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Regional gray matter volume correlates with anxiety, apathy, and resilience in geriatric depression

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ABSTRACT

Objectives: Geriatric depression (GD) is associated with significant medical comorbidity, cognitive impairment, brain atrophy, premature mortality, and suboptimal treatment response. While apathy and anxiety are common comorbidities, resilience is a protective factor. Understanding the relationships between brain morphometry, depression, and resilience in GD could inform clinical treatment. Only few studies have addressed gray matter volume (GMV) associations with mood and resilience.

Participants: Forty-nine adults aged >60 years (38 women) with major depressive disorder undergoing concurrent antidepressant treatment participated in the study.

Measurements: Anatomical T1-weighted scans, apathy, anxiety, and resilience data were collected. Freesurfer 6.0 was used to preprocess T1-weighted images and qdec to perform voxel-wise whole-brain analyses. Partial Spearman correlations controlling for age and sex tested the associations between clinical scores, and general linear models identified clusters of associations between GMV and clinical scores, with age and sex as covariates. Cluster correction and Monte-Carlo simulations were applied (corrected alpha = 0.05).

Results: Greater depression severity was associated with greater anxiety ($r = 0.53$, $p = 0.0001$), lower resilience ($r = -0.33$, $p = 0.03$), and greater apathy ($r = 0.39$, $p = 0.01$). Greater GMV in widespread, partially overlapping clusters across the brain was associated with reduced anxiety and apathy, as well as increased resilience.

Conclusion: Our results suggest that greater GMV in extended brain regions is a potential marker for resilience in GD, while GMV in more focal and overlapping regions may be markers for depression and anxiety. Interventions focused on improving symptoms in GD may seek to examine their effects on these brain regions.

Key words: Geriatric depression, resilience, anxiety, apathy, brain, gray matter, MRI

Introduction

Ten to fifteen percent of adults over the age of 60 years suffer from clinical depression (Ismail *et al.*, 2013). Geriatric depression (GD) is characterized by more treatment-resistant depressive and cognitive symptoms, as well as alterations in brain structure, compared to that for depression at a younger age (Dillon *et al.*, 2009; Mackin *et al.*, 2014; Sachs-Ericsson *et al.*, 2013). Some of its debilitating consequences include lower remission rates and poorer treatment prognosis, comorbid cognitive impairment, and impaired daily functioning leading to an increased risk of injuries and falls requiring hospitalization (Carpenter *et al.*, 2014; Tunvirachaisakul *et al.*, 2018). Only approximately 70% of patients respond favorably to selective serotonin reuptake inhibitors after 2–3 months (Chen *et al.*, 2011), and even fewer achieve remission (only 30–40%) (Nelson *et al.*, 2008).

Apathy and anxiety are common comorbid symptoms in GD and can further complicate successful recovery (Funes *et al.*, 2018; Groeneweg-Koolhoven *et al.*, 2016), while psychological resilience is a protective factor and is counter-correlated with various stress response

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measures (Charney, 2004; Laird *et al.*, 2019a; Southwick *et al.*, 2005; Stainton *et al.*, 2018). For example, higher resilience is associated with reduced mortality and depression onset and higher well-being in older age (MacLeod *et al.*, 2016; Zeng and Shen, 2010). More resilient individuals are more likely to respond to treatment, as we previously demonstrated (Laird *et al.*, 2018a, 2018b, 2019). Therefore, resilience is a potentially modifiable protective factor and a promising target for depression prevention and intervention.

GD is associated with cortical atrophy across large portions of the frontal, temporal, and parietal lobes, although some regions show increases in gray matter volume (GMV) (Mackin *et al.*, 2013). Several meta-analyses report reductions in regional GMV in GD, including the hippocampus, amygdala, right lentiform nucleus and portions of the parahippocampal region, medial frontal and orbitofrontal cortices, right subcallosal gyrus, putamen, and thalamus compared to healthy older adults (Du *et al.*, 2014; Sexton *et al.*, 2013). The functional significance of cortical gray matter changes is less clear in GD. That is, while most studies report differences compared to healthy controls, only few find correlations between GMV and symptom severity (Szymkowicz *et al.*, 2016). In a large, mixed sample of treated and untreated patients with GD, we previously found that lower GMV in the insula was associated with increased anxiety and depression (Laird *et al.*, 2019b). Neural correlates of apathy in depression are largely unknown, even in younger populations. However, we previously found associations between GMV and depression in bilateral orbitofrontal cortices and reduced anterior cingulate GMV in those with higher apathy (Lavretsky *et al.*, 2007). Only few studies using functional and structural (white matter connectivity) imaging methods have found associations with apathy and resilience (Laird *et al.*, 2019b; Robert *et al.*, 2021; Vlasova *et al.*, 2018). Investigating both the complicating comorbid symptoms and the protective factors of GD in the same sample population can demonstrate both the overlapping and distinct representations of each variable in the brain.

