treatment outcome after consideration for the effects of clinical/demographic characteristics. Percent change in PHQ-9 scores (from baseline to follow-up) was used as the primary outcome variable of the multiple regression analysis. A second, *post hoc* regression model was computed using backward elimination to further clarify the association between baseline cognitive functioning and follow-up depression scores. Attrition from treatment was also predicted using cognitive and affective measures, as in hypothesis one. Finally, a planned exploratory one-way ANOVA was conducted to determine whether treatment type represented an independent predictor of depression four to six months following baseline.

Results

With regard to treatment responsive PHQ-9 scores improved an average of 46% within four to six months following intake, with most participants improving from moderately severe depression at baseline to mild depression at follow-up (see Table 1 above). Over half the sample experienced a 50% or larger reduction in depression symptoms. Thirty-two percent of the sample scored within the minimal range of depression on the PHQ-9 at follow-up.

To address our hypothesis that cognitive test performance would significantly predict response to usual treatment, a two-step multiple regression was computed using the percent change in follow-up PHQ-9 scores as the outcome variable. The first step of the model using education, age and baseline PHQ-9 scores was significant, $F(3,73) = 4.79, p < .01, R^2 = .17$ (see Table 2). When the EF and AP variables were added as predictors in the second step, R^2 notably increased [$F(8,68) = 3.35, p < .01, R^2 = .28$], enhancing the prediction of treatment outcomes from 14% to 28%. Among the cognitive variables entered in the model, only PSIR added significant, unique variance to the model, with faster PSIR predicting a greater percent change in PHQ-9 follow-up scores (illustrated in Figure 2, $B = -.34, p = .01$). The other cognitive factors scores were not significant unique predictors in the model. Better emotion/visual processing accuracy was at the trend level for prediction of treatment response ($B = .22, p = .09$). In a larger model with all participants, we used the same predictors to evaluate ability to predict attrition to treatment or PHQ follow-up. Step 1 was the same as above, now predicting binary continue vs attrition ($X^2 = 4.79, p = .19, R^2 = 0.03$). We also compared those who were included to those who were lost to attrition. Of the 226 individuals who were lost to attrition, they were significantly slower in PSIR relative to those who remained in treatment and completed multiple PHQ measurements ($F(1,310) = 37.61, p < .0001, B = .02, p < .0001, sR^2 = .16$). Those who did not complete treatment and/or complete multiple PHQ measurements were not different in age, education, initial PHQ score, or age of onset relative to those who continued on in treatment and completed multiple PHQ measurements ($ps > .25$). More males tended to be lost to attrition in measurement, but this was not significant ($X^2 = 1.27, p = .26$). Models had similar predictive value if those with Mood Disorder NOS were excluded, or if those with PHQ scores in the mild range were excluded, consistent with current formulations for how treatment evaluation and prediction might be transdiagnostic³⁶.

In an effort to further evaluate the meaningfulness of PSIR as a predictor of treatment outcome, a *post hoc* regression model was computed using backward elimination to determine whether PSIR would remain a significant contributor to the model when additional demographic characteristics were considered (i.e., age at disease onset, presence of medical or psychiatric comorbidity, and gender). The combination of age, education, percent change in PHQ-9 scores, the presence of a comorbid medical or psychiatric condition, and PSIR explained approximately 30% of the variance in the percent change in PHQ-9 scores, $F(4, 70) = 7.43, p < .01, R^2 = .30$. PSIR remained a significant unique predictor (semi-partial correlation = .11).

Finally, a planned, exploratory *post hoc t*-test was computed to evaluate whether the type of treatment the patients received was associated with the percent change in depression scores

at follow-up. Possible treatment outcomes were limited to 1. medication change only ($n = 47$) versus 2. combined medication change and completed psychotherapy ($n = 19$) because very few participants completed psychotherapy only ($n = 4$). There were no significant differences in the change in PHQ-9 scores between treatment groups ($t = 1.50$, $df = 25$, $p = .14$; see Supplemental Figure 1). Likewise, there was no difference between groups based upon subsequent treatment allocation in baseline PHQ scores ($F(3,64) = 0.26$, $p = 0.85$, Supplemental Figure 1).

