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RESEARCH ARTICLE

Associations Between Social Network Characteristics and Brain Structure Among Older Adults

Mohit K. Manchella[1,2] | **Paige E. Logan**[2] | **Brea L. Perry**[3] | **Siyun Peng**[3] | **Shannon L. Risacher**[4,5] | **Andrew J. Saykin**[2,3,4,5] | **Liana G. Apostolova**[2,3,4,5]

[1]Harvard Medical School, Boston, Massachusetts, USA

[2]Department of Neurology, Indiana University School of Medicine, Indianapolis, Indiana, USA

[3]Indiana University Network Science Institute, Indiana University, Bloomington, Indiana, USA

[4]Indiana Alzheimer's Disease Research Center, Indianapolis, Indiana, USA

[5]Center for Neuroimaging, Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, Indiana, USA

Correspondence
Liana G. Apostolova, Indiana University School of Medicine, 355 W 16th Street, Suite 4022, Indianapolis, IN 46202, USA.
Email: lapostol@iu.edu

Abstract

INTRODUCTION: Social connectedness is associated with slower cognitive decline among older adults. Recent research suggests that distinct aspects of social networks may have differential effects on cognitive resilience, but few studies analyze brain structure.

METHODS: This study includes 117 cognitively impaired and 59 unimpaired older adults. The effects of social network characteristics (bridging/bonding) on brain regions of interests were analyzed using linear regressions and voxel-wise multiple linear regressions of gray matter density.

RESULTS: Increased social bridging was associated with greater bilateral amygdala volume and insular thickness, and left frontal lobe thickness, putamen, and thalamic volumes. Increased social bonding was associated with greater bilateral medial orbitofrontal and caudal anterior cingulate thickness, as well as right frontal lobe thickness, putamen, and amygdala volumes.

DISCUSSION: The associations between social connectedness and brain structure vary depending on the types of social enrichment accessible through social networks, suggesting that psychosocial interventions could mitigate neurodegeneration.

KEYWORDS
bonding, bridging, cognitive impairment, magnetic resonance imaging, neuroimaging, social connectedness, social networks

Highlights

- Distinct forms of social capital are uniquely linked to gray matter density (GMD).
- Bridging is associated with preserved GMD in limbic system structures.
- Bonding is associated with preserved GMD in frontal lobe regions.
- Bridging is associated with increased brain reserve in sensory processing regions.
- Bonding is associated with increased brain reserve in regions of stress modulation.

1 | INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative condition affecting approximately 6.7 million Americans aged ≥ 65 as of 2022.[1] Given the lack of medical treatments for AD, social scientists have considered the potential therapeutic benefits of social connectedness in slowing cognitive impairment in older adults[2–4] and in improving health outcomes.[5] Other studies have identified a relationship between social connectedness and reduced mortality risk.[6–8]

Recent work suggests that social connectedness confers resilience against cognitive impairment, even among patients diagnosed with AD.[9] However, specific types of relationships and social network properties tend to be more effective at protecting cognition than others. For instance, having a larger social network was associated with a lower risk of dementia over a 4-year follow-up period in older women, after controlling for age, education, depression, and other health conditions.[10] Weak social ties, characterized by infrequent contact, low emotional intensity, and limited intimacy, have similarly been demonstrated to preserve cognition.[11] Two main hypotheses have emerged that propose distinct mechanisms about the types of social enrichment that protect cognition among older adults: the social bridging and social bonding hypotheses.

The social bridging hypothesis suggests that access to diverse and novel social stimuli, including exposure to new ideas, information, and activities can augment cognitive function.[12,13] Social bridging is conferred through irregular contact with less familiar individuals (i.e., weak ties) and interactions with dissimilar others (e.g., neighbors, colleagues, casual friends) as opposed to familiar exchanges with similar others (e.g., close friends and family).[14,15] The cognitive stimulation conferred by social bridging throughout the life course has thus been postulated to increase one's cognitive reserve and protect their cognition in later life.[16] A recent study found that social bridging was positively associated with older adults' global cognitive function, episodic memory, and executive function.[17]

The social bonding hypothesis suggests that the social benefits provided by close and supportive relationships drives cognitive protection in older adults.[18] Social bonding is conferred by close, high-quality relationships typically characterized by connections with kin and other close confidantes. This type of connectedness promotes a sense of purpose in life and increases perception of security and control that may stave off the chronic neurodegenerative effects of stress.[17,19,20]

Few studies in the literature have examined the associations between social networks and neuroimaging biomarkers.[21–23] Those that have failed to consider additional social network measures that reflect distinct social mechanisms, specifically bridging and bonding. The use of a broad generic measure of social network size does not allow for a nuanced exploration of how social bridging and social bonding associate with various cortical structures.

Subcortical structures, such as the thalamus, putamen, hippocampus, and amygdala, responsible for different elements of sensory integration and sensory information flow, are affected by early AD pathology.[24–29] Individuals with high levels of social bridging have high sensory processing demands to navigate a vast, diverse social environment, and are likely to heavily recruit these subcortical regions to integrate all this sensory information. Therefore, we hypothesize:

Hypothesis 1: Social bridging networks are associated with greater cortical thickness and volumes in subcortical regions associated with sensory integration.

As AD pathology progresses, cerebral structures (i.e., the frontal lobe and medial orbitofrontal cortex) become vulnerable to neurodegeneration. These regions have been previously linked to emotional regulation and processing[30] and to minimizing the effects of stress. *Post mortem* morphological studies of posttraumatic stress disorder of the brain suggest the crucial role these regions play in stress and trauma management.[31] Given that individuals with high levels of social bonding capital have a greater proportion of network ties that provide a sense of security and comfort due to regular contact with familiar individuals, it is plausible that these ties reduce stress. Therefore, we hypothesize:

Hypothesis 2: Social bonding networks are associated with greater cortical thickness and volumes in prefrontal cortex structures associated with emotional regulation and processing.

RESEARCH IN CONTEXT

Systematic review: Using specific sociological search terms in traditional search engines, we examined and referenced several publications of prior work detailing the augmentation of cognition resulting from social connectedness. Despite a broad review of the literature, virtually no studies examine associations between social capital and neuroimaging markers.

Interpretation: Our findings demonstrate that the benefits individuals derive from social connectedness differ depending on the preponderance of social bridging capital and social bonding capital, suggesting that different social relationships may buffer against age-related neurodegeneration through distinct mechanisms.

Future directions: Investigations in larger datasets including a more ethnically diverse sample can increase the generalizability of our findings to a larger population of older adults. Furthermore, investigating associations between social capital and other biomarkers, such as amyloid and tau deposition, may further our understanding of how social connections mediate age-related neurodegenerative processes.

2 | METHODS

2.1 | Sample selection

The data used in this analysis were sourced from the Social Networks and Alzheimer's Disease (SNAD) study, which recruits participants from the Indiana Alzheimer's Disease Research Center (IADRC) and

adds extensive characterization of social networks and other aspects of the social environments of older adults. The IADRC also collects longitudinal clinical and magnetic resonance imaging (MRI) data from a cohort of older adults. The IADRC enrollment criteria excludes participants with a history of schizophrenia, bipolar disorder, other major psychiatric disorders, history of cancer with chemotherapeutic or radiation interventions, traumatic brain injury with loss of consciousness, developmental disorders, and history of or present alcohol and other substance abuse disorders.

