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Cognitive Performance in Antidepressant-Free Recurrent Major Depressive Disorder

Kimberly Albert, PhD[a], **Guy G. Potter, PhD**[b], **Douglas R. McQuoid, MPH**[b], and **Warren D. Taylor, MD, MHSc**[a,c]

[a]The Center for Cognitive Medicine, Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center, Nashville, TN, 37212, USA

[b]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, 27710, USA

[c]Geriatric Research, Education and Clinical Center, Department of Veterans Affairs Medical Center, Tennessee Valley Healthcare System, Nashville, TN, 37212, USA

Abstract

Background—Cognitive complaints are common in depression, and cognition may be an important treatment target as cognitive problems often remain during remission and may contribute to recurrence risk. Previous studies of cognitive performance in depression have mainly examined late-life depression, with a focus on older adults, or assessed performance in specific cognitive tasks rather than cognitive domains.

Methods—This study examined cognitive performance across multiple cognitive domains in antidepressant-free depressed adults with early onset recurrent depression compared to never-depressed controls. Domain scores were calculated for episodic memory, executive function, processing speed, and working memory, and the effect of depression diagnosis, depression severity, and depression duration on each domain score was examined, including interactions with age, sex, and education.

Results—Currently depressed adults (n = 91) exhibited poorer performance in the processing speed domain compared with never-depressed adults (n = 105). Additionally, there was an interactive effect of depression duration and age on processing speed and executive function domain performance, such that performance was worse with older age and longer duration of depression. There were no effects of depression severity on performance across the cognitive domains.

Conclusions—These findings support that processing speed deficits appear in young adults with early onset depression that may not be related to current mood. Additionally, the effects of cumulative depressive episodes may interact with aging such that cognitive performance deficits worsen with recurrence over the lifespan.

Address for correspondence: Kimberly Albert, PhD, Vanderbilt Center for Cognitive Medicine, Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center, 1601 23rd Ave. South, Nashville, TN 37212, Phone: 615-936-4559, kimberly.albert@vanderbilt.edu.

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INTRODUCTION

Cognitive complaints and subjective difficulties with cognitively demanding tasks are common in major depressive disorder (MDD). Difficulty with thinking and concentration is a key diagnostic criterion for MDD (American Psychiatric Association, 2013) and approximately two-thirds of depressed individuals experience deficits in cognitive performance (Abas et al., 1990; Afridi et al., 2011). Cognitive complaints and poorer task performance may both be a consequence of depressive episodes and also contribute to the onset and maintenance of depressive states.

Cognitive problems often persist during remission from depression (Bhalla et al., 2006; Bora et al., 2013; Hasselbalch et al., 2011; Rock et al., 2014) and may contribute to recurrence vulnerability (Maeshima et al., 2012). Remitted depressed individuals show biases in attention and memory for negative information even while euthymic (Albert et al., 2017; Fritzsche et al., 2010; Joormann and Gotlib, 2007; Sears et al., 2011). Suboptimal cognitive performance that persists during remission may reflect underlying neural network alterations and contribute to recurrence risk by reducing the ability to maintain attention and memory for relevant information. Diminished cognitive capacity may result in cognitive resources being preferentially allocated to information that is congruent with remaining depressive symptoms (Kaser et al., 2017). This would play a role in making depressogenic information seem more salient and potentially triggering depressive episodes (Joormann and Quinn, 2014). Better understanding the cognitive domains that are affected in MDD may help identify targets for cognitive interventions.

Recent meta-analyses examining cognitive performance during both depressive episodes and remission support that depression is associated with poor executive function, memory, and attention performance; however the majority of these studies have primarily examined performance on specific cognitive tasks rather than in broader cognitive domains (Bora et al., 2013; Hasselbalch et al., 2011; Rock et al., 2014). It is also unclear how chronicity or duration of depression may influence cognitive performance, or whether depression accelerates age-associated cognitive changes. Previous studies assessing cognitive performance in depression have largely focused on late-onset depression and older adults with fewer large studies assessing multiple cognitive domains in depressed early- or midlife-adult (18–60 years of age) populations (Darcet et al., 2016). Recent research in elderly populations has found that, in contrast to late-onset depression, older adults with an adolescent or early adulthood onset of their first depressive episode exhibit more rapid decline in their geriatric years (Riddle et al., 2015). This finding suggests that depression could have a negative effect on cognitive performance earlier in life. However, these findings are not generalizable to younger populations, and investigating cognition in young adults with early onset depression is integral to understanding the relationship between cognition and depression independent of aging.