Discussion

This study evaluated whether performance on a brief computerized cognitive screening battery would prospectively predict responsiveness to usual treatment among adults with depressive disorders in a naturalistic clinical setting. We hypothesized that better executive functioning and affect perception at baseline would be associated with a greater reduction in depressive symptoms four to six months after treatment initiation. As expected, faster processing speed with interference resolution was a significant predictor of greater improvement in depressive symptoms at follow-up, contributing variance beyond that explained by baseline depression symptoms and educational attainment. Therefore, inefficient executive functioning at baseline, exemplified by slowed interference resolution, appears to represent a risk factor for poorer response to standard treatments. Visual processing speed and accuracy and other attention/inhibition variables did not contribute significant unique variance in the change in depression severity.

Response inhibition has been assessed as a prospective predictor of treatment outcome using paper-and-pencil tests, with variable results.^{10,11} Some of this variability may be related to the relatively small number of participants in most of these studies in proportion to the relatively large number of cognitive variables, which increases the risk for Type II errors. Paper-and-pencil tests are also unable to measure inhibitory processing speed, which is a unique capability of computerized Go/No Go tasks such as the PGNG. Executive functioning, more broadly, appears well-supported as a meaningful predictor of treatment responsiveness.^{6,8,10,37,38} These findings are consistent with the theory that the executive system regulates behavior, and also support the potential role of the executive system in emotion regulation and/or perseveration of negative mood states in depression.^{22,26,39} Additionally, this is the first study of which we are aware to demonstrate that cognitive measures can be incorporated into the intake process at outpatient psychiatry clinics, thereby supporting the direct translation of research findings to clinical practice.

Our primary finding that efficient behavioral responses on a contextual inhibition task predicts treatment responsiveness among depressed adults fits well with available literature on the structural and functional impact of depression on neural circuits. Specifically, the dorsolateral prefrontal cortex, orbital frontal cortex, and anterior cingulate cortex, regions associated with cognitive and inhibitory control, are often reduced in volume and/or underactive at rest in depressed adults compared to healthy adults^{39–41} and have been implicated in responsiveness to treatment for depression. Several studies support the utility of neuroimaging techniques for identifying individuals at risk for treatment resistance or individuals who may respond better to one treatment versus another,^{9,39,42–44} yet

neuroimaging is typically costly, time-consuming, and limited in availability, and is sometimes medically contraindicated. As a more feasible alternative, the current results support the administration of a brief computerized screening battery for this purpose. Computerized neuropsychological screening batteries can easily be administered by supervised trainees, technicians, and research assistants; require minimal resources; and, as this study illustrates, can be easily adapted as part of the intake process in any outpatient setting. Additional measures might be added to the PGNG task, such as auditory memory, to increase the predictive power. Furthermore, this added intake procedure could be useful for identifying individuals who might benefit from a more thorough neuropsychological evaluation—to rule out significant cognitive impairment that could impede the patient's ability to effectively participate in psychotherapy, manage his/her medications, or successfully function in social, familial, and occupational domains.

The sample treated herein is a relatively large sample and had a similar level of treatment response compared to that observed in STAR-D (32% remission rate compared to ~33% STAR-D, not accounting for relapse). In fact, as UM was a site in STAR-D, drawing patients from some of the same clinics, some of these patients in the present study could have been previously enrolled in STAR-D.

The present study has limitations to acknowledge. First, a naturalistic sample is less well-controlled and restricts the ability to compare efficacy of different treatments. We were, therefore, unable to reliably assess the potential relationships among cognitive functioning and specific treatment methods. The sample is also restricted to those who continued to receive care in our clinics for at least four months. The strength though, is the representativeness of this sample to other outpatient settings and the substantial implications in real-world settings, particularly because medical and psychiatric comorbidities among depressed individuals are common and relevant to treatment considerations yet are often exclusionary in treatment trials. Second, there was substantial heterogeneity in initial depression severity, also related to our sample selection method. There is substantial attrition in the sample, including about 44% of those who were prescribed psychotherapy following through with the advised number of sessions. It is unclear if this might be related to patient burden (more frequent visits are needed), or more rapid return to wellness, and we did not have data available to answer these questions. Another limitation is that, with the current sample, we were unable to model specific cognitive variables by depression severity, and the current test battery was selected based on its relative ease of application and its relevance to the cognitive domains frequently implicated in depression but was therefore limited in scope. Also, unfortunately, broader measures of functioning were not evaluated. Finally, we were unable to reliably control for type of intervention on depression severity at follow-up due to range restriction.

