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Distinct neural correlates of emotional and cognitive empathy in older adults

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ABSTRACT

Empathy is thought to be a mechanism underlying prosocial behavior across the lifespan, yet little is known about how levels of empathy relate to individual differences in brain functioning among older adults. In this exploratory study, we examined the neural correlates of affective and cognitive empathy in older adults. Thirty older adults ($M=79$ years) underwent fMRI scanning and neuropsychological testing and completed a test of affective and cognitive empathy. Brain response during processing of cognitive and emotional stimuli was measured by fMRI in *a priori* and task-related regions and was correlated with levels of empathy. Older adults with higher levels of affective empathy showed more deactivation in the amygdala and insula during a working memory task, whereas those with higher cognitive empathy showed greater insula activation during a response inhibition task. Our preliminary findings suggest that brain systems linked to emotional and social processing respond differently among older adults with more or less affective and cognitive empathy. That these relationships can be seen both during affective and non-emotional tasks of "cold" cognitive abilities suggests that empathy may impact social behavior through both emotional and cognitive mechanisms.

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1. Introduction

A strong relationship between social connectedness, quality of life, and health in older adults has been demonstrated (Danner et al., 2001; Doyle et al., 2006; Holt-Lunstad et al., 2010; Waugh and Fredrickson, 2006), and there is a growing scientific and public health interest in understanding factors that can moderate the relationship between physical and emotional health and subjective quality of life among older adults. The availability of social support for older adults depends on life circumstances and environment, but may also be facilitated by personality traits and attitudes that promote closer ties with other people. Empathy is a trait that may play a role in good health and well-being in late-life. Empathy implies a shared interpersonal experience and can be defined as the process of understanding the emotional state of, and feeling with, another person, while also understanding that the origin of the emotional state is the other and not oneself (Sprecher and Fehr, 2005). Indeed, among older adults a relationship between higher empathy and lower self-reported loneliness has been observed (Beadle et al., 2012). However, the neural underpinnings of empathy in late-life are not well understood, and an understanding of these neural mechanisms can help advance our understanding of typical aging processes and prosocial behavior in late life. Such studies can also provide insight into neurodegenerative conditions associated with socioemotional deficits, such as frontotemporal dementia (Gleichgerrcht et al., 2011; Lough et al., 2006), or late-life mental illnesses such as geriatric depression.

Empathy is a multidimensional construct composed of two components: 1) cognitive empathy and 2) affective empathy. Cognitive empathy is defined as the ability to explain, predict, and interpret another's emotions accurately (Decety et al., 2012). Cognitive empathy has considerable overlap with theory of mind (i.e., the ability to infer other people's mental states); age-related changes in theory of mind have been found to be mediated by

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age-related executive dysfunction (Duval et al., 2011; Pardini and Nichelli, 2009). Additionally, cognitive empathy is sometimes referred to in the literature as perspective taking (O'Brien et al., 2013). For the purposes of this study, we did not disentangle the differences between cognitive empathy, theory of mind, and perspective taking, although our measurement of cognitive empathy focused on understanding emotions rather than other types of mental states (e.g., lying). Affective empathy, also sometimes referred to as empathic concern (O'Brien et al., 2013), is the capacity to share another's emotions (i.e., feeling with) and a mechanism by which to monitor the distinction between one's own and another's feelings (Eisenberg and Fabes, 1990). Cognitive and affective empathy are thought to have overlapping but non-identical neural bases (Fan et al., 2011). The amygdala and insula, in particular, are limbic regions which have been associated with the perception of emotions in others (Banks et al., 2007; Wager et al., 2008). In a meta-analytic study, the left anterior insula was active in both cognitive and affective empathy (Fan et al., 2011). In a recent study of patients with behavioral variant frontotemporal dementia, gray-matter reduction in the insula and the amygdala were associated with impairment in affective empathy (Cerami et al., 2014). Additionally, lesions in the insula and the amygdala (along with networked frontal and temporal structures) have been found to be associated with acute impairment in affective empathy (Leigh et al., 2013).