In order to better understand the relationship between regional GMV and the most common comorbid symptoms and protective factors of GD, we investigated the relationships between GMV and resilience, depression, anxiety, and apathy in a group of older adults with major depressive disorder. In addition, we aimed to demonstrate brain regions of overlap between the clinical scores, as well as score-specific regions.

Methods

Participants

Forty-nine older adults over the age of 60 years diagnosed with major depressive disorder and on stable antidepressant treatment (Table 1 and supplementary Table 1) for at least the prior 4 months participated in this study. This subsample was part of a larger clinical trial (NCT02460666) (Lavretsky *et al.*, 2022). Eligibility criteria were as follows: (1) a score of ≥ 14 on the 24-item Hamilton Depression Rating Scale (HAMD-24; Hamilton, 1960, 1967), moderate to severe depression; (2) a Mini-Mental State Examination (MMSE) score greater than 24 (Folstein *et al.*, 1975); (3) sufficient English proficiency to follow the testing procedures and main trial interventions (a minimum of an eighth grade reading level on the word reading subtest of the Wide Range Achievement Test-IV; Wilkinson and Robertson, 2006); (4) the mental capacity to provide informed consent; and (5) on stable antidepressant treatment for at least 4 months prior to participation. Exclusion criteria included (1) a history of other psychiatric conditions, such as drug or alcohol dependence, psychosis, bipolar disorder, or a neurological disorder; (2) a severe visual or hearing impairment that could prevent participation in the study; (3) insufficient English proficiency; (4) a diagnosis of dementia; (5) an MMSE score below 24; (6) current effective antidepressant treatment or psychotropic medication; and (7) a HAMD score below 14. Additionally, MRI exclusion criteria included unsafe or unverifiable metallic implants, tattoos in the head and neck region, permanent makeup, and claustrophobia. All participants signed written informed consent to participate in the trial as approved by the UCLA Institutional Review Board. This study was conducted in accordance with the Declaration of Helsinki of 1975.

Clinical and cognitive measures

Depressive symptom severity was assessed using the HAMD-24 (Hamilton, 1960, 1967), anxiety using the Hamilton Anxiety Scale (Hamilton, 1967; Maier *et al.*, 1988), apathy using the Apathy Evaluation Scale (AES) (Marin *et al.*, 1991), and resilience using the Connor–Davidson Resilience Scale (CD-RISC) (Connor and Davidson, 2003). Higher AES scores represent lower apathy. Higher CD-RISC scores represent greater resilience.

Procedure

Participants underwent an initial phone screening and proceeded to in-person screening if they met the inclusion criteria. The baseline visit began with the

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Table 1. Demographics and clinical variables

$N = 49$	Mean	Standard deviation
Sex	38 women/11 men	
Age (years)	67.98	6.12
Education	15.98	1.98
BMI	26.52	6.20
Age of depression onset	42.8	18.3
MMSE	29.0	1.16
HAMD	18.57	3.51
HAMA	10.84	3.60
AES	54.33	7.82
CD-RISC	61.35	14.09

Means and standard deviations are shown.
BMI = body mass index, HAMD = Hamilton Depression Rating Scale, MMSE = Mini-Mental State Examination, HAMA = Hamilton Anxiety Scale, AES = Apathy Evaluation Scale, CD-RISC = Connor–Davidson Resilience Scale.

participant signing their written informed consent, and baseline measures were taken, including mood and cognitive assessments, as well as vital signs (pulse rate, systolic blood pressure, body weight, and electrocardiogram). If the participant qualified for the study, an MRI scan was performed.

MRI acquisition and analysis

Structural 3D T1-weighted multi-echo magnetization-prepared rapid gradient-echo sequence (MEMPRAGE) images were acquired at the Ahmanson & Lovelace Brain Mapping Center at UCLA using a Siemens 3T Prisma system (Siemens, Erlangen, Germany) with a 32-channel head coil (TEs = 1.74, 3.6, 5.46, and 7.32 ms; TR = 2,530 ms; TI = 1,260 ms; flip angle = 7°; voxel size = 1 mm^3; double GRAPPA and matrix size = 256 × 192; acquisition time = 5:18 min). Freesurfer 6.0 (http://surfer.nmr.mgh.harvard.edu/) was used to perform cortical reconstruction. Preprocessing involved magnetic field inhomogeneity corrections, non-brain tissue removal from the image, and parcellation and segmentation of cortical and subcortical gray matter from white matter and cerebrospinal fluid. The resulting scans were visually inspected for tissue misclassifications. Manual corrections were performed wherever necessary. Resulting cortical maps were smoothed with a Gaussian kernel of 10 mm full-width half-maximum. First, whole-brain volume-based voxel-wise general linear models (GLMs) were performed for each hemisphere using qdec (www.surfer.nmr.mgh.harvard.edu). We performed whole-brain voxel-wise GLMs on GMV with depressive symptom severity, anxiety, apathy, and resilience as continuous variables. Age and sex served as covariates in all models. We applied a cluster-wise correction for multiple comparisons (Hagler *et al.*, 2006) and Monte-Carlo simulation corrected cluster thresholds of $p < 0.05$ for bidirectional effects (Greve and Fischl, 2018). In addition, to demonstrate the inverse relationship between mood symptoms (depression, apathy, anxiety) and resilience, we performed partial Spearman correlations between clinical scores using age and sex as covariates and an unadjusted alpha of 0.05.