As a proof of concept study, this is the first of which we are aware that uses a brief, computer-administered cognitive screening battery as a clinical tool in tertiary care mental health clinics. We found that patients demonstrating slower reaction times during a task involving response inhibition (i.e., PGNG) on intake responded less robustly to outpatient treatment for depression. Indeed, response inhibition efficiency in this study represented a primary predictor of treatment responsiveness, beyond other demographic characteristics

previously associated with treatment outcomes. These findings suggest that patients with impaired executive functioning may benefit from augmented or alternative treatment, if such impairments can be identified early, thereby supporting the utility of streamlining the inclusion of a brief cognitive screen as part of the intake process in outpatient mental health clinics. Selection accuracy with cognitive and affective measures could decrease time to wellness, a key concept in the precision medicine initiative of NIMH^{16–18}. This may be particularly valuable if some newer medications and treatments are available to potentially improve executive functioning^{13,45}. Future studies might iteratively develop a battery of sensitive measures that is somewhat broader-based, with the ultimate goal of reducing time to recovery and incidence of relapse through more personalized care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Flow chart depicting recommended treatment (i.e., medication change, initiation of psychotherapy, or both) and actual treatment received.

Figure 2.

A. Scatterplot illustrating that those with faster PSIR endorsed fewer depressive symptoms at follow-up ($R^2 = .12$). B. Illustration of PSIR times in tertile split by initial and change in PHQ scores. C. PSIR Z score (effect size) based upon treatment outcome, including those lost to follow-up/attrition.

Table 1

Sample Demographic Variables, Depression Scores, and Cognitive Factors

Variable	<i>M</i>	<i>SD</i>
Age (years)	37.8	11.7
Education (years)	15.4	2.6
Shipley estimated IQ	104.5	8.5
Age at disease onset (years)	23.9	11.8
PHQ-9 (raw score)		
Baseline	15.5	5.2
4–6 month follow-up	7.9	5.4
Percent change from baseline	46.1	37.6
Cognitive Factors		
Visual-Perceptual Processing Speed (ms)	1157.8	336.8
Processing Speed with Interference Resolution (ms)	488.3	49.8
Attention Percent Accuracy	89.5	7.8
Inhibitory Control Percent Accuracy	75.2	16.5
Visual-Perceptual Percent Accuracy	88.9	7.3

Note. *N* = 75; PHQ-9 = Patient Health Questionnaire, 9th edition

Table 2

Multiple Regression Models Predicting Follow-Up PHQ-9 Scores From Demographic and Cognitive Variables

Model	β	sr^2	t	p
Model 1 (using step-wise entry)				
Step 1				
Education (years)	.20	.20	1.88	.07
PHQ-9 (baseline)	.30	.29	2.80	.01
Step 2				
Visual-Perceptual Processing Speed (ms)	.07	.06	.56	.58
Processing Speed with Interference Resolution	-.37	-.32	-3.04	.01
Attention Percent Accuracy	-.10	-.08	-.76	.45
Inhibitory Control Percent Accuracy	-.06	-.05	-.51	.61
Visual-Perceptual Percent Accuracy	.17	.14	1.35	.18
Model 2 (using backward elimination)*				
Education (years)	.20	.20	1.95	.06
PHQ-9 (baseline)	.34	.34	3.39	.01
Medical and/or Psychiatric Comorbidity	.21	.21	2.05	.04
Processing Speed with Interference Resolution	-.33	-.33	-3.29	.01

*
= Excluded variables included gender and age at disease onset