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Neurocognitive Correlates of Resilience in Late-Life Depression

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Abstract

Objectives.—Increasing understanding of the neurocognitive correlates of resilience in late-life depression (LLD) could inform interventions to promote more sustained remission. We investigated cross-sectional relations between baseline resilience and domains of neurocognitive functioning in depressed older adults enrolled in one of four trials.

Methods.—Participants (N=288) completed neurocognitive tests of memory, language performance, and executive functioning, as well as measures of subjective memory performance and components of resilience (grit, active coping self-efficacy, accommodative coping self-efficacy, and spirituality).

Results.—Medium-sized associations were observed between greater resilience (overall resilience, accommodative coping) and lower frequency of self-reported forgetting. Small positive associations were observed between language performance and total resilience, active coping self-efficacy, and accommodative coping self-efficacy. Small negative associations were observed between spirituality and each objective measure of cognitive performance.

Conclusions.—Future longitudinal studies will help elucidate the complex relation between resilience and cognitive functioning in LLD. In addition, randomized controlled trials targeting coping self-efficacy may inform the development of more effective and personalized interventions.

Late-life depression (LLD) is a common and debilitating disorder, with roughly 8–16% of older adults experiencing clinically significant symptoms (1) and 2% meeting criteria for major depressive disorder (MDD)(2). LLD is more chronic than depression experienced earlier in life (3) and significantly predicts cognitive decline (4). With the population rapidly aging, identifying factors that support sustained remission is a high public health priority.

Self-reported resilience (the capacity to adapt and thrive in the face of adversity (5)) may predict treatment response in LLD (6). We recently investigated the clinical correlates of

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resilience in a sample of 337 depressed older adults using the Connor-Davidson Resilience Scale (CD-RISC)(7), which was found to have the best psychometric properties of the 17 resilience scales identified by a recent review (8). Exploratory factor analysis (EFA) revealed a four-factor model with items assessing (1) grit (e.g., “When things look hopeless, I don’t give up”), (2) active coping self-efficacy (e.g., “I am in control of my life”), (3) accommodative coping self-efficacy (e.g., “I am able to adapt to change”), and (4) spirituality (e.g., “I believe things happen for a reason”). A reliability analysis yielded the following Cronbach’s α estimates: Total CD-RISC: 0.92, Factor 1: 0.89, Factor 2: 0.91, Factor 3: 0.90, Factor 4: 0.71 (7). Total resilience and each factor was associated with decreased depressive symptoms, apathy, and anxiety as well as increased quality of life. Furthermore, baseline total resilience and accommodative coping self-efficacy significantly predicted remission following 16 weeks of antidepressant treatment (6). To our knowledge, no studies have investigated the association between resilience and domains of neurocognitive functioning in LLD.

Research conducted with other populations suggests that resilience may be positively associated with cognitive functioning. For example, a study of 1,395 community-dwelling older women found a strong negative association between resilience and self-reported cognitive problems (9). However, no significant association emerged between resilience and participants’ score on a brief mental status exam (the Cognitive Abilities Screening Test - Revised) (10). The authors concluded that a brief mental status exam may be insufficiently sensitive to detect an effect. This is particularly likely if certain domains of cognition are more strongly associated with resilience than others. The current study addresses this gap by using validated assessments designed to detect subtle differences in neurocognitive performance. We focused on three cognitive deficits that often co-occur with LLD: memory performance (11), language performance (12), and executive functioning (13–15).

Methods

Participants

Data comprised baseline interviews from four clinical trials conducted with adults 60 years with MDD (7). The interventions tested in these trials included Methylphenidate (16) (NCT00602290), Memantine (NCT01902004), tai chi (NCT02460666), and levomilnacipran (NCT02466958). Eligibility criteria included: (1) DSM-IV-TR or DSM 5 diagnosis of MDD; (2) MMSE ≥ 24 . Exclusion criteria included: (1) history of any psychiatric disorder (with the exception of stable comorbid anxiety or insomnia); (2) acute suicidal ideation; (3) severe or acute unstable medical illness.

Mood and Self-report Measures

Depressive symptom severity was assessed with the 24-item clinician-rated Hamilton Depression Rating Scale (HAM-D)(17). Resilience was assessed via the 25-item CD-RISC (18). Subjective memory performance was assessed in a subset of participants (N=71) via the General Frequency of Forgetting scale of the Memory Functioning Questionnaire (MFQ) (19).

Neurocognitive Testing

Memory performance was assessed via the California Verbal Learning Test-II (20-minute delay free recall) and the Rey-Osterrieth complex figure test (30-minute delay recall). Language performance was assessed via the Controlled Oral Word Association test (FAS form), Animal Fluency, and Boston Naming Test. Executive functioning was assessed via the Trail Making Test Part B and the Stroop Interference task. Raw scores were transformed to z-scores (reversing z-scores as needed such that higher z-scores represented better performance), then averaged within each domain to produce composite scores.

Analyses

Data were inspected for outliers, skewness, and homogeneity of variance to ensure appropriateness of parametric statistical tests. General linear models (GLMs) were used to examine associations between resilience factors and cognitive domain scores. A separate GLM was estimated for total resilience and each resilience factor, with each of the cognitive domains as predictors and age, sex, ethnicity and years of education as covariates. We also explored whether associations remained significant when depressive symptom severity was added as a covariate. Finally, we investigated whether resilience was associated with subjective memory performance (self-reported general frequency of forgetting) after controlling for covariates. Significance was set at $p < 0.05$ for all inferences.

Results

Sample Characteristics

The majority of participants ($N=288$) were White (78.8%), female (59.4%), and highly educated, with an average of nearly 16 years of education. The average age was 70.4 ($SD=7.0$; range=60–89 years).