The IADRC Clinical Core's interdisciplinary team consisting of psychiatrists, neurologists, and neuropsychologists determined participant diagnoses. Participants without significant memory concerns (12-item Cognitive Change Index < 20) and without significant cognitive testing deficits were diagnosed as cognitively normal (CN), while participants with elevated memory concerns (12-item Cognitive Change Index ≥ 20), with or without increased levels of informant-based concerns, and no significant deficits on cognitive testing were characterized as having subjective cognitive decline (SCD).[32] Individuals were diagnosed with mild cognitive impairment (MCI), or AD dementia based on previously established and standard criteria.[33,34]

Informed consent was obtained from all participants in accordance with the Indiana University Institutional Review Board and the ethical standards laid down in the Declaration of Helsinki.

Since April 2019, 54% of all eligible-for-SNAD IADRC participants were approached to voluntarily complete the SNAD protocol. SNAD enrollment criteria excluded IADRC participants who scored < 10 on the Montreal Cognitive Assessment (MoCA), participants with known family history of dominantly inherited dementia, and participants < 65 years of age. Data for SNAD were collected face to face using computer-assisted personal interviewing.

The analyses detailed below include baseline data from 176 participants from SNAD: 63 CN, 54 with SCD, 47 with MCI, and 12 with AD dementia.

2.2 | Social network measures

Social network data were collected using an expanded PhenX Social Network Battery tailored for use among participants with cognitive impairment.[35] SNAD interviewers obtained the names of individuals in the study participant's social network called upon in the past 6 months for discussions regarding important topics and health matters.[36] Questions were asked about each person in the participant's network, yielding structural, functional, and compositional variables about a person's core social network.

A composite measure of social bridging was calculated using density, effective size, sole bridge status, network diversity, weak ties, and network size.[37] Network density was calculated using the mean of the closeness of ties between each network member in a participant's network, ranging from 0 to 3. Response categories were "don't know each other," "not very close," "sort of close," and "very close." Effective size of a person's network, which estimates the number of non-redundant network members, was calculated using the number of network members that a person has, minus the average number of ties that each network member has to other members. Sole bridge status was a dichotomous indicator of whether the respondent reports that at least one pair of network members do not know each other. Network diversity assessed participation in 12 types of social relationships (ranged from 0 to 12). These include relationships with a spouse, close neighbors, friends, workmates, and more. The presence of weak ties in the network was assessed using the minimum value of the strength of ties between a participant and each of his/her network members, which had a potential range of 1 to 10 on a sliding scale. Network size was measured by the number of unique people mentioned in response to name generators.

Social bonding was primarily operationalized through participants' quality of social relationships. Quality of social relationships was measured by taking the average of all non-missing values for three items in the Quality of Life in Alzheimer's Disease scale.[38] Subscale items included relationships with family members, relationships with a marital or romantic partner (or if none, the person they are closest to), and relationships with friends. The resulting index ranged from 1 to 4 (corresponding to "poor," "fair," "good," or "excellent") with higher values indicating better quality.

2.3 | MRI data acquisition and processing

T1-weighted MRI data were acquired on a single Siemens Prisma 3T scanner with a 64-channel RF receiver head coil by the IADRC Neuroimaging Core. A three-dimensional magnetization rapid gradient echo (MPRAGE) sequence was used; imaging parameters match the Alzheimer's Disease Neuroimaging Initiative 2 protocols.

The T1- weighted MRI scans were processed using FreeSurfer, version 6.0, to extract intracranial volume, cortical thicknesses, gray matter volumes, and subcortical volumes, by regions of interests (ROIs). For analysis in imaging space, the scans were processed using voxel-based morphometry (VBM) standard methods in SPM12 to produce gray matter density (GMD) images for each subject.

2.4 | Statistical analyses and parametric mapping

A comprehensive review of the literature for areas of the brain that have been previously associated with social function yielded several MRI ROIs selected for this analysis. The measures selected for this analysis included global, frontal lobe, frontal pole, medial orbitofrontal, lateral orbitofrontal, caudal anterior cingulate, and insular cortical thickness, as well as hippocampal, putamen, thalamic, amygdala, and pallidum volumes. The left- and right-hemispheric regions were analyzed separately to check for a potential laterality association with social bridging or bonding.

To increase statistical power for the statistical and parametric mapping analyses, CN and SCD participants were grouped together into a cognitively unimpaired (CU) group ($n = 117$) and the MCI and AD participants were grouped together into a cognitively impaired (CI) group ($n = 59$).

TABLE 1 Demographic and biomarker characteristics of SNAD sample.

Demographics and biomarkers	Cognitively unimpaired ($n = 117$)	Cognitively impaired ($n = 59$)	p-value
Age, years, mean (SD)	68.29 (11.98)	69.10 (12.87)	0.6830
Sex, % female	73.5%	54.2%	0.0103
Education, years, mean (SD)	16.47 (2.55)	16.29 (2.59)	0.6578
MoCA, mean (SD)	24.37 (4.11)	24.02 (4.79)	0.6244
APOE ε4 status, % with ε4 allele	38.8%	57.6%	0.0179
Social bridging, mean (SD)	0.19 (0.88)	−0.40 (0.90)	<0.0001
Social bonding, mean (SD)	3.37 (0.47) $N = 109$	3.23 (0.51) $N = 49$	0.0958
Total bilateral total hippocampal volume, mm^3, mean (SD)	7390.63 (986.53)	7702.46 (1363.93)	0.0848
Bilateral total amygdala volume, mm^3, mean (SD)	2957.76 (415.40)	2708.35 (594.22)	0.0014
Global cortical thickness, mm, mean (SD)	2.43 (0.10)	2.43 (0.10)	0.9600
Bilateral insula thickness, mm, mean (SD)	2.84 (0.15)	2.78 (0.17)	0.0223
Left insula thickness, mm, mean (SD)	2.84 (0.16)	2.77 (0.19)	0.0208
Right insula thickness, mm, mean (SD)	2.85 (0.16)	2.80 (0.18)	0.0579
Intracranial volume, mm^3, mean (SD)	1485177.65 (157769.43)	1442956.28 (176972.69)	0.1096
Right frontal lobe thickness, mm, mean (SD)	2.37 (0.14)	2.36 (0.12)	0.6058
Left frontal lobe thickness, mm, mean (SD)	2.45 (0.11)	2.41 (0.11)	0.0291
Right frontal pole thickness, mm, mean (SD)	2.56 (0.20)	2.55 (0.26)	0.7139
Left frontal pole thickness, mm, mean (SD)	2.60 (0.21)	2.60 (0.21)	0.9021
Bilateral medial orbitofrontal cortex thickness, mm, mean (SD)	2.32 (0.11)	2.32 (0.13)	0.9748
Left medial orbitofrontal cortex thickness, mm, mean (SD)	2.33 (0.13)	2.32 (0.16)	0.5611
Right medial orbitofrontal cortex thickness, mm, mean (SD)	2.56 (0.20)	2.32 (0.16)	0.5787
Bilateral lateral orbitofrontal cortex thickness, mm, mean (SD)	2.54 (0.11)	2.54 (0.13)	0.8405
Bilateral caudal anterior cingulate thickness, mm, mean (SD)	2.55 (0.21)	2.52 (0.23)	0.3240
Left caudal anterior cingulate thickness, mm, mean (SD)	2.64 (0.27)	2.61 (0.30)	0.4651
Right caudal anterior cingulate thickness, mm, mean (SD)	2.44 (0.25)	2.42 (0.26)	0.5384
Left putamen volume, mm^3, mean (SD)	4263.09 (474.73)	4168.80 (539.17)	0.2365
Right putamen volume, mm^3, mean (SD)	4317.05 (490.59)	4214.72 (614.70)	0.2327
Left thalamus volume, mm^3, mean (SD)	6301.51 (732.58)	6105.25 (776.16)	0.1019
Right thalamus volume, mm^3, mean (SD)	6238.76 (675.08)	6138.19 (732.02)	0.3657
Left pallidum volume, mm^3, mean (SD)	1871.14 (199.51)	1924.85 (255.57)	0.1277
Right pallidum volume, mm^3, mean (SD)	1796.89 (220.50)	1830.97 (270.29)	0.3715
Left amygdala volume, mm^3, mean (SD)	1430.72 (225.12)	1300.23 (317.23)	0.0019
Right amygdala volume, mm^3, mean (SD)	1527.04 (218.52)	1408.12 (314.90)	0.0039