Functional neuroimaging studies of young adults have supported a "shared representations" theory of empathy, which proposes that sharing of emotions of others activates similar neural structures to those involved in the direct experience of the same emotions (Singer and Lamm, 2009). It has also been shown that differences between young adults in levels of self-reported empathy correlate with the degree of neural engagement in empathy-related frontal lobe brain systems (Chakrabarti and Baron-Cohen, 2006).

Current research on empathy in older adults indicates that cognitive empathy may decline with increasing age (Ruffman et al., 2008). Among older adults, reduced cognitive empathy has been found to be related to reduced inhibitory control (Bailey and Henry, 2008). A component of empathy is the ability to inhibit the natural human tendency to be self-focused to instead attend to the needs and emotions of another, which may help explain the aforementioned relationship between cognitive empathy and inhibitory control. Furthermore, there is evidence that processing of emotional stimuli either facilitate or hinder working memory processing (Luo et al., in press). In the aging literature, the cognitive processes of executive control, including inhibitory control and perspective taking, are known to steadily decline in late life (Li et al., 2001). In order to be empathic, one presumably needs to be able to keep two perspectives in mind, yet it remains unknown whether there is a relationship between these "cold" cognitive brain systems and individual variance in levels of cognitive or affective empathy.

In contrast to research indicating declines in cognitive empathy with age, affective empathy appears more stable or may even increase with age (Ruffman et al., 2008; Sze et al., 2012), but see (Chen et al., 2014). In terms of brain functioning in older adults, we know that despite older adults showing large variability in cognitive abilities and brain function (Eyler et al., 2011), they have relatively preserved or even enhanced emotional responding. The well-maintained emotional responding among older adults has been referred to as "the emotion paradox in the aging brain" (Mather, 2012). This "emotion paradox" is based on research demonstrating that, despite cognitive and physical declines, older adults have less reactivity to negative situations/stimuli (e.g., Mather et al., 2004) and ignore irrelevant negative stimuli better than younger adults (e.g., Thomas and Hasher, 2006), as well as have a positivity bias for remembering positive information better than negative information. Thus, given that emotional responding becomes more salient in older age even while cognitive processes decrease (Carstensen et al., 2003; Ruffman et al., 2008), is it likely that affective and cognitive empathy may be differentially affected by aging and that the neural correlates of these may differ. Therefore, it is important for neuroscience research on empathy in older adults to examine both emotional responding brain systems and those implicated in cognitive regulation strategies.

Therefore, the purpose of our study was to investigate the neural correlates of both cognitive and affective empathy among older adults. We chose functional magnetic resonance imaging (fMRI) tasks known to engage neural systems of interest based on the existing empathy and aging literature. See Table 1 for relationships between the chosen fMRI tasks and their putative involvement in empathy. We examined associations within *a priori* regions of interest, specifically the insula and amygdala, and also explored other possible associations with appropriate controls for multiple testing. Despite the exploratory nature of this study, we were interested in addressing the following questions: 1) Is affective empathy more related to brain response in emotional systems in older adults? and 2) Is cognitive empathy more related to response in systems important for information processing in older adults?

2. Methods

2.1. Subjects

Thirty older adults (mean age = 79 years, S.D. = 10) enrolled in the Successful AGing Evaluation (SAGE) study were concurrently enrolled in this study. The SAGE study, previously described elsewhere (Jeste et al., 2013), used a multicohort longitudinal design to enroll adults aged 20–99, with an overrepresentation of adults in their 80s and 90s. SAGE participation included completion of a comprehensive survey on areas related to successful aging, including physical and health status, positive psychological traits, and psychosocial and cognitive functioning. Recruitment for the present study was based on self-reported compassion/empathy

Table 1
fMRI Tasks and their putative involvement with empathy.