The aim of this study was to examine cognitive performance across multiple cognitive domains (including tasks of episodic memory, executive function, processing speed, and working memory) in antidepressant-free depressed adults with early onset recurrent depression compared to healthy controls. Examination of medication-free individuals may

be particularly important as some have reported antidepressant effects on neurospychological tests (Kalb et al., 2006; Solé et al., 2015). Exploratory analysis examined the interactive effects between age and depression. Performance in many cognitive domains declines with age (Park et al., 2002), so we examined how the presence of depression influences that relationship. Additionally, as longer duration of depression is associated with atrophy in brain areas important for cognitive performance (Sheline et al., 1999), we examined whether duration of depression was associated with cognitive performance.

METHODS

Participants

Participants between the ages of 20 and 50 years were enrolled at Duke University Medical Center and Vanderbilt University Medical Center. Depressed participants had a DSM-IV diagnosis of recurrent MDD, as assessed by the Mini-International Neuropsychiatric Interview (MINI, version 5.0) (Sheehan et al., 1998) and interview with a study psychiatrist. Additional entry criteria included onset of first depressive episode before age 35 years and a Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) of 15 or greater. Entry criteria specified that participants were not in current psychotherapy and no antidepressant use in the last month (six weeks for fluoxetine); however, most participants reported no antidepressant use for at least three months or longer. Eligible control participants had no lifetime history of psychiatric disorders and no history of psychotropic medication use.

Exclusion criteria included other lifetime DSM-IV Axis I disorders including substance abuse or dependence. Participants were excluded for Axis II disorders determined by the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (Spitzer et al., 1992). Additional exclusion criteria included: history of psychosis, acute suicidality, use of illicit substances in the last month, ECT in the last 6 months, a family history of bipolar disorder, any unstable medical condition, or any history of neurological illness or head injury.

Both the Duke University Medical Center Institutional Review Board and the Vanderbilt University Institutional Review Board approved this study. All study participants provided informed consent.

Clinical Assessment and Neuropsychological Testing

Participants initially provided demographic data through a structured interview. A study psychiatrist assessed depression severity with the MADRS and medical comorbidity using the Cumulative Illness Rating Scale (CIRS) (Linn et al., 1968). Participants then completed a battery of neuropsychological tests that covered cognitive domains relevant to depression. A trained psychometric technician supervised by a clinical neuropsychologist administered the testing.

As previously described (Taylor et al., 2017), we created rationally constructed composite domain variables from a broad test battery. To combine tasks, we created z-scores for each

measure based on the performance of all participants and averaged the z-scores for all tests within each domain for each individual. Internal consistency for each domain was assessed using Cronbach's coefficient alpha (CoA). This resulted in four composite neuropsychological measures: a) episodic memory: Logical Memory 1 and 2 from the Wechsler Memory Scale (Weschsler, 1997); Benton Visual Retention Test (number correct) (Manna et al., 2011); Rey's Auditory Verbal Learning Test (total I-V and total VII) (Schmidt, 1996), CoA = 0.87; b) executive function: Controlled Oral Word Association (COWA) test (letters: C,F,L, total score)(Ruff et al., 1996); Trail Making B time (reverse scored time to completion)(Bowie and Harvey, 2006); semantic fluency (Animal Naming); Stroop Color-Word interference condition (number completed) (Golden, 1978); CoA = 0.75); c) processing speed: Symbol-Digit Modality (number completed)(Smith, 1982); Trail Making A (reverse scored time to completion) (Bowie and Harvey, 2006); Stroop Color Naming condition (verbal, number completed) (Golden, 1978); CoA = 0.70); and d) working memory: Digit Span forward from the Wechsler Memory Scale (number of trials correctly completed); Digit Span backward from the Wechsler Memory Scale (number of trials correctly completed); CoA = 0.75 (Weschsler, 1997).