Abbreviations: *APOE ε4*, apolipoprotein E ε4; MoCA, Montreal Cognitive Assessment; SD, standard deviation.

The statistical distribution of clinical and demographic characteristics (i.e., age, sex, education), and MRI ROIs across groups were analyzed in SAS 9.4 using a one-way analysis of variance. Linear regressions were conducted in SAS 9.4 to identify significant associations between various MRI ROIs and social bridging and bonding. A false discovery rate (FDR) correction was conducted to correct for multiple comparisons.

The predictor variable in these linear regression models was either the composite bridging measure (bridging) or the quality of relationships measure (bonding), and the outcome measures were the ROIs listed above. The covariates included in the model were age, sex, education, intracranial volume, diagnosis, apolipoprotein E ε4 (*APOE ε4*) carrier status, and MoCA score. Regression scatter plots showing the association of each ROI with bridging or bonding separated by diagnostic group were also generated.

A post hoc neuroimaging analysis was used to examine which brain regions are associated with social bridging and bonding. These analyses were subjected to stringent false discovery correction using family-wise error (FWE) correction for multiple comparisons. Voxel-wise linear regression models of GMD images were conducted in

TABLE 2 Beta coefficients for social bridging obtained from linear regression models in pooled, cognitively unimpaired, and cognitively impaired samples. Note: (*) indicates $p_{FDR} < 0.05$.

Regions of interest	Pooled ($n = 176$)	Cognitively unimpaired ($n = 117$)	Cognitively impaired ($n = 59$)
Total hippocampal volume (mm^3)	−50.50	−64.50	−110.49
Total amygdala volume (mm^3)	112.37*	32.78	186.69*
Global cortical thickness (mm)	−0.0000042	−0.010	−0.0022
Bilateral insula thickness (mm)	0.029*	0.021	0.031
Left insula thickness (mm)	0.030*	0.019	0.021
Right insula thickness (mm)	0.028*	0.022	0.040
Right frontal lobe thickness (mm)	0.016	0.023	0.0037
Left frontal lobe thickness (mm)	0.020*	0.012	0.022
Right frontal pole thickness (mm)	0.0075	0.022	−0.070
Left frontal pole thickness (mm)	0.023	0.032	0.016
Bilateral medial orbitofrontal cortex thickness (mm)	−0.0016	0.0090	−0.030
Left medial orbitofrontal cortex thickness (mm)	0.0018	0.0016	−0.012
Right medial orbitofrontal cortex thickness (mm)	−0.0054	0.017	−0.050
Bilateral lateral orbitofrontal cortex thickness (mm)	0.017	0.028	0.0013
Bilateral caudal anterior cingulate thickness (mm)	0.0024	0.017	−0.035
Left caudal anterior cingulate thickness (mm)	0.016	0.040	−0.021
Right caudal anterior cingulate thickness (mm)	−0.011	−0.0031	−0.043
Left putamen volume (mm^3)	83.87	55.07	108.27
Right putamen volume (mm^3)	70.75	69.59	35.62
Left thalamus volume (mm^3)	136.57	60.52	182.99
Right thalamus volume (mm^3)	62.26	15.82	70.80
Left pallidum volume (mm^3)	26.80	26.27	27.25
Right pallidum volume (mm^3)	29.65	20.98	46.20
Left amygdala volume (mm^3)	55.47*	14.89	106.17*
Right amygdala volume (mm^3)	56.90*	17.89	80.51*

Abbreviation: FDR, false discovery rate.

SPM12 using bridging or bonding as predictors of GMD in the pooled sample while controlling for diagnosis, age, sex, education, *APOE* ε4 carrier status, and intracranial volume to produce statistical brain maps. Because of the exploratory nature of our secondary results, we allowed a less stringent primary or cluster-defining visualization threshold of $P < 0.01$ (uncorrected). FWE correction for multiple comparisons was applied at the cluster level. Only clusters surviving the FWE correction at $p_{FWE} < 0.05$ with the minimum cluster size (k) depending on the minimum threshold level were displayed. The cluster-corrected maps were saved and rendered in Surf Ice.

3 | RESULTS

3.1 | Demographic and ROI comparison

Of the SNAD participants, 67% were women, mean age was 69 years, and mean education was 16 years. Clinical and demographic characteristics of the diagnostic groups are listed in Table 1. No significant differences were observed between the two diagnostic groups for age and education. Significant differences were observed in sex ($p = 0.01$), *APOE* ε4 carrier status ($p = 0.02$), mean bridging ($p < 0.01$), total insular thickness ($p = 0.02$), left frontal lobe thickness ($p = 0.03$), left insular thickness ($p = 0.02$), and bilateral amygdala volume (left $p < 0.01$; right $p < 0.01$).

3.2 | Linear regression results

Tables 2 and 3 show the beta coefficients of social bridging and bonding, respectively, in each linear regression model tested. The regressions were also separately conducted in each diagnostic group to determine whether the effects of social bridging and bonding were more pronounced in either the cognitively impaired or unimpaired population. Tables 4 and 5 display the beta coefficients of the covariates included in the social bridging and bonding models, respectively.

TABLE 3 Beta coefficients for social bonding obtained from linear regression models in pooled, cognitively unimpaired, and cognitively impaired samples. Note: (*) indicates $p_{FDR} < 0.05$.