Results

Participant demographics and clinical scores are listed in Table 1. Greater depressive symptom severity was associated with greater anxiety ($r = 0.53$, $p = 0.0001$) and lower resilience ($r = -0.33$, $p = 0.03$), but not apathy ($r = -0.07$, $p = 0.6$). Resilience correlated inversely with apathy ($r = 0.39$, $p = 0.01$).

Gray matter volume

Greater GMV was associated with reduced anxiety in the left caudal frontal cortex, stretching across the precentral toward the postcentral cortex; the left postcentral cortex from superior to inferior, with a branch crossing the supramarginal cortex; the left lingual to pericalcarine cortex; the right medial superior part of the superior frontal cortex, with a tip in the medial orbitofrontal cortex (OFC); the right inferior parietal to lateral occipital cortex; and the right border of the caudal and rostral middle frontal to pars opercularis (Figure 1; all clusters are listed in Supplementary Table 2).

Greater GMV was also associated with reduced apathy in the left superior frontal cortex, stretching into the paracentral, precuneus, and posterior cingulate cortex (PCC); the left postcentral cortex, with a small branch crossing the precentral cortex; a smaller region in the left lateral occipital cortex; the right medial OFC; right superior, middle, and inferior temporal cortices; and the right lingual-to-isthmus cingulate cortex and precuneus (Figure 2).

Greater GMV was associated with increased resilience in the left superior to caudal middle frontal cortex, reaching into the superior precentral cortex; the length of the postcentral cortex, dipping into the superior parietal and supramarginal cortices; the left insula, transverse, and superior temporal cortices; a small region of the lateral and a larger part of the ventromedial OFC; the anterior tip of the middle temporal cortex and the inferior middle and inferior temporal cortices; the right ventromedial OFC; the right inferior posterior and isthmus cingulate, reaching into the lingual and posterior parahippocampal cortices; and the right insula

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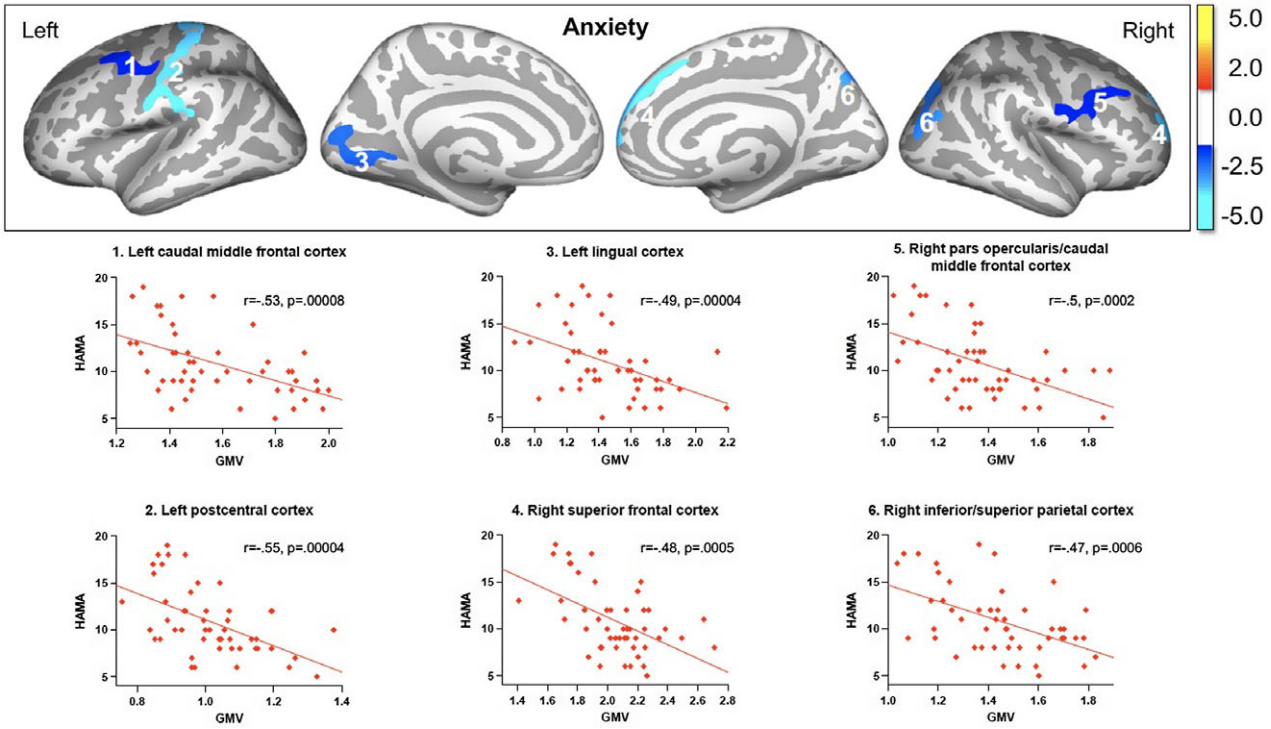