Estimation of total time depressed

In depressed participants, the duration of depression was determined using the Life Charting Method (Post et al., 1988), an approach previously used to examine the effects of depression duration on brain morphology (Sheline et al., 1999). The number of DSM-IV depressive symptoms were assessed concurrently with duration of each episode and the presence or absence of pharmacological antidepressant treatment. Diagnostic criteria were used to establish each episode, with the total cumulative duration of depression calculated by summing all episodes. When possible, corroborating information was obtained from family members or medical records. Individuals who could not clearly identify past episodes and who did not have sufficient corroborating information were not included in these analyses.

Analytic Plan

All analyses were conducted with SAS 9.4 (Cary, NC). Initial univariate analyses of demographic variables and unadjusted cognitive domain scores were conducted using pooled two-tailed t-tests for continuous variables and chi-square tests for categorical variables. Satterthwaite's t-test was used for continuous variables with unequal variances.

Statistical analyses utilized general linear models (SAS PROC GLM), examining the four z-transformed cognitive domain scores as dependent variables, $\alpha = 0.95$. Data was normally distributed with no missing data. The use of composite variable limited the number of dependent variables to four and thus corrections for multiple comparisons were not conducted. Diagnostic group was the primary independent variable of interest, but models also included covariates of age, sex, education (in years), depression duration, race, and medical morbidity measured by the CIRS.

RESULTS

The study included 91 depressed and 105 never-depressed comparison participants. The depressed group was older and exhibited greater medical comorbidity as measured by the CIRS (Table 1). There was no significant difference between the groups in sex representation or education level; there was a trend for the comparison group to have a higher minority participant representation, but this did not reach statistical significance. In univariate analyses, the depressed group exhibited significantly poorer performance in cognitive domains of processing speed, episodic memory, and executive function.

Performance differences by depression diagnosis

Statistical models tested for differences between diagnostic groups while controlling for age, sex, race, education level, and medical morbidity measured by the CIRS. The z-scored processing speed domain exhibited a group difference ($F_{1,189} = 4.82$, $p = 0.0294$) wherein the depressed group exhibited poorer performance than the nondepressed group. Group differences were not observed for other z-scored cognitive domains, including episodic memory ($F_{1,189} = 3.78$, $p = 0.0533$), working memory ($F_{1,189} = 0.18$, $p = 0.6753$), or executive function ($F_{1,189} = 2.96$, $p = 0.0522$).

Interactive effects between depression diagnosis and demographic differences

In exploratory analyses, we sought to examine whether sex or age affected the relationship between depression diagnosis and cognitive performance. To examine this issue, in the statistical models described above we added interaction terms between diagnosis and sex and diagnosis and age. We observed no statistically significant interaction term between depression and sex or depression and age for any cognitive domain (data not shown).

Effects of depression severity on performance in the depressed group

We examined the effect of depression severity measured by the MADRS on cognitive performance in the depressed group. After age, sex, race, education level, and medical morbidity, we did not find a statistically significant relationship between performance on any z-scored cognitive domain and MADRS score.

Effects of depression duration on performance in the depressed group

Finally, we examined the effect of depression duration on cognitive performance in the depressed group. The mean duration of depression for the depressed group was 2116.20 days (SD = 1792.00) with a minimum of 90.00 days and a maximum of 7500.00 days. There was no significant main effect of depression duration in any of the cognitive performance domains. There was a significant interaction effect between depression duration and age on processing speed ($F_{8,64} = 10.96$, $p = 0.0021$) and executive function ($F_{8,64} = 4.98$, $p = 0.0291$), and no significant interaction effect on working or episodic memory. In depressed participants, older age and longer duration of depression were associated with worse processing speed and executive function performance. There were no significant interactions between depression duration and either sex or MADRS score on any of the cognitive performance domains.

DISCUSSION

The primary result of this study is that currently depressed adults exhibited poorer performance on tests of processing speed compared with non-depressed adults. These results are consistent with previous findings of slower processing speed in depressed older adults (Nebes et al., 2017; Sanders et al., 2011) and late onset depression (Elderkin-Thompson V et al., 2011) and reduced cognitive processing speed in depressed young adults (Khanahmadi et al., 2013; Tsourtos et al., 2002). The effect of depression on cognitive performance did not vary based on sex or age, at least in the 20–50 year age range examined. These results support that psychomotor and cognitive processing speed are slower in young, unmedicated, depressed adults.