Regions of interest	Pooled ($n = 158$)	Cognitively unimpaired ($n = 109$)	Cognitively impaired ($n = 49$)
Total hippocampal volume (mm^3)	−192.22	−186.91	−268.81
Total amygdala volume (mm^3)	78.14	−26.42	234.44
Global cortical thickness (mm)	−0.0037	−0.0020	−0.020
Bilateral insula thickness (mm)	0.022	0.024	0.0032
Left insula thickness (mm)	0.016	0.019	0.0015
Right insula thickness (mm)	0.026	0.030	0.0037
Right frontal lobe thickness (mm)	0.049	0.042	0.038
Left frontal lobe thickness (mm)	0.021	0.010	0.033
Right frontal pole thickness (mm)	0.12*	0.062	0.20
Left frontal pole thickness (mm)	−0.025	−0.0060	−0.022
Bilateral medial orbitofrontal cortex thickness (mm)	0.057	0.038	0.11
Left medial orbitofrontal cortex thickness (mm)	0.027	0.0070	0.064
Right medial orbitofrontal cortex thickness (mm)	0.085*	0.068	0.15
Bilateral lateral orbitofrontal cortex thickness (mm)	0.031	0.0072	0.093
Bilateral caudal anterior cingulate thickness (mm)	0.076	0.085	0.10
Left caudal anterior cingulate thickness (mm)	0.064	0.084	0.066
Right caudal anterior cingulate thickness (mm)	0.096	0.10	0.14
Left putamen volume (mm^3)	102.09	79.23	164.92
Right putamen volume (mm^3)	206.34*	166.29	293.52
Left thalamus volume (mm^3)	−40.91	−79.49	−63.49
Right thalamus volume (mm^3)	−38.02	−154.82	91.21
Left pallidum volume (mm^3)	−10.18	−2.39	−14.08
Right pallidum volume (mm^3)	4.58	18.46	−3.17
Left amygdala volume (mm^3)	6.22	−39.76	87.10
Right amygdala volume (mm^3)	71.91	13.34	147.33

Abbreviation: FDR, false discovery rate.

For results in each diagnostic category please see Tables S1–S4 in supporting information.

In the pooled sample, greater social bridging was associated with increased left and right amygdala volume ($p_{FDR} < 0.01$, $p_{FDR} = 0.02$, resp), left and right insula thickness ($p_{FDR} = 0.03$, $p_{FDR} = 0.04$, resp), and left frontal lobe thickness ($p_{FDR} = 0.01$). In the CU group, greater social bridging was not significantly associated with any MRI ROI. In the CI group, greater social bridging was associated with increased left and right amygdala volume ($p_{FDR} < 0.01$ and $p_{FDR} = 0.02$). Figure 1 displays scatterplots of significant associations between social bridging and the MRI ROIs separated by diagnostic group.

In the pooled sample, greater social bonding is associated with increased right frontal pole thickness ($p_{FDR} = 0.01$), right medial orbitofrontal cortex thickness ($p_{FDR} = 0.01$), and right putamen volume ($p_{FDR} = 0.04$). In both the CU and CI groups, greater social bonding had no significant associations to any MRI ROI. Figure 2 displays scatterplots of significant associations between social bonding and MRI ROIs separated by diagnostic group.

3.3 | Parametric mapping

The FWE cluster-level corrected statistical brain maps of GMD confirmed the differing patterns between social bridging and bonding (Figure 3). In social bridging, the structural benefits appear to be left lateralized and situated in the frontal pole, dorsolateral prefrontal cortex, the insula, the medial and lateral temporal, and medial occipital lobes. Social bonding by contrast appears to have a greater bias toward the right hemisphere with strongest associations with the medial frontal, cingulate, orbitofrontal, anterior, inferior temporal, and dorsolateral parietal cortices. Areas that seemed to be associated with social bridging were not associated with social bonding and vice versa.

TABLE 4 Beta coefficients for covariates in social bridging linear regression models. Note: (*) indicates $p_{FDR} < 0.05$.

Regions of interest	Sample	Age	Sex	Education	ICV	MoCA	*APOE ε4 carrier status*
Total hippocampal volume (mm^3)	Pooled	−11.41	−11.98	3.41	−0.0033*	–	207.31
	CU	−15.27	−57.43	−19.88	−0.0033	111.89	47.76
	CI	−14.87	131.29	23.53	−0.0047*	79.52	−35.38
Total amygdala volume (mm^3)	Pooled	−21.45*	−162.94	5.72	0.00038	–	−13.87
	CU	−17.89*	−270.22	4.12	0.00012	0.35	69.09
	CI	−24.96*	−42.39	6.40	0.00047	3.89	−35.11
Global cortical thickness (mm)	Pooled	−0.00047	−0.011	0.0031	2.82E-8	–	0.021
	CU	−0.00080	−0.017	0.0024	−8.22E-9	0.010	0.0068
	CI	−0.0010	−0.023	0.0013	−1.09E-7	0.0088*	−0.0042
Bilateral insula thickness (mm)	Pooled	−0.0054	−0.0040	0.0030	5.10E-8	–	−0.0091
	CU	−0.0060*	0.012	0.0042	9.90E-10	0.00073	0.0055
	CI	−0.0048	−0.058	−0.00014	6.53E-8	−0.0048	−0.0031
Left insula thickness (mm)	Pooled	−0.0048	0.0079	0.0067	1.83E-8	–	0.00066
	CU	−0.0051*	0.027	0.0083	−3.82E-8	−0.000054	0.021
	CI	−0.0048	−0.052	0.0050	2.79E-8	−0.0057	0.025
Right insula thickness (mm)	Pooled	−0.0060	−0.014	−0.00046	8.48E-8	–	−0.020
	CU	−0.0069*	−0.00080	0.00044	4.25E-8	0.0014	−0.0094
	CI	−0.0048	−0.063	−0.0053	9.88E-8	−0.0037	−0.033
Right frontal lobe thickness (mm)	Pooled	−0.0012	−0.0014	0.0040	3.85E-8	–	−0.011
	CU	−0.0027*	0.048	0.0055	5.48E-9	−0.0014	−0.0040
	CI	0.00071	−0.060	0.0052	5.64E-8	−0.0019	−0.021
Left frontal lobe thickness (mm)	Pooled	−0.0041*	0.0054	0.0024	9.14E-9	–	0.0065
	CU	−0.0045*	0.036	0.0025	−3.41E-8	0.0017	0.019
	CI	−0.0044	−0.045	0.0043	2.43E-8	−0.0051	0.022
Left frontal pole thickness (mm)	Pooled	−0.0018	0.047	−0.00021	5.05E-8	–	0.035
	CU	−0.0030	0.067	−0.0060	3.45E-8	0.0037	0.053
	CI	−0.00058	0.016	0.012	5.97E-8	−0.0089	0.019
Right frontal pole thickness (mm)	Pooled	−0.0021	0.048	−0.0040	2.86E-8	–	−0.014
	CU	−0.0026*	0.11	−0.0055	−5.75E-8	0.0023	−0.013
	CI	−0.0042	−0.041	0.0090	1.30E-7	0.00055	0.037
Bilateral medial orbitofrontal cortex thickness (mm)	Pooled	−0.0019	−0.032	−0.0044	1.15E-7	–	0.0034
	CU	−0.0018	−0.036	−0.0058	7.99E-8	0.0023	0.017
	CI	−0.0035	−0.038	−0.00088	1.46E-7	−0.0056	−0.0025
Left medial orbitofrontal cortex thickness (mm)	Pooled	−0.0030	−0.046	−0.0046	9.79E-8	–	0.010
	CU	−0.0026	−0.055	−0.0058	3.57E-8	0.0032	0.036
	CI	−0.0046	−0.059	−0.0035	1.33E-7	−0.0094	−0.0037
Right medial orbitofrontal cortex thickness (mm)	Pooled	−0.0010	−0.018	−0.0042	1.34E-7	–	−0.0033
	CU	−0.00098	−0.014	−0.0055	1.29E-7	0.0014	−0.000019
	CI	−0.0025	−0.024	0.0013	1.55E-7	−0.0027	−0.050
Bilateral lateral orbitofrontal cortex thickness (mm)	Pooled	−0.0024	−0.021	−0.0021	4.06E-8	–	0.0035
	CU	−0.0028*	−0.0094	−0.00046	5.37E-8	−0.0015	0.015
	CI	−0.0019	−0.025	−0.0036	−2.24E-9	−0.0019	−0.019