Task	Information processing domain	Known brain areas of activation	Empathy component	References
Go/No-go	•Selection of appropriate behavior •Inhibit proponent self-focus	•Presupplementary motor area	Cognitive	•(Bailey and Henry, 2008) •(Simmonds et al., 2008) •(Ze et al., 2014)
Facial Affect Matching	•Emotion processing: subjective feeling state and processing the experiences of others	•Amygdala •Insula •Anterior cingulate cortex	Affective	•(Hariri et al., 2000) •(Fan et al., 2011)
n-Back	•Information processing •Executive control •Perspective taking	•Frontoparietal networks •Dorsolateral prefrontal cortices •Superior parietal lobules including precuneus •Frontoinsular network	Cognitive	•(Li et al., 2001) •(Luo et al., 2014) •(Chen et al., 2014)

scores on the Santa Clara Brief Compassion Scale, described below (SCBCS; Hwang et al., 2008). To ensure a diverse group of participants in regard to compassion/empathy scores, we over-recruited participants from the top decile (90% and above) and bottom decile (10% and below) of SCBCS scores. Participants were screened on the phone prior to enrollment to ensure they were eligible based on the following criteria: right-handed, no history of neurological (e.g., stroke), psychiatric, or substance use disorders, and did not have MRI contraindications (e.g., pacemaker or other implanted metallic devices, claustrophobia, or metallic dental implants). Participation involved 1) additional assessments of empathy, 2) a neuropsychological assessment, and 3) an fMRI exam while performing emotional and cognitive tasks. These assessments were completed over 2 days, with the additional assessments and fMRI completed in visit 1 and the neuropsychological assessment completed in visit 2. The study was approved by the Internal Review Board at the University of California at San Diego and the UCSD Human Research Protections Program. Participant informed consent and data collection was acquired according to the guidelines established by the Helsinki Declaration.

2.2. Empathy and compassion

2.2.1. Santa Clara Brief Compassion Scale (SCBCS; Hwang et al., 2008)

A 5-item self-report measure of compassion/empathy was used to recruit participants for this study. Example items include: "When I hear about someone (a stranger) going through a difficult time, I feel a great deal of compassion for him or her" and "One of the activities that provides me with the most meaning to my life is helping others in the world when they need help". Items are scored on a 7-point Likert scale, with higher scores indicating greater compassion/empathy. Scores are averaged to create a total score ranging from 1 to 7.

2.2.2. Multifaceted Empathy Test (MET; Dziobek et al., 2008)

The MET is an objective measure used to assess multidimensional empathic processes, including cognitive and affective empathy. This assessment was administered immediately upon completion of the fMRI session. During this computerized task, participants view a series of photographs of people in an emotionally laden context (see Supplementary Fig. 1). To assess cognitive empathy, participants are provided with four emotions (e.g., fearful, annoyed, indecisive, sad) and asked to select which emotion depicts the mental state of the individuals in a photograph. Immediate feedback (i.e., answer correct or incorrect) is provided. To assess affective empathy, participants are then asked to rate their emotional reactions ("How calm/aroused does this picture make you feel?" and "How concerned are you for this person?") in response to the pictures on a scale from 1=calm/no concern to 9=highly aroused/highly concerned. Pictures include scenes with and without people. Separate total scores for mental state recognition, empathic concern, and arousal are calculated. Internal consistency of the MET's subscales was assessed by calculation of Cronbach's alpha, which revealed good to highly satisfactory values. Alpha was 0.71 for the cognitive empathy scale, 0.91 for the empathic concern scale, and 0.92 for the arousal scale (Dziobek et al., 2008). For this study, we created a composite variable of affective empathy by averaging the *z*-scores of the MET empathic concern and arousal total scores. These two variables are highly related to each other and arousal is believed to be a proxy for empathic concern.

2.3. Neuropsychological assessment

Participants completed a neuropsychological test battery that included tests from the Wide-Range Achievement Test (WRAT; Wilkinson, 1993) to assess for premorbid IQ and the Montreal Cognitive Assessment (MOCA; Nasreddine et al., 2005) to assess for current cognitive status. Other cognitive domains tested included: 1) Attention: Continuous Performance Test 4-digit correct and d-prime (Cornblatt et al., 1988); 2) Memory: California Verbal Learning Test encoding, recall, and recognition scores (Delis et al., 1987); 3) Working Memory: Letter Number Sequencing subtest from the Wechsler Adult Intelligence Test – Third Edition (WAIS-III; Wechsler, 1997); 4) Language: FAS and animal fluency (Delis et al., 2001); 5) Executive Functioning: Trails B (Reitan, 1958) and Stroop Interference (Golden and Freshwater, 2002); 6) Motor Speed: Grooved Pegboard dominant and non-dominant hand performance (Heaton et al., 2004); and 7) Processing Speed: Trails A (Reitan, 1958) and Digit Symbol subtest from the WAIS-III (Wechsler, 1997). Composite scores of each domain were created by converting *t*-scores to *Z*-scores and averaging the *Z*-scores per domain. Additionally, an overall neurocognitive composite score was created which was an average of the seven individual domain composite scores. Composite scores were only created for participants with complete neuropsychological data.