Figure 1. Greater GMV was associated with reduced anxiety. Six clusters across both hemispheres indicated an association between GMV and anxiety scores.

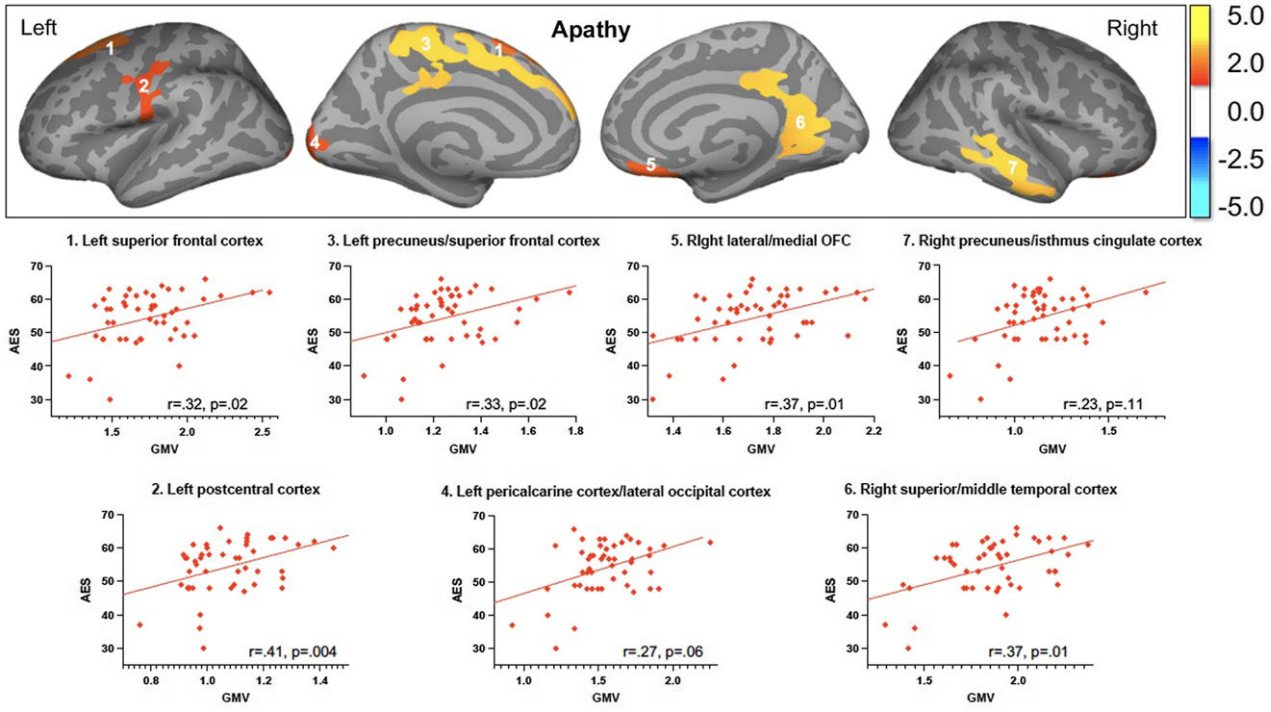

Figure 2. Greater GMV was associated with reduced apathy. There were seven clusters in which GMV was associated with apathy.

and supramarginal cortices, with a thin branch into the pars opercularis. The latter cluster continued into the right superior and middle temporal cortices, including the transverse temporal cortex (Figure 3). Figure 4 depicts the overlap between anxiety, resilience, and apathy clusters.