(Continues)

TABLE 4 (Continued)

Regions of interest	Sample	Age	Sex	Education	ICV	MoCA	*APOE ε4 carrier status*
Bilateral caudal anterior cingulate thickness (mm)	Pooled	−0.000061	0.052	−0.0041	2.09E-7	–	−0.036
	CU	−0.00057	0.0018	−0.014	1.66E-7	0.0028	−0.016
	CI	0.00055	0.095	0.013	2.15E-7	0.00064	−0.056
Left caudal anterior cingulate thickness (mm)	Pooled	−0.0012	0.048	−0.0056	3.56E-7*	–	−0.044
	CU	−0.00043	−0.012	−0.0098	3.09E-7	−0.0054	−0.011
	CI	−0.0016	0.12	0.0000056	5.01E-7	−0.0037	−0.055
Right caudal anterior cingulate thickness (mm)	Pooled	0.00024	0.055	−0.0029	1.25E-7	–	−0.023
	CU	−0.0015	0.012	−0.018	1.10E-7	0.012	−0.027
	CI	0.0016	0.077	0.025	−2.76E-9	0.00050	−0.037
Left putamen volume (mm^3)	Pooled	−18.40*	−199.62	19.57	0.00016	–	65.95
	CU	−15.45*	−333.35	28.51	0.00028	1.16	−1.68
	CI	−21.04	21.94	1.75	0.000035	14.96	193.87
Right putamen volume (mm^3)	Pooled	−19.96*	−176.28	12.66	0.00027	–	57.78
	CU	−16.88*	−335.25	24.11	0.00040	−1.30	−20.96
	CI	−23.04	113.53	−3.41	0.00017	27.44	189.97
Left thalamus volume (mm^3)	Pooled	−25.55*	−506.00	47.47*	0.000057	–	103.38
	CU	−24.44*	−505.22	61.58*	0.000016	−3.22	55.81
	CI	−27.31	−568.96	27.76	0.00013	−2.93	336.78
Right thalamus volume (mm^3)	Pooled	−26.00*	−490.02	58.19*	0.00015	–	113.98
	CU	−25.55*	−531.92	60.39*	0.00015	2.41	61.14
	CI	−27.22	−500.70	56.84	0.00016	−1.93	314.22
Left pallidum volume (mm^3)	Pooled	−2.47	−102.53	5.89	0.000034	–	41.79
	CU	0.51*	−133.96	8.39	0.000066	1.00	32.81
	CI	−7.07	−44.49	−0.26	0.000098	4.97	69.06
Right pallidum volume (mm^3)	Pooled	−1.99	−128.11	−0.69	0.000024	–	20.81
	CU	1.11*	−146.11	6.58	0.000081	−6.17	−0.68
	CI	−6.11	−93.34	−12.43	0.00010	3.10	105.28
Left amygdala volume (mm^3)	Pooled	−12.03*	−46.64	4.61	0.00019	–	−10.86
	CU	−10.33*	−96.13	8.90	0.00011	1.17	20.80
	CI	−13.30	10.37	−7.06	0.00015	5.07	−30.89
Right amygdala volume (mm^3)	Pooled	−9.42*	−116.31	1.11	0.00019	–	−3.01
	CU	−7.58*	−174.09	−4.78	0.0000097	−0.82	17.89
	CI	−11.66	−52.75	13.46	0.00032	−1.18	−4.22

Abbreviations: *APOE ε4*, apolipoprotein E ε4; CI, cognitively impaired; CU, cognitively unimpaired; FDR, false discovery rate; ICV, intracranial volume; MoCA, Montreal Cognitive Assessment.

4 | DISCUSSION

The present study aimed to evaluate hypothesized relationships between brain structure and social bridging and bonding among CN and CI subjects. Through this analysis, we sought to pinpoint cortical regions that may be associated with social cognitive benefits and elucidate the mechanisms by which different social network characteristics affect the brain. The brain regions significantly associated with social bridging provide evidence supporting our first hypothesis: individuals with greater social bridging potential in their networks have greater cortical thickness and volumes in regions associated with effective integration of novel social stimuli. The associations observed for social bonding confirmed our second hypothesis: social bonding networks are associated with greater cortical thickness and volumes in the cortical areas that have been associated with emotional regulation and processing.

TABLE 5 Beta coefficients for covariates in social bonding linear regression models. Note: (*) indicates $p_{FDR} < 0.05$.