2.4. fMRI tasks

Three functional MRI (fMRI) experimental tasks that have previously been shown to engage cognitive and emotional processes in older adults were administered: an affective facial matching task, Go/No-Go task, and *n*-Back working memory task. The reliability of the facial affect matching task depends on the contrast used, but ranges from ICCs= −0.12 to 0.63 (Sauder et al., 2013). Reliability estimates do not exist for the particular versions of the other tasks used, but are presumed to be moderate based on general reliability values seen for cognitive neuroimaging challenges (Plichta et al., 2012). Prior to scanning, participants were trained to perform the tasks and completed practice runs. All stimuli were generated on a computer and back-projected onto a screen which the participants were able to view through a mirror placed above their eyes. To minimize motion, participants were instructed to remain still and not move their heads.

2.4.1. Facial affect matching task

During a modification of Hariri's block design affective facial matching task (Hariri et al., 2000), participants viewed a target human face that depicted an emotion (e.g. happy, angry or fearful) and were asked to pick one of two additional faces that matched the target in affect. A sensorimotor control condition also directed participants to match one of two geometric forms of different dimensions (oval or circle) to a target form. The task consisted of a total of 6 blocks: three blocks consisted of facial emotion matching and three blocks consisted of geometric matching. Each image was presented for 5 s, and total block length was 30 s. Total scan time was 8 min and 33 s. A fixation cross appeared between blocks. All participants completed one run of this task, and accuracy and response times were calculated.

2.4.2. Go/No-go task

The Go/No-go task, a test of response inhibition, involves a response selection stimulus (Go) and a response inhibition stimulus (No-go) (Owen et al., 2005). Participants were asked to press a button, as rapidly as possible, when presented with a Go stimulus (X's and Y's alternatively presented on the screen) and not respond when presented with a No-go stimulus (X or Y repeated). The task was weighted towards Go stimuli in order to build up a prepotency to respond, which increases the inhibitory effort necessary to successfully withhold responding to the No-go stimulus. Prior to completing the task in the scanner, participants completed a trial run of the Go/No-go task with stimulus display time frequencies ranging from 200 ms to 900 ms. The display time for which participants performed with approximately 50% accuracy was used while scanning to maximum brain activation during this task. Total scan time was 8 min and 8 s. One run of this task was completed, and Go hits, Go misses, No-go hits, and No-go misses were calculated.

2.4.3. n-Back working memory task

Working memory was assessed with the *n*-Back task consisting of 0-Back, 1-Back, and 2-Back blocks (Braver et al., 1997; Cohen et al., 1997). During each block, a series of 11 individual consonants (3 targets) were presented in a random order for 500 ms each, followed by an asterisk for 1000 ms. In the 0-Back condition, participants were instructed to respond with a button press every time they saw the pre-specified target letter (X). In the 1-Back condition, the target for response was any letter that was identical to the one presented one stimuli before (e.g., B–Y–Y, target is second Y), and in the 2-Back condition the target was any letter identical to the one presented two stimuli before (e.g., C–S–P–S, target is second S). Each participant completed six 0-back blocks, five 1-back blocks, and five 2-back blocks that alternated in a pre-determined sequence throughout the run. Mean accuracy was calculated for each condition.