We did not observe group differences in measures of episodic memory, executive function, or working memory. In contrast to our findings, previous work has reported executive function, memory, and attention detriments in both currently depressed and remitted adult samples (Bora et al., 2013; Roca et al., 2015; Rock et al., 2014). However, these findings have generally been observed with isolated neuropsychological tasks that may be more influenced by deficits in specific cognitive task components than the composite domain measures used in this study. Additionally, this study did not include a separate domain for attention and used low -demand measures (digit-span) in the working memory domain which may not have sufficiently tasked memory to reveal depression effects. In the current study the performance difference between groups was not related to depression severity supporting that cognitive deficits in depression are not entirely explained by negative mood or other depressive symptoms, which accords with previous findings of cognitive deficits that persist during depression remission (Bhalla et al., 2006; Bora et al., 2013; Hasselbalch et al., 2011; Rock et al., 2014).

Our observations may be specific to younger adults with early life onset of depression; the mean age for each group was in the early 30’s and the entry criteria required depression onset prior to the age of 35. The relationship between depression and cognitive performance may differ across the lifespan, as depression may accelerate cognitive change observed with aging or interact with age such that the ability to compensate for cognitive detriment related to depression is reduced in older depressed adults. The range of performance scores in the depressed group indicate that while the mean processing speed performance was lower in the depressed group, not all depressed participants would qualify as exhibiting impaired performance.

We did not observe a significant interaction effect between depression diagnosis and age on cognitive performance. However, there was a significant interaction effect of depression duration and age on processing speed and executive function performance. Similarly, depression duration has been found to be associated with reduced hippocampal volume in recurrent depression in a study including a wide age range of women (Sheline et al., 1999). These results support a cumulative effect of experiencing depressive episodes on cognitive function that may interact with age. In young depressed adults cognitive resources may be available to compensate for cognitive changes related to depression and performance may be maintained through altered neurocognitive function. As the negative cognitive effects of

depression accumulate with greater depression duration and interact with aging into the fifth decade, compensation may be less effective at maintaining cognitive performance. Neuroimaging approaches may be useful in revealing differences in brain activity or functional connectivity related to cognitive performance in depressed adults.

The strengths of this study include examining a large sample of unmedicated adults with recurrent early onset depression and non-depressed controls. In studies that include late life depression it is difficult to separate the cognitive problems related to depression from those that may be due to neurodegenerative processes or changes with age. Investigating cognitive performance in relatively young adults with early onset depression and controlling for the effect of age provides evidence of cognitive alterations that may be more strongly related to depression or depression risk than neurodegeneration or age. In older adults with late-life depression, impairment in neuropsychological testing is mediated in large part by processing resources (processing speed and working memory), and accounting for these effects results in similar performance in a variety of cognitive tasks between depressed and healthy older adults (Nebes et al., 2017). Processing speed is a core feature of cognitive functioning, and reduced processing speed may contribute to cognitive impairment in aging (Salthouse, 1996). The current results suggest that deficits in processing speed may begin earlier in life in depressed adults rather than being strictly associated with aging. Further, processing speed deficits may accumulate with greater depression duration following recurrent episodes and provide a mechanism for the increased risk for late-life cognitive impairment in depression.

Limitations of this study include cross-sectional examination of currently depressed individuals. This precludes the examination of the nature of poor cognitive performance as trait vs. state, thus we cannot address whether cognitive differences precede the onset of depression or remain during remission. Additionally, this study did not include assessments of emotional cognition. Cognitive processing of emotional information may be particularly affected in depression (Joormann and Quinn, 2014); tasks that include emotionally valenced stimuli may better distinguish between depressed and non-depressed individuals. The results of this study suggest an interaction effect of depression duration and age on executive function and processing speed performance. However, the examination of executive function separate from processing speed is limited by the use of executive function tasks which also include a component of processing speed and in which speed and accuracy may be conflated. Further examination of the effects of age and depression duration on executive function would benefit from including measures that do not include a speed component.