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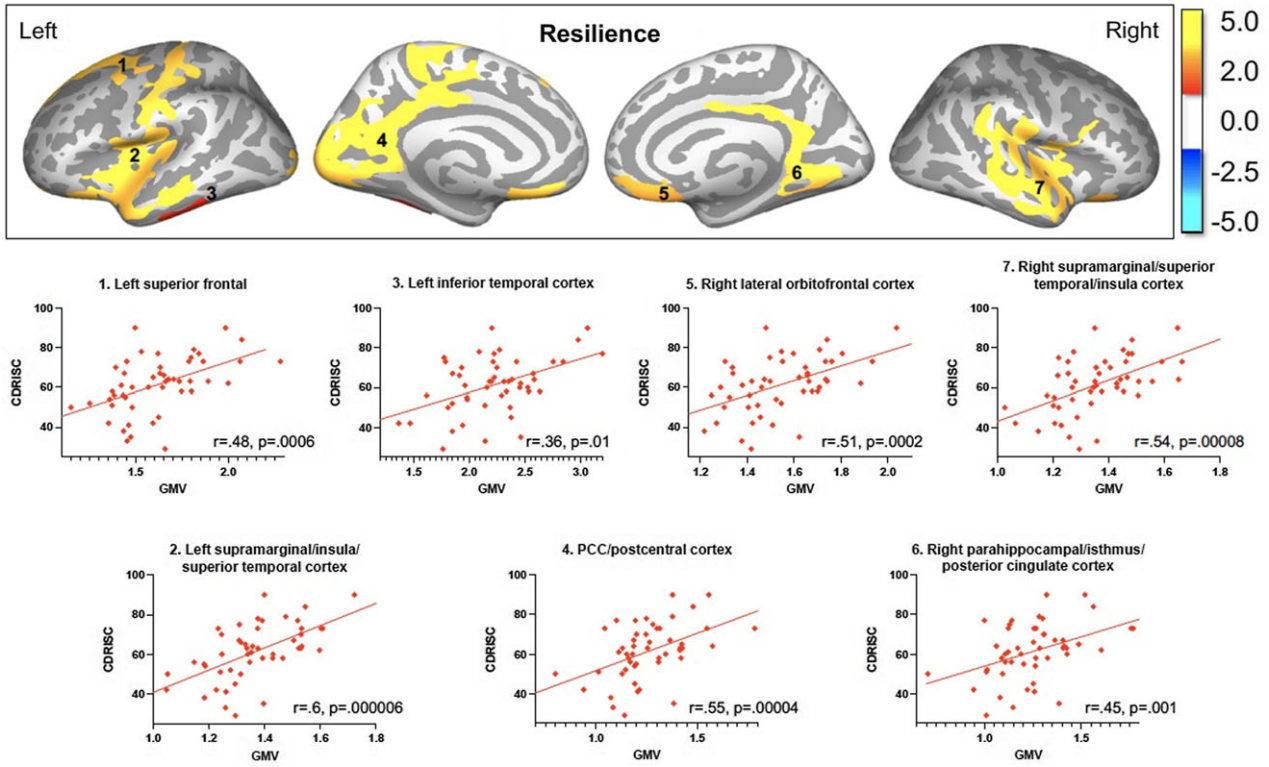

Figure 3. Greater GMV was associated with increased resilience. There were seven clusters in which GMV was associated with resilience scores.

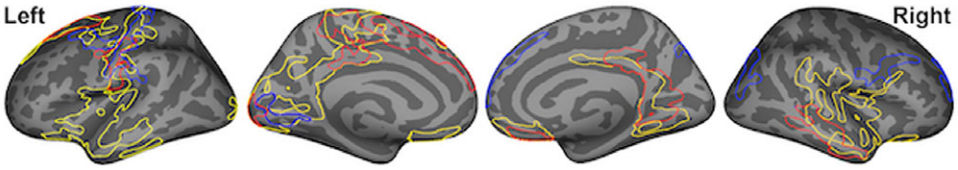

Figure 4. Overlap between GMV clusters for anxiety, apathy, and resilience. Greater GMV was associated with lower anxiety (blue), apathy (red), and increased resilience (yellow) in various large regions of both hemispheres.

Discussion

In 49 older adults with major depression, we found that those with higher depressive symptom severity also suffered from increased anxiety and reduced resilience. Apathy, however, was not associated with depression severity. Higher resilience was further associated with reduced apathy. We were able to demonstrate regions in which GMV correlated with individual clinical scores, in addition to being able to show the overlap in these correlations for anxiety, apathy, and resilience within the same sample. Subsequently, we will discuss both individual scores and overlap in detail.

Anxiety

At the neuroanatomical level, lower GMV in frontal, parietal, and occipital regions (but not temporal cortices) was associated with greater anxiety; there was no symmetry between the hemispheres. Anxiety specifically showed associations with GMV in the bilateral posterior cingulate cortices. Other anxiety regions included the left posterior superior frontal cortex, the middle-to-inferior somatosensory cortex, primary visual, and an extensive cluster from the medial anterior superior cortex reaching all the way toward the medial posterior parietal cortex. Unique to the right hemisphere were the right middle-to-anterior medial superior frontal and mid-anterior lateral superior frontal, precentral-to-caudal middle frontal, and superior occipital cortices. We previously found that greater subclinical anxiety symptoms were associated with lower GMV in the bilateral insula in GD (Laird *et al.*, 2019b). In older adults with a history of depression, greater trait anxiety was associated with reduced cortical thickness in the amygdala, anterior cingulate cortex (ACC), insula, OFC, and temporal cortices, as

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found by a region of interest study (Potvin *et al.*, 2015). A recent meta-analysis in depression across the lifespan found increased amygdala volume in those with comorbid anxiety, while those without anxiety showed reduced volume in the hippocampus, putamen, globus pallidus, and thalamus (Espinoza Oyarce *et al.*, 2020). However, these regions do not necessarily correlate with symptom severity, and subcortical regions were not examined in the current study.