2.5. Image acquisition

Data were acquired with magnetic resonance imaging (MRI) on a research-dedicated 3 T General Electric Excite MRI scanner with an 8-channel head coil. High-resolution structural T1-weighted MRI images were acquired using a magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence. This image was used for localization of functional signal. We measured blood oxygenation-level dependent (BOLD) signal using fMRI during the three tasks. Functional images were acquired using gradient echo echoplanar imaging (Facial Affect Matching Task: time repetition (TR)=2000 ms, time echo (TE)=30 ms, 3-mm slice thickness, 1.4-mm gap between slices, field of view (FOV)=25.6 cm, bandwidth=250, 290 repetitions; Go/No-go Task: TR=2000 ms, TE=32 ms, 4-mm slice thickness/no gap, FOV=25.6 cm, bandwidth=125, 195 repetitions; *n*-Back Task: TR=2500 ms, TE=32 ms, 4-mm slice thickness/no gap, FOV=25.6 cm, bandwidth=125, 195 repetitions). 2d flash field maps were collected to correct for distortion of the EPI images due to inhomogeneities in the static magnetic field.

2.6. Data processing and analysis

2.6.1. Neuroimaging processing and analysis

fMRI data processing for all three tasks was implemented with the AFNI (Analysis of Functional NeuroImages) software package from the National Institutes of Health (Cox, 1996). fMRI data were analyzed and overlaid onto structural T1-weighted images. The first two images of each session were discarded to account for signal stabilization. Field map and slice timing corrections were applied to the EPI images, and individual functional-to-anatomical alignment was conducted to the center image of the functional time series. Following automated motion correction, visual inspection was used to examine uncorrected motion outliers, and time points with excessive motion were rejected. Data were excluded if more than one third of total time points were deleted due to excessive motion. The following data were excluded due to excessive

motion: three participants for Facial Affect Matching Task, two participants for the Go/No-go Task, and three participants for the *n*-Back Task. Additionally, some participants did not complete the entire scan protocol due to time constraints, resulting in the following number of participants with usable data per task: Facial Affect Matching Task, $N=27$; Go/No-go Task, $N=28$; *n*-Back Task, $N=15$. A spatial blur to 6 mm full-width at half-maximum was applied and the functional data were transformed into a standardized coordinate system corresponding to Talairach space (Talairach and Tournoux, 1988) and resampled at 4 mm^3 resolution. Associations between BOLD signal and task parameters in all three tasks were calculated with multiple regressions using AFNI 3Ddeconvolve program. The model accounted for linear and quadratic trends, as well as degree of motion in three angles of rotation.

2.6.1.1. Functional tasks. For the facial affect matching task, contrasts comparing combined angry and fearful faces versus shape conditions were examined to identify brain regions associated with fear and anger while controlling for other cognitive processes such as visual attention and motor response. Anger and fear were chosen due to known differences in emotional processing of negative emotions among older adults (Mather, 2012), which may have implications for empathic/compassionate responding. For the Go/No-go task, contrasts comparing Go versus No-go hits were examined to determine brain regions associated with sustained attention and response inhibition, while for the *n*-Back task contrasts comparing 2-back versus 1-back conditions were designed to determine changes in brain activation in response to increasing task demand.

For all three functional tasks, voxel-wise whole brain response was evaluated using *t*-tests with the contrast coefficient as the dependent variable. Functional regions of interest (ROIs) were identified as clusters of group response to contrasts that were significant at a whole-brain $p<0.05$ based on a Monte Carlo simulation (clusters of 32 contiguous voxels with each voxel significant at $p<0.01$). We assumed the same smoothness in the Monte Carlo simulation that was applied to the functional data (6 mm full-width at half-maximum). In addition, bilateral amygdala and insula ROIs were applied to data from each task given the known involvement of these regions in emotion processing and empathy. These ROIs were defined in standard space using AFNI's Talairach Atlas daemon (Fig. 1). In each functional and anatomical ROI, the mean fit coefficient for the contrast of interest was calculated for each individual.

2.6.2. Statistical analysis

Distributions of the brain and behavioral variables were examined and Pearson correlations were calculated to examine associations between affective empathy, cognitive empathy, cognitive performance, and brain activation in response to all three fMRI tasks. Correlations of $p<0.05$ were considered significant for *a priori* regions of interest. For areas not selected *a priori*, we applied a Bonferroni-adjusted critical value of $p<0.01$ to control for multiple comparisons within cognitive and affective empathy (Facial Affect Matching Task: 