Regions of interest	Sample	Age	Sex	Education	ICV	MoCA	*APOE ε4 carrier status*
Total hippocampal volume (mm^3)	Pooled	−18.67	−86.78	−1.84	−0.0033*	–	130.84
	CU	−18.52*	−94.88	−0.36	−0.0029*	−21.30	50.31
	CI	−22.13	64.26	58.35	−0.0039*	18.80	229.77
Total amygdala volume (mm^3)	Pooled	−32.30*	−142.88	4.41	0.00042	–	−62.50
	CU	−25.83	−281.11*	−2.91	0.000044	5.65	63.37
	CI	−42.77*	−112.11	7.47	0.00056	−17.21	−265.05
Global cortical thickness (mm)	Pooled	−0.0015	−0.0097	0.0027	1.54E-8	–	0.013
	CU	−0.00052	−0.0061	0.0032	−2.83E-8	−0.0024	0.023
	CI	−0.0052	−0.036	0.0027	−3.26E-8	0.0083	−0.0056
Bilateral insula thickness (mm)	Pooled	−0.0054*	0.017	0.0029	2.24E-8	–	−0.0040
	CU	−0.0052*	0.026	0.0025	4.06E-9	−0.00014	0.031
	CI	−0.0058	−0.032	−0.0010	1.62E-8	0.00049	−0.033
Left insula thickness (mm)	Pooled	−0.0055*	0.020	0.0065	−1.72E-8	–	0.0012
	CU	−0.0047*	0.026	0.0054	−3.95E-8	0.00081	0.038
	CI	−0.0074	−0.037	0.0037	−1.57E-8	0.0010	−0.028
Right insula thickness (mm)	Pooled	−0.0053*	0.017	−0.00050	6.34E-8	–	−0.0098
	CU	−0.0057*	0.028	0.000043	4.99E-8	−0.00098	0.024
	CI	−0.0043	−0.025	−0.0057	4.64E-8	−0.000088	−0.040
Right frontal lobe thickness (mm)	Pooled	0.0014	0.022	0.0056	6.16E-8	–	−0.00078
	CU	0.00016	0.059	0.0067	1.89E-8	0.0012	0.015
	CI	0.0032	−0.031	0.0017	9.48E-8	0.0070	−0.015
Left frontal lobe thickness (mm)	Pooled	−0.0035*	0.021	0.0016	1.33E-8	–	0.013
	CU	−0.0038*	0.039	0.0017	−3.04E-8	0.00087	0.032
	CI	−0.0024	−0.021	0.00046	2.75E-8	−0.0047	−0.012
Left frontal pole thickness (mm)	Pooled	−0.0023	0.068	−0.000063	2.58E-8	–	0.041
	CU	−0.0023	0.098	−0.0041	−4.96E-9	−0.000097	0.070
	CI	−0.0034	0.035	0.0050	6.52E-8	−0.0054	−0.045
Right frontal pole thickness (mm)	Pooled	0.0022	0.070	−0.0058	9.92E-8	–	0.010
	CU	0.0023	0.14*	−0.0045	−6.52E-8	−0.0051	0.029
	CI	0.0000038	−0.015	−0.0033	2.50E-7	−0.010	−0.018
Bilateral medial orbitofrontal cortex thickness (mm)	Pooled	0.0011	−0.023	−0.0066	1.28E-7	–	0.025
	CU	0.00035	−0.028	−0.0066	8.53E-8	−0.00078	0.043
	CI	0.0033	0.00066	−0.013	1.63E-7	−0.0076	−0.033
Left medial orbitofrontal cortex thickness (mm)	Pooled	−0.00048	−0.033	−0.0058	8.85E-8	–	0.033
	CU	−0.0012	−0.042	−0.0053	2.58E-8	−0.0027	0.060
	CI	0.0020	−0.012	−0.011	1.08E-7	−0.0054	−0.024
Right medial orbitofrontal cortex thickness (mm)	Pooled	0.0027	−0.012	−0.0073	1.67E-7	–	0.017
	CU	0.0019	−0.012	−0.0075	1.47E-7	0.0013	0.027
	CI	0.0047	0.0094	−0.015	2.12E-7	−0.010	−0.042
Bilateral lateral orbitofrontal cortex thickness (mm)	Pooled	−0.0012	−0.0054	−0.0030	3.28E-8	–	0.017
	CU	−0.0016	0.0082	0.00047	3.63E-8	0.00024	0.024
	CI	0.00012	−0.013	−0.016	−1.44E-8	−0.0091	−0.035

(Continues)

TABLE 5 (Continued)

Regions of interest	Sample	Age	Sex	Education	ICV	MoCA	*APOE ε4 carrier status*
Bilateral caudal anterior cingulate thickness (mm)	Pooled	0.0043	0.062	−0.0041	2.14E-7	–	−0.0066
	CU	0.0028	0.035	−0.011	1.73E-7	0.0018	0.0087
	CI	0.0087	0.15	0.015	2.29E-7	0.00051	−0.022
Left caudal anterior cingulate thickness (mm)	Pooled	0.0038	0.076	−0.0030	3.35E-7	–	−0.018
	CU	0.0039	0.033	−0.0041	2.24E-7	0.0047	−0.0031
	CI	0.0048	0.18	−0.000091	4.71E-7	0.00051	−0.033
Right caudal anterior cingulate thickness (mm)	Pooled	0.0046	0.050	−0.0064	1.51E-7	–	0.013
	CU	0.0017	0.034	−0.017	2.20E-7	−0.000043	0.017
	CI	0.011	0.15	0.024	1.65E-8	0.000029	−0.00023
Left putamen volume (mm^3)	Pooled	−20.08*	−164.34	23.05	0.00014	–	57.96
	CU	−15.40*	−317.21*	20.13	0.00023	11.42	15.28
	CI	−24.95*	−5.94	24.31	0.000065	−2.15	203.51
Right putamen volume (mm^3)	Pooled	−25.86*	−166.32	17.41	0.00031	–	40.03
	CU	−21.58*	−346.62*	7.15	0.00037	11.56	2.48
	CI	−29.30*	27.66	31.29	0.00029	2.90	211.04
Left thalamus volume (mm^3)	Pooled	−35.86*	−437.73*	59.47*	−0.000065	–	−15.09
	CU	−32.58*	−486.71*	62.29*	−0.00029	1.01	−62.83
	CI	−35.04	−514.77	77.13	0.000073	−32.10	171.67
Right thalamus volume (mm^3)	Pooled	−31.07*	−422.96*	69.87*	0.000086	–	44.63
	CU	−29.07*	−519.75*	63.71*	−0.000026	4.00	−3.04
	CI	−29.21	−366.62	90.74	0.000071	−9.26	173.80
Left pallidum volume (mm^3)	Pooled	−1.89	−75.14	8.15	−0.000016	–	54.77
	CU	0.66	−113.21*	8.77	−0.000038	7.16	29.55
	CI	−6.49	−7.20	12.99	0.00010	−2.29	121.82
Right pallidum volume (mm^3)	Pooled	−2.25	−98.87	2.84	0.000021	–	14.95
	CU	1.32	−139.56*	6.62	−0.000021	7.60	18.46
	CI	−8.70	−47.26	−1.24	0.00016	−11.67	63.74
Left amygdala volume (mm^3)	Pooled	−18.15*	−41.02	5.07	0.00021	–	−38.69
	CU	−15.27*	−103.11	5.23	0.000076	3.21	9.98
	CI	−22.31*	−22.94	−2.95	0.00022	−9.95	87.10
Right amygdala volume (mm^3)	Pooled	−14.16*	−101.86	−0.65	0.00021	–	−23.81
	CU	−10.56*	−178.01*	−8.14	−0.000032	2.44	53.39
	CI	−20.46	−89.16	10.42	0.00035	−7.26	−149.38

Abbreviations: *APOE ε4*, apolipoprotein E ε4; CI, cognitively impaired; CU, cognitively unimpaired; FDR, false discovery rate; ICV, intracranial volume; MoCA, Montreal Cognitive Assessment.

Social bridging was found to be associated with greater GMD primarily in frontal and temporal cortices and limbic system structures of the left hemisphere, such as the amygdala, thalamus, putamen, and insula. Previous studies have related the amygdala volume to modulation of an individual's level of trust in others and ability to infer emotions in others.[39–43] Therefore, preserved volume of the amygdala could provide significant advantage in decoding the complex social information conveyed by the novelty of social connections in bridging.