Apathy

Reduced GMV in various extended clusters of all four lobes was also associated with greater apathy. We previously demonstrated that older depressed adults present with reduced GMV in the OFC compared to that in non-depressed older adults, and that higher apathy is associated with reduced GMV in the right ACC across both depressed and non-depressed older adults (Lavretsky *et al.*, 2007). Presently, we did not find a correlation between GMV in the ACC and apathy; however, the current study included only older adults diagnosed with major depression. In younger depressed adults, higher apathy has been shown to be associated with increased fractional anisotropy (a measure of white matter connectivity) in the anterior and posterior cingulum and bilateral internal capsules, increased functional activity in the ACC during a congruent affect task with greater apathy, and greater right functional connectivity between the Dorso-Lateral Prefrontal Cortex (DLPFC) and the ACC during an attention affect task (Robert *et al.*, 2021). The cingulum consists of far-reaching fibers from the ACC, running along the length of the cingulate gyrus and bending into the entorhinal cortex, passing the posterior end of the corpus callosum. Our results show associations between GMV and apathy scores in the PCC bilaterally, across the isthmus cingulate that ends in the parahippocampal cortex and at its tip the entorhinal cortex. The internal capsule projects to the motor cortex, including our left inferior cluster, which represents the face control area. In another of our previous studies, we found that apathy in older adults with and without dementia was associated with reduced hippocampal and cortical gray matter, smaller white matter volume, and increased lacunar volumes in the white matter (Lavretsky *et al.*, 2008). In Parkinson's disease, a different neurodegenerative disorder characterized by altered brain connectivity, it was found that increased glucose metabolism measured using positron emission tomography correlated with poorer emotional face recognition in the bilateral PCC and bilateral superior frontal gyri (Robert *et al.*, 2014). These regions correlated with apathy in our current study. In addition, the Parkinson's study found a positive correlation, that is, decreased glucose metabolism, between the right precuneus and left inferior occipital cortex and emotional face recognition. Similarly, we found these regions to correlate with apathy in our current sample of older adults with depression.

Resilience

Lastly, greater GMV was associated with greater resilience in extensive regions across the cortex and the effects were similar in both hemispheres. These included widespread clusters in bilateral insulae, lateral temporal and orbitofrontal cortices, and middle cingulate-to-parahippocampal cortices. Associations in the left superior frontal, medial parietal, medial primary visual, and somatosensory cortices tended a more right-lateralized representation. We found no clusters where GMV correlated with depression severity. In healthy younger adults, resilience measured using the CD-RISC correlates positively with GMV in the sub-parietal sulcus and negatively with GMV in the inferior parietal cortex (Gupta *et al.*, 2017). Both regions (bilateral sub-parietal sulci and the left inferior parietal cortex) were also found to show associations in the current study. We previously demonstrated a relationship between the CD-RISC and white matter fractional anisotropy, brain activity within the amygdala, and amygdala to default mode network activity in GD (Leaver *et al.*, 2018; Vlasova *et al.*, 2018). However, to our best knowledge, this is the first study in GD investigating the relationship between cortical GMV and resilience in GD based on the CD-RISC.

Anxiety, apathy, and resilience

All three measures showed associations with GMV in the inferior primary somatosensory cortex. The primary somatosensory cortex is a common cluster found in structural and functional studies in depression, potentially due to its role in emotion regulation (Kropf *et al.*, 2019) or perhaps indicating a dysfunctional integration of sensory information. This might explain the involvement of this large region found in the current study.

Anxiety and resilience

The left primary somatosensory cortex and a smaller isolated cluster in the caudal middle frontal cortex were associated with anxiety and resilience in overlapping regions. In addition, another region of overlap was observed in a cluster across the left pericalcarine and lingual cortex.

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Apathy and resilience

Furthermore, the left middle-to-posterior superior frontal cortex showed great overlap between resilience and apathy, as did the medial primary somatosensory cortex, left posterior primary visual cortex, right OFC, right isthmus cingulate/lingual/precuneus region, and right middle and slightly inferior temporal cortices. Only a few of these overlapping clusters were mirrored in the contralateral hemisphere; the somatosensory cortex only showed clusters in the left but not the right hemisphere. Similarly, the superior frontal cortex only showed extensive clusters in the left, but not right hemisphere, for apathy.

Depressive symptoms

While a multitude of studies report voxel-wise group differences between depressed and non-depressed adults, fewer studies have reported correlations between GMV and depressive symptom severity, particularly in older populations. It is possible that our mood measures were less sensitive to the underlying neuro-morphometric correlates to detect associations with GMV. In addition, a variety of depressive symptom measures are available, possibly leading to a less consistent understanding of the neuroanatomical phenotype of mood in GD.

Limitations

The current study had several limitations. While the parent clinical trial included a much larger sample, the reported findings are for a subsample consisting of only 49 participants, since many older adults did not qualify for MRI scanning due to implant safety criteria and claustrophobia. Additionally, while we applied corrections for multiple comparisons within each model, we did not correct for the number of models we performed (i.e. for anxiety, apathy, resilience, and depression). Furthermore, our models did not control for intracranial volume or head size. Lastly, the cross-sectional design of the study precludes drawing causal relationships between brain structure and mood and resilience symptoms.

Conclusion

Nevertheless, the current study suggests that greater GMV in extended and partially overlapping clusters across both hemispheres is associated with reduced anxiety and apathy, as well as increased resilience. GMV in these regions is therefore a potential marker for these clinical symptoms and resilience in GD. Future studies should also examine the effects of treatments on GMV in these regions.

Conflicts of interest

None.

Description of author(s)' roles

HL is the PI of the study, KLN designed the neuroimaging component and advised on result interpretation, BKS and MMM acquired the data, LAK processed the imaging data, BKS analyzed the imaging data, PS analyzed the clinical data, PS and BKS wrote the results section, and BKS wrote the manuscript. All authors provided critical input on the written manuscript and data interpretation.

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Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S1041610223000510.

References

Carpenter, C. R., Avidan, M. S., Wildes, T., Stark, S., Fowler, S. A. and Lo, A. X. (2014). Predicting geriatric falls following an episode of emergency department care: a systematic review. *Academic Emergency Medicine*, 21, 1069–1082.

Charney, D. S. (2004). Psychobiological mechanisms of resilience and vulnerability: implications for successful adaptation to extreme stress. *American Journal of Psychiatry*, 161, 195–216.

Chen, Y. M., Huang, X. M., Thompson, R. and Zhao, Y. B. (2011). Clinical features and efficacy of escitalopram treatment for geriatric depression. *Journal of International Medical Research*, 39, 1946–1953.

Connor, K. M. and Davidson, J. R. (2003). Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depression and Anxiety*, 18, 76–82.

Dillon, C. *et al.* (2009). Late- versus early-onset geriatric depression in a memory research center. *Neuropsychiatric Disease and Treatment*, 5, 517–526.

Du, M. *et al.* (2014). Brain grey matter volume alterations in late-life depression. *Journal of Psychiatry & Neuroscience*, 39, 397–406.

Espinoza Oyarce, D. A., Shaw, M. E., Alateeq, K. and Cherbuin, N. (2020). Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *Journal of Psychiatry & Neuroscience*, 45, 406–429.

Folstein, M. F., Folstein, S. E. and McHugh, P. R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.

Funes, C. M., Lavretsky, H., Ercoli, L., St Cyr, N. and Siddarth, P. (2018). Apathy mediates cognitive difficulties in geriatric depression. *The American Journal of Geriatric Psychiatry*, 26, 100–106.

Greve, D. N. and Fischl, B. (2018). False positive rates in surface-based anatomical analysis. *Neuroimage*, 171, 6–14.

Groeneweg-Koolhoven, I., Comijs, H. C., Naarding, P., de Waal, M. W. and van der Mast, R. C. (2016). Apathy in older persons with depression: course and predictors: the NESDO study. *Journal of Geriatric Psychiatry and Neurology*, 29, 178–186.

Gupta, A. *et al.* (2017). Morphological brain measures of cortico-limbic inhibition related to resilience. *Journal of Neuroscience Research*, 95, 1760–1775.

Hagler, D. J., Jr., Saygin, A. P. and Sereno, M. I. (2006). Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. *Neuroimage*, 33, 1093–1103.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*, 23, 56–62.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology*, 6, 278–296.

Ismail, Z., Fischer, C. and McCall, W. V. (2013). What characterizes late-life depression? *Psychiatric Clinics of North America*, 36, 483–496.

Kropf, E., Syan, S. K., Minuzzi, L. and Frey, B. N. (2019). From anatomy to function: the role of the somatosensory cortex in emotional regulation. *Brazilian Journal of Psychiatry*, 41, 261–269.

Laird, K. T. *et al.* (2019). Clinical correlates of resilience factors in geriatric depression, *International Psychogeriatrics*, 31, 193–202.

Laird, K. T., Krause, B., Funes, C. and Lavretsky, H. (2019a). Psychobiological factors of resilience and depression in late life. *Translational Psychiatry*, 9, 88.

Laird, K. T., Lavretsky, H., St Cyr, N. and Siddarth, P. (2018a). Resilience predicts remission in antidepressant treatment of geriatric depression. *International Journal of Geriatric Psychiatry*, 33, 1596–1603.

Laird, K. T., Lavretsky, H., Wu, P., Krause, B. and Siddarth, P. (2018b). Neurocognitive correlates of resilience in late-life depression. *The American Journal of Geriatric Psychiatry*, 27, 12–17.

Laird, K. T. *et al.* (2019b). Anxiety symptoms are associated with smaller insular and orbitofrontal cortex volumes in late-life depression. *Journal of Affective Disorders*, 256, 282–287.

Lavretsky, H., Ballmaier, M., Pham, D., Toga, A. and Kumar, A. (2007). Neuroanatomical characteristics of geriatric apathy and depression: a magnetic resonance imaging study. *The American Journal of Geriatric Psychiatry*, 15, 386–394.

Lavretsky, H. *et al.* (2008). The MRI brain correlates of depressed mood, anhedonia, apathy, and anergia in older adults with and without cognitive impairment or dementia. *International Journal of Geriatric Psychiatry*, 23, 1040–1050.

Lavretsky, H. *et al.* (2022). A randomized controlled trial of Tai Chi Chih or health education for geriatric depression. *The American Journal of Geriatric Psychiatry*, 30, 392–403.

Leaver, A. M. *et al.* (2018). Resilience and amygdala function in older healthy and depressed adults. *Journal of Affective Disorders*, 237, 27–34.

Mackin, R. S. *et al.* (2014). Association of age at depression onset with cognitive functioning in individuals with late-life depression and executive dysfunction. *The American Journal of Geriatric Psychiatry*, 22, 1633–1641.

Mackin, R. S. *et al.* (2013). Patterns of reduced cortical thickness in late-life depression and relationship to psychotherapeutic response. *The American Journal of Geriatric Psychiatry*, 21, 794–802.

MacLeod, S., Musich, S., Hawkins, K., Alsgaard, K. and Wicker, E. R. (2016). The impact of resilience among older adults. *Gerontological Nursing*, 37, 266–272.

Maier, W., Buller, R., Philipp, M. and Heuser, I. (1988). The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. *Journal of Affective Disorders*, 14, 61–68.

Marin, R. S., Biedrzycki, R. C. and Firinciogullari, S. (1991). Reliability and validity of the Apathy Evaluation Scale. *Psychiatry Research*, 38, 143–162.

Nelson, J. C., Delucchi, K. and Schneider, L. S. (2008). Efficacy of second generation antidepressants in late-life depression: a meta-analysis of the evidence. *The American Journal of Geriatric Psychiatry*, 16, 558–567.

Potvin, O. *et al.* (2015). Gray matter characteristics associated with trait anxiety in older adults are moderated by depression. *International Psychogeriatrics*, 27, 1813–1824.

Robert, G. *et al.* (2021). Multimodal brain imaging connectivity analyses of emotional and motivational deficits in depression among women. *Journal of Psychiatry & Neuroscience*, 46, E303–e312.

Robert, G. *et al.* (2014). Apathy and impaired emotional facial recognition networks overlap in Parkinson's disease: a PET study with conjunction analyses. *Journal of Neurology, Neurosurgery, and Psychiatry*, 85, 1153–1158.

Sachs-Ericsson, N. *et al.* (2013). A longitudinal study of differences in late- and early-onset geriatric depression: depressive symptoms and psychosocial, cognitive, and neurological functioning. *Aging and Mental Health*, 17, 1–11.

Sexton, C. E., Mackay, C. E. and Ebmeier, K. P. (2013). A systematic review and meta-analysis of magnetic resonance imaging studies in late-life depression. *The American Journal of Geriatric Psychiatry*, 21, 184–195.

Southwick, S. M., Vythilingam, M. and Charney, D. S. (2005). The psychobiology of depression and resilience to

https://doi.org/10.1017/S1041610223000510 Published online by Cambridge University Press

stress: implications for prevention and treatment. *Annual Review of Clinical Psychology*, 1, 255–291.

Stainton, A. *et al.* (2018). Resilience as a multimodal dynamic process. *Early Intervention in Psychiatry*, 13, 725–732.

Szymkowicz, S. M. *et al.* (2016). Depressive symptom severity is associated with increased cortical thickness in older adults. *International Journal of Geriatric Psychiatry*, 31, 325–333.

Tunvirachaisakul, C. *et al.* (2018). Predictors of treatment outcome in depression in later life: a systematic review and meta-analysis. *Journal of Affective Disorders*, 227, 164–182.

Vlasova, R. M. *et al.* (2018). Resilience and white matter integrity in geriatric depression. *The American Journal of Geriatric Psychiatry*, 26, 874–883.

Wilkinson, G. S. and Robertson, G. J. (2006). *Wide Range Achievement Test Professional Manual*. Bloomington, MN: NCS Pearson, Inc.

Zeng, Y. and Shen, K. (2010). Resilience significantly contributes to exceptional longevity. *Current Gerontology and Geriatrics Research*, 2010, 9.

https://doi.org/10.1017/S1041610223000510 Published online by Cambridge University Press