Another limitation is the use of neurocognitive measures that do not separate cognitive processing speed and motor reaction time, although the Stroop color naming was completed verbally to reduce the effect of motoric slowing. There are conflicting findings for motoric slowing in depressed younger adults (Caligiuri and Ellwanger, 2000; Tsourtos et al., 2002); future work should include tasks that allow distinguishing between cognitive processing speed and motoric speed. However, the use of multiple measures and a composite processing speed domain score in this study provide evidence that depressed adults show reduced speed across a variety of processing speed measures compared to non-depressed adults. These

results suggest general processing speed deficits rather than slowed performance on specific cognitive tasks.

CONCLUSION

This study supports that processing speed is reduced in currently depressed, un-medicated, adults with early onset depression compared to never-depressed adults, and that both processing speed and executive function are worse among those who are relatively older and have experienced a longer duration of depression symptoms. These findings are consistent with previous work and suggest that processing speed may be the primary cognitive domain affected in depression among younger adults, and that longer duration of depression may have cumulative adverse effects in some cognitive domains. Processing speed in depressed adults was not related to depression severity, again supporting previous work and suggesting that processing speed slowing may be related to depression risk or a consequence of depression but not a marker of current mood dysregulation. Future work should include neuroimaging methods that may reveal alterations in brain activity or functional connectivity that may maintain cognitive performance in depressed younger adults as well as assessments in remitted or at risk depressed individuals to further define the role of processing speed reduction as a risk factor or trait consequence of depression.

Table includes univariate comparisons. All comparisons of continuous measures with equal variances used pooled, two-tailed t-tests with 195 degrees of freedom. For comparisons of continuous measures with unequal variances, we used Satterthwaite's t-test, specifically for CIRS with 151.67 df and MADRS with 100.03 degrees of freedom. Comparisons of categorical variables conducted using the chi square test with 1 df.

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References

Abas MA, Sahakian BJ, Levy R. Neuropsychological deficits and CT scan changes in elderly depressives. Psychol. Med. 1990; 20:507–520. DOI: 10.1017/S0033291700017025 [PubMed: 2236360]

Afridi MI, Hina M, Qureshi IS, Hussain M. Cognitive disturbance comparison among drug-naive depressed cases and healthy controls. J. Coll. Physicians Surg. Pakistan. 2011; 21:351–355. doi: 07.2011/JCPSP.351355.

Albert K, Gau V, Taylor WD, Newhouse PA. Attention bias in older women with remitted depression is associated with enhanced amygdala activity and functional connectivity. J. Affect. Disord. 2017; 210:49–56. DOI: 10.1016/j.jad.2016.12.010 [PubMed: 28012352]

American Psychiatric Association. DSM-V, American Journal of Psychiatry. 2013.

Bhalla RK, Butters MA, Mulsant BH, Begley AE, Zmuda MD, Schoderbek B, Pollock BG, Reynolds CF, Becker JT. Persistence of neuropsychologic deficits in the remitted state of late-life depression. Am. J. Geriatr. Psychiatry. 2006; 14:419–27. DOI: 10.1097/01.JGP.0000203130.45421.69 [PubMed: 16670246]

Bora E, Harrison BJ, Yücel M, Pantelis C. Cognitive impairment in euthymic major depressive disorder: a meta-analysis. Psychol. Med. 2013; 43:2017–2026. DOI: 10.1017/S0033291712002085 [PubMed: 23098294]

Bowie CR, Harvey PD. Administration and interpretation of the Trail Making Test. Nat. Protoc. 2006; 1:2277–2281. DOI: 10.1038/nprot.2006.390 [PubMed: 17406468]

Caligiuri MP, Ellwanger J. Motor and cognitive aspects of motor retardation in depression. J. Affect. Disord. 2000; 57:83–93. DOI: 10.1016/S0165-0327(99)00068-3 [PubMed: 10708819]

Darcet F, Gardier AM, Gaillard R, David DJ, Guilloux J-P. Cognitive Dysfunction in Major Depressive Disorder. A Translational Review in Animal Models of the Disease. Pharmaceuticals (Basel). 2016; :9.doi: 10.3390/ph9010009

Elderkin-Thompson V, Moody T, Knowlton B, Hellemann G, Kumar A. Explicit and implicit memory in late-life depression. Am. J. Geriatr. Psychiatry. 2011; 19:249–255. DOI: 10.1097/JGP.0b013e3181e89a5b