The significant association between the thalamus and social bridging can also be explained by the thalamic role in relaying sensory information to other parts of the cortex controlling processes of attention, speed of information processing, and working and episodic memory.[44] Thus, the preserved thalamic volume in individuals with greater levels of social bridging capital would allow them to process novel social information more efficiently. Furthermore, the left putamen plays a fundamental role in language comprehension and semantic retrieval.[45] Additionally, the relationship between social bridging and

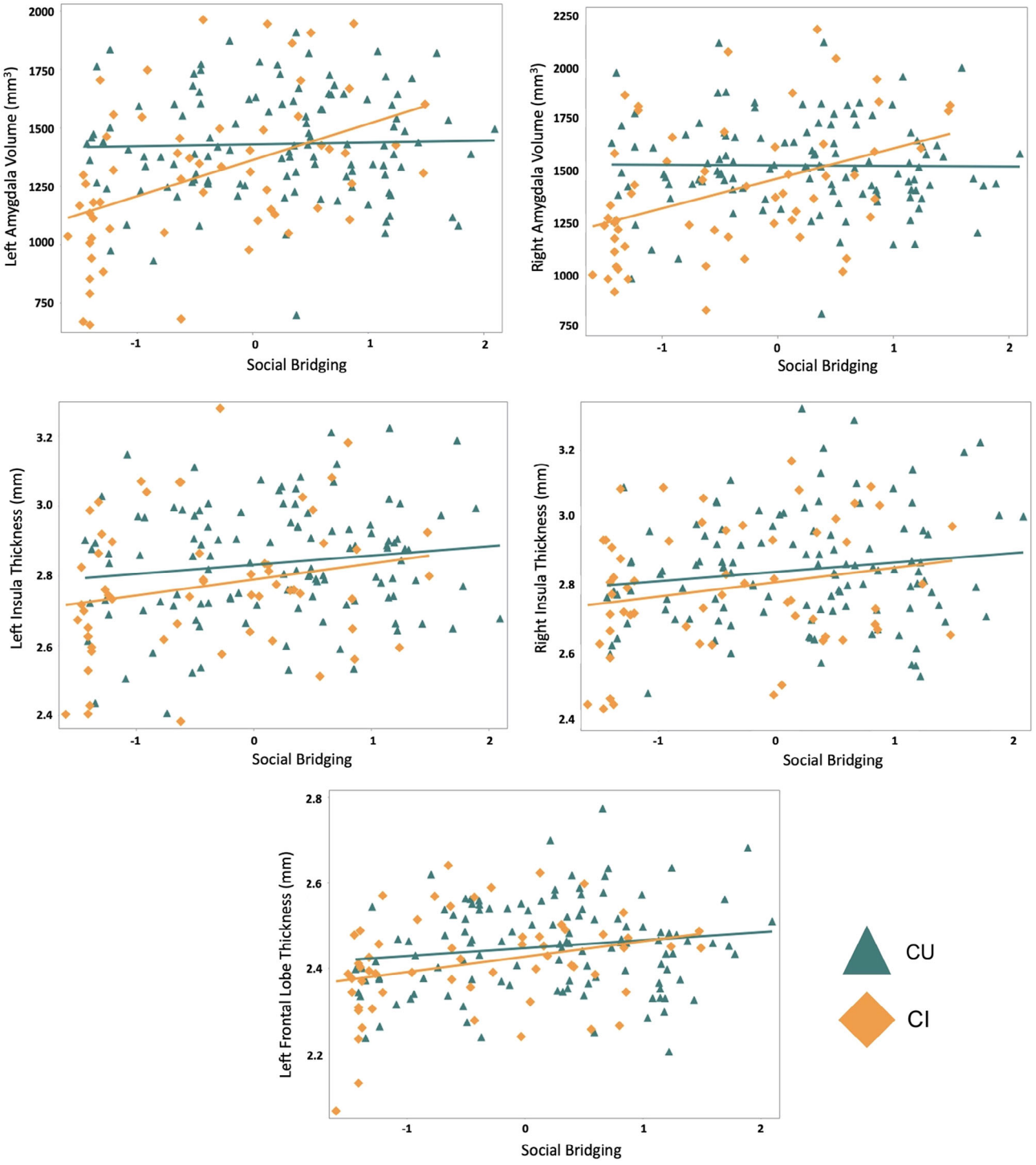

FIGURE 1 Scatterplots displaying significant associations between social bridging and MRI ROIs separated by diagnosis. CI, cognitively impaired; CU, cognitively unimpaired; MRI, magnetic resonance imaging; ROI, region of interest.

insula thickness can be attributed to the insula's role in empathy and intuiting another's emotional state.[46–48] Thus, greater insular thickness would afford individuals the ability to better maintain these novel social connections through a better understanding of others' feelings.

Alongside these limbic system-related subcortical structures, a significant relationship was found between social bridging capital and left frontal lobe thickness. Given the frontal lobe's function in higher-order planning and executive function,[49] it is plausible that maintenance of the numerous, diverse social connections characteristic of a high social bridging capital requires greater GMD in the frontal lobe to effectively manage these relationships.

Social bonding, measured primarily through quality of relationships, is associated with greater GMD in the frontal lobe, medial orbitofrontal