Association of Resilience with Neurocognitive Measures

Language was the only domain of cognitive functioning that emerged as statistically significant in the GLM for total resilience ($F[1,282]=6.72$, $r=0.14$, $p=0.01$). Specifically, higher language performance was associated with increased resilience. With regard to the resilience factors, higher language performance was associated with greater accommodative coping self-efficacy ($F[1,282]=10.20$, $r=0.18$, $p=0.002$) and active coping self-efficacy ($F[1,282]=4.81$, $r=0.13$, $p=0.03$). All three domains of cognitive functioning emerged as statistically significant in the GLM for spirituality; however, the direction of these effects were opposite of those observed for the other resilience factors (see Figure 1). That is, poorer memory performance ($F[1,282]=6.38$, $r=-.15$, $p=0.01$), poorer language performance ($F[1,282]=5.15$, $r=-.14$, $p=0.02$), and poorer executive functioning ($F[1,281]=5.95$, $r=-.14$, $p=0.02$) were each significantly associated with greater spirituality. Findings were similar when depressive symptom severity and trial in which the participant was enrolled were added as additional covariates.

Association of Resilience to Subjective Memory Complaints

Total resilience ($F[1,65]=7.83$, $r=0.43$, $p=0.0003$) and accommodative coping self-efficacy ($F[1,65]=0.45$, $r=0.51$, $p<0.0001$) were significantly associated with lower self-reported frequency of forgetting. Grit ($F[1,65]=0.19$, $r=0.23$, $p=0.06$) and active coping self-efficacy ($F[1,65]=0.20$, $r=0.23$, $p=0.07$) were marginally associated with lower self-reported frequency of forgetting. No association was found between self-reported memory performance and spirituality.

Discussion

This is the first study to our knowledge to investigate the association between resilience and domains of neurocognitive functioning in LLD. When using objective measures of neurocognitive performance, observed associations were small (for language) or non-significant (for memory and executive functioning). On the other hand, the magnitude of association between overall resilience and cognitive functioning was moderate for self-reported forgetting. These findings warrant replication, as subjective memory performance was only assessed in a subset ($N=71$) of participants. However, this finding is consistent with previous studies that have found stronger associations between resilience and subjective vs. objective measures (9). Associations between language performance and overall resilience, active coping self-efficacy, and accommodative coping self-efficacy remained statistically significant after controlling for depressive symptom severity. Of course, due to the cross-sectional nature of the study, the causality of these effects is unknown. Superior language abilities may increase one's confidence in his/her coping skills; alternatively or in addition, low coping self-efficacy may influence language. Several studies have documented differences in language use among depressed vs. non-depressed individuals (20). It is possible that depression affects language performance directly via neuropathology or indirectly via patterns of cognition and language use.

None of the cognitive domains assessed in the current study were significantly associated with grit. This finding is in contrast to the results of a cross-sectional study of 120 adults living with HIV (21) as well as a longitudinal study finding that adolescent grit (approximated by class rank controlling for IQ) significantly predicted late-life memory performance (22). Of note, a recent review found that greater purpose in life appears to reduce the negative impact of neuropathology on cognitive functioning (23). Although we found no statistically significant associations between grit and objective cognitive performance, results approached significance for self-reported frequency of forgetting.

Spirituality showed significant negative associations with memory, language, and executive functioning performance after controlling for demographic variables. Although these effects were small, it is notable that the direction of association was consistently negative across all three cognitive domains. These results are in contrast to those of several previous studies. A recent systematic review of the relation between cognitive functioning and religion/spirituality found that of 17 studies comprising primarily geriatric samples, 14 reported positive associations (24). However, these association may be due to increased social engagement (25–27), an established protective factor against cognitive decline (28). In contrast to studies whose definitions have included religious attendance, the spirituality

factor in the current study focused exclusively on beliefs. Evidence for the importance of distinguishing between religious beliefs vs. behavior comes from an investigation of associations between multiple aspects of religious involvement (religious affiliation, attendance, beliefs, and practices) and cognitive functioning among 2,930 older Taiwanese adults (29). Frequency of religious attendance showed the strongest association with improved cognitive functioning, and this effect remained significant after controlling for health behaviors, social support, and prior health status. Together, these results suggest that religious attendance, rather than religious beliefs, may account for previously-reported associations between spirituality and cognition. It is also possible that race, ethnicity, culture, generational cohort, and/or socioeconomic status moderate the relation between spirituality and cognitive functioning. Due to the limited diversity of our sample, we were unable to test this possibility in the current study. We found no evidence that religious beliefs are associated with higher cognitive functioning.

Future longitudinal studies are needed to determine whether interventions targeting language may be useful for improving coping self-efficacy in LLD. In addition, randomized controlled trials targeting components of resilience may help elucidate the complex relationships between resilience and cognitive functioning in depressed older adults. Continued research in this area will inform the development of more effective and personalized interventions to promote more sustained remission from LLD.

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Highlights

- The neurocognitive correlates of resilience were evaluated in 288 depressed older adults. Participants completed neurocognitive tests of memory, language, and executive functioning as well as self-report measures of memory performance and resilience.
- Medium-sized associations were observed between components of resilience (overall resilience and accommodative coping self-efficacy) and self-reported memory performance. Small positive associations were observed between resilience (overall resilience, active coping self-efficacy, and accommodative coping self-efficacy) and language performance.
- Clinical trials will determine the utility of targeting active and accommodative coping self-efficacy in treating late-life depression.

Figure 1. Scatterplots depicting the association between language performance and two resilience factors: accommodative coping self-efficacy ($r=0.18$, $p=0.002$; 1A) and spirituality ($r=-0.14$, $p=0.02$; 1B).