Fritzsche A, Dahme B, Gotlib IH, Joormann J, Magnussen H, Watz H, Nutzinger DO, von Leupoldt A. Specificity of cognitive biases in patients with current depression and remitted depression and in patients with asthma. Psychol. Med. 2010; 40:815–26. DOI: 10.1017/S0033291709990948 [PubMed: 19719897]

Golden CJ. Stroop Color and Word Test: A manual for clinical and experimental uses. Chicago: Stoelting; 1978. 1–46. doi:10.1002

Hasselbalch BJ, Knorr U, Kessing LV. Cognitive impairment in the remitted state of unipolar depressive disorder: A systematic review. J. Affect. Disord. 2011; doi: 10.1016/j.jad.2010.11.011

Joormann J, Gotlib IH. Selective attention to emotional faces following recovery from depression. J. Abnorm. Psychol. 2007; 116:80–5. DOI: 10.1037/0021-843X.116.1.80 [PubMed: 17324018]

Joormann J, Quinn ME. Depression and Anxiety. 2014. Cognitive processes and emotion regulation in depression; 308–315.

Kalb R, Dörner M, Kalb S. Opposite effects of depression and antidepressants on processing speed and error rate. Prog. Neuropsychopharmacol. Biol. Psychiatry. 2006; 30:244–50. DOI: 10.1016/j.pnpbp.2005.10.009 [PubMed: 16310918]

Kaser M, Zaman R, Sahakian BJ. Cognition as a treatment target in depression. 2017; doi: 10.1017/S0033291716003123

Khanahmadi M, Malmir M, Eskandari H, Orang T. Evaluation of Visual Information Processing Speed in Depressed People. Iran. J. Public Health. 2013; 42:1266–73. [PubMed: 26171339]

Linn BS, Linn MW, Gurel L. CUMULATIVE ILLNESS RATING SCALE. J. Am. Geriatr. Soc. 1968; 16:622–626. DOI: 10.1111/j.1532-5415.1968.tb02103.x [PubMed: 5646906]

Maeshima H, Baba H, Nakano Y, Satomura E, Namekawa Y, Takebayashi N, Suzuki T, Mimura M, Arai H. Residual memory dysfunction in recurrent major depressive disorder - A longitudinal study from Juntendo University Mood Disorder Project. J. Affect. Disord. 2012; 143:84–88. DOI: 10.1016/j.jad.2012.05.033 [PubMed: 22832170]

Manna CG, Alterescu K, Borod JC, Bender HA. Encyclopedia of Clinical Neuropsychology. Springer; New York, New York, NY: 2011. Benton Visual Retention Test; 392–394.

Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. Br. J. Psychiatry. 1979; 134:382–389. DOI: 10.1192/bjp.134.4.382 [PubMed: 444788]

Nebes RD, Butters MA, Mulsant BH, Pollock BG, Zmuda MD, Houck PR, Reynolds CF Iii. Decreased working memory and processing speed mediate cognitive impairment in geriatric depression. Psychol. Med. 2017; 30:679–691.

Park DC, Lautenschlager G, Hedden T, Davidson NS, Smith AD, Smith PK. Models of visuospatial and verbal memory across the adult life span. Psychol. Aging. 2002; 17:299–320. DOI: 10.1037/0882-7974.17.2.299 [PubMed: 12061414]

Post RM, Roy-Byrne PP, Uhde TW. Graphic representation of the life course of illness in patients with affective disorder. Am. J. Psychiatry. 1988; 145:844–8. DOI: 10.1176/ajp.145.7.844 [PubMed: 3381929]

Riddle M, Mcquoid DR, Potter GG, Steffens DC, Taylor WD. Disability but not social support predicts cognitive deterioration in late-life depression. Int. Psychogeriatrics C Int. Psychogeriatr. Assoc. 2015; 27:707–714. DOI: 10.1017/S1041610214002543

Roca M, Vives M, Lopez-Navarro E, Garcia-Campayo J, Gili M. Cognitive impairments and depression: a critical review. Actas Esp Psiquiatr. 2015; 43:187–193. [PubMed: 26320897]

Rock PL, Roiser JP, Riedel WJ, Blackwell AD. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol. Med. 2014; 44:2029–40. DOI: 10.1017/S0033291713002535 [PubMed: 24168753]