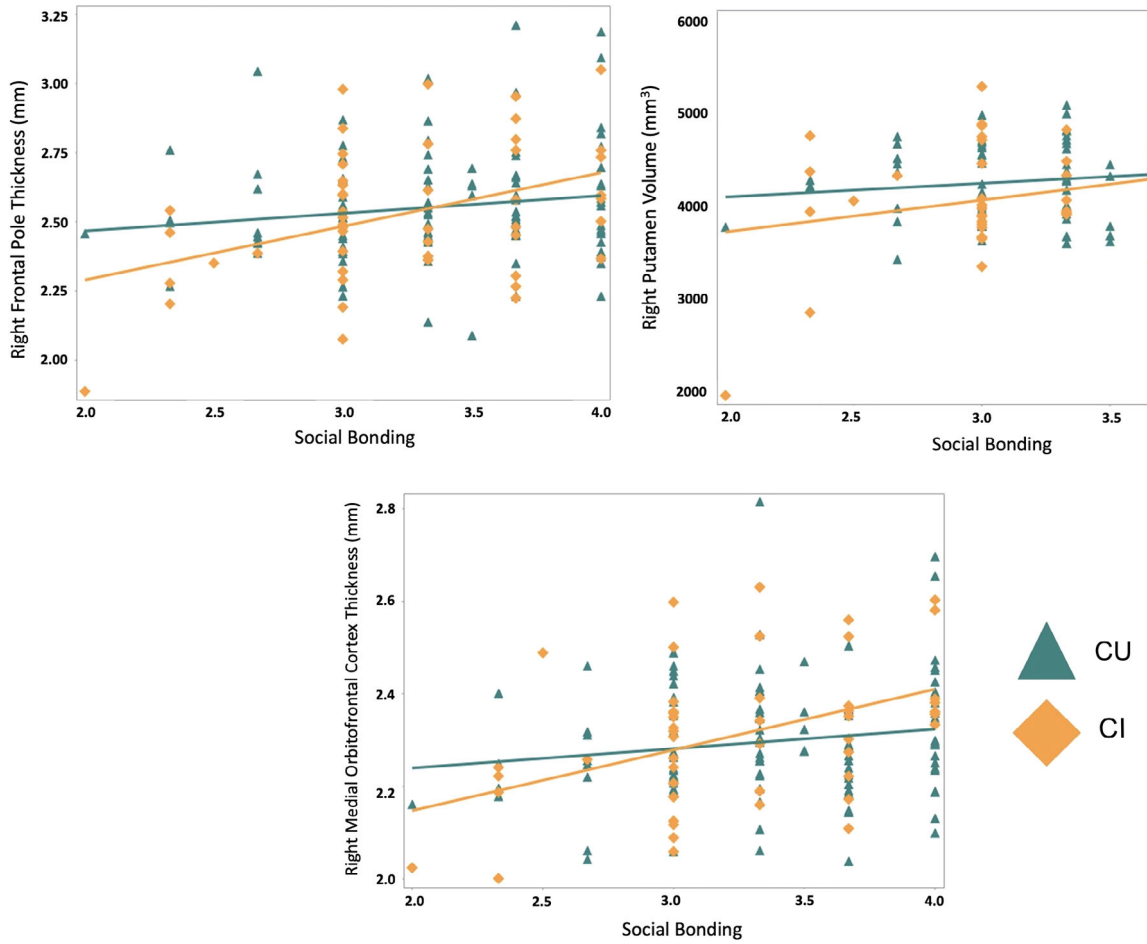

FIGURE 2 Scatterplots displaying significant associations between social bonding and MRI ROIs separated by diagnosis. CI, cognitively impaired; CU, cognitively unimpaired; MRI, magnetic resonance imaging; ROI, region of interest.

and caudal anterior cingulate cortices, as well as greater putamen and amygdala volumes with a right hemispheric bias. These results are corroborated by previous studies that indicate that these regions, particularly the amygdala and anterior cingulate cortex, play a role in assessing threats to social connection.[50,51] As social bonding is typically characterized by connections with kin and close friends, it would be reasonable to posit that increased social bonding would be associated with preservation of these regions.

A positive association between putamen volume and social bonding would be expected as the demands of the language processing and semantic retrieval functions of the putamen would increase proportionally to the number of connections to close confidants. Furthermore, the significant association between the medial orbitofrontal cortex and social bonding is likely due to the orbitofrontal cortex's role in emotional processing.[52,53] Maintaining the close relationships that characterize social bonding can be both stress-inducing and stress-relieving. Thus, having greater GMD in the medial orbitofrontal cortex can provide increased emotional processing functionality useful in navigating these relationships.

Last, the significant associations between frontal lobe and frontal pole thickness and social bonding capital can be explained through these regions' function in social judgement.[54,55] Many of the connections that compose social bonding capital require one to judge the feelings of others to maintain a high-quality relationship. Therefore, individuals experiencing a high social demand to maintain a close relationship are also likely to have greater GMD in the frontal lobe and frontal pole.

An important consideration to note is that these associations may simply be a parallel expression of anatomical and behavioral traits. Cognitive impairment, the criteria we use to separate CI and CU participants, is representative of anatomical change. Social network characteristics are also reflected in these groups as individuals with cognitive impairment are likely concurrently experiencing social isolation. This correlation should moderate expectations of therapeutic breakthrough.

4.1 | Study limitations and future directions

Although these results indicate associations between social network characteristics and brain structure, it is difficult to distinguish whether social enrichment results in neurostructural changes or neurostructural changes drive the formation and maintenance of particular types of social connections given a cross-sectional study design. Future

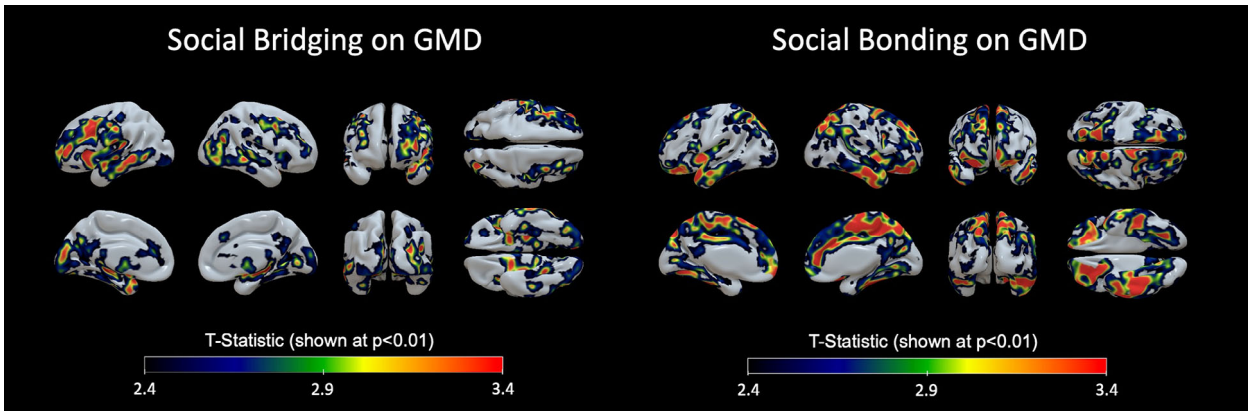

FIGURE 3 Voxel-wise multiple linear regression statistical maps across the pooled sample (CU and CI) demonstrating positive associations between social bridging and bonding and regions of increased GMD while controlling for age, sex, education, and intracranial volume. Cluster corrected images shown rendered in Surf Ice at a FWE correction of $p < 0.05$. CI, cognitively impaired; CU, cognitively unimpaired; FWE, family-wise error; GMD, gray matter density.

work should consider conducting longitudinal social network and neuroimaging analysis to elucidate the directionality of this relationship. Another limitation of this analysis is the lack of racial and ethnic diversity in the selected cohort, limiting the generalizability of these findings to the population at large. However, the SNAD study is taking steps to increase the enrollment of individuals from historically marginalized groups. Furthermore, investigations into alternative neuroimaging biomarkers, such as amyloid and tau deposition, could yield greater insights into the relationship between social connectedness and specific diseases such as AD. Additionally, examining the strength of this relationship depending on one's demographic risk factors, such as sex, race, social determinants of health, and so on, could help identify which patients may receive the greatest benefit from these social interventions. Furthermore, in the current study we combined CN and SCD (CU), and MCI and AD (CI) groups to increase statistical power in our regression and neuroimaging analysis; however, we understand that this limits the interpretation of our results to more specific diagnostic groups. Our findings will benefit from replication in a separate cohort when such data become available. The study is continuously enrolling. Further, it would be beneficial to perform a longitudinal analysis of the effects of bridging and bonding on disease progression in MCI and AD, and conversion to MCI or dementia among CN and SCD. This could help us elucidate the directionality of or causality in the relationship between bridging, bonding, and dementia.

5 | CONCLUSIONS

Some hypotheses for the observed increases in volume and GMD of regions associated with bridging or bonding include:

1. The types of connections defined as social bridging potentially buffer against age-related cognitive impairment and neurodegeneration by protecting regions integral to sensory processing.
2. The types of connections defined as social bonding may combat cognitive impairment by enhancing stress-reduction pathways, mitigating the harmful effects of stress on cognition.

Future studies analyzing longitudinal changes in brain structure and cognition are needed to elucidate the effects of social bridging and bonding. In particular, randomized controlled social intervention studies may be a promising avenue to discover the directionality of this relationship.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENT

All authors have read and provided consent to be associated with this manuscript.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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