Ruff RM, Light RH, Parker SB, Levin HS. Benton controlled Oral Word Association Test: Reliability and updated norms. Arch. Clin. Neuropsychol. 1996; 11:329–338. DOI: 10.1016/0887-6177(95)00033-X [PubMed: 14588937]

Salthouse TA. The processing-speed theory of adult age differences in cognition. Psychol. Rev. 1996; 103:403–428. DOI: 10.1037/0033-295X.103.3.403 [PubMed: 8759042]

Sanders JB, Bremmer MA, Comijs HC, Deeg DJH, Lampe IK, Beekman ATF. Cognitive Functioning and the Natural Course of Depressive Symptoms in Late Life. Am. J. Geriatr. Psychiatry. 2011; 19:664–672. DOI: 10.1097/JGP.0b013e3181f7d8e9 [PubMed: 21709612]

Schmidt M. Rey Auditory Verbal Learning Test: RAVLT: a Handbook - Michael Schmidt - Google Books. Western Psychological Services; 1996.

Sears CR, Newman KR, Ference JD, Thomas CL. Attention to emotional images in previously depressed individuals: An eye-tracking study. Cognit. Ther. Res. 2011; 35:517–528. DOI: 10.1007/s10608-011-9396-5

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry. 1998; :22–33. DOI: 10.1016/S0924-9338(99)80239-9

Sheline YI, Sanghavi M, Mintun MA, Gado MH. Depression duration but not age predicts hippocampal volume loss in medically healthy women with recurrent major depression. J. Neurosci. 1999; 19:5034–43. DOI: 10.1001/ARCHPSYC.1991.01810320017003 [PubMed: 10366636]

Smith A. Symbol digits modalities test: manual. Western Psychological Services; Los Angeles: 1982.

Solé B, Jiménez E, Martinez-Aran A, Vieta E. Cognition as a target in major depression: New developments. Eur. Neuropsychopharmacol. 2015; 25:231–247. DOI: 10.1016/j.euroneuro.2014.12.004 [PubMed: 25640673]

Spitzer RL, Williams JB, Gibbon M, First MB. The Structured Clinical Interview for DSM-III-R (SCID) - History, rationale, and description. Arch. Gen. Psychiatry. 1992; 49:624–629. DOI: 10.1001/archpsyc.1992.01820080032005 [PubMed: 1637252]

Taylor WD, Boyd B, Turner R, McQuoid DR, Ashley-Koch A, MacFall JR, Saleh A, Potter GG. APOE ε4 associated with preserved executive function performance and maintenance of temporal and cingulate brain volumes in younger adults. Brain Imaging Behav. 2017; 11:194–204. DOI: 10.1007/s11682-016-9522-9 [PubMed: 26843007]

Tsourtos G, Thompson JC, Stough C. Evidence of an early information processing speed deficit in unipolar major depression. Psychol. Med. 2002; 32:259–265. DOI: 10.1017/S0033291701005001 [PubMed: 11866321]

Weschsler D. Wechsler Memory Scale. Third. 1997.

Table 1

Demographics

	Depressed Mean (SD) N = 91	**Nondepressed Mean (SD) N = 105**	**Test value**	**P value**
Age	35.9 (9.0)	30.2 (9.1)	T = 4.48	< 0.0001
Sex (%F)	66.3% (61)	64.8% (68)	X2 = 0.05	0.8203
Race (%W)	37.0% (34)	50.4% (53)	X2 = 3.63	0.0566
Education	15.3 (2.4)	15.8 (2.1)	T = 1.56	0.1207
CIRS	0.68 (1.11)	0.30 (0.73)	T = 2.82	0.0055
MADRS	24.0 (4.4)	0.7 (1.1)	T = 49.26	< 0.0001
zProc Speed	−0.20 (0.80)	0.17 (0.77)	T = 3.37	0.0009
zWork Mem	−0.09 (0.83)	0.08 (0.94)	T = 1.34	0.1805
zEpi Mem	−0.21 (0.84)	0.17 (0.74)	T = 3.37	0.0009
zExec Fxn	−0.13 (0.77)	0.12 (0.74)	T = 2.31	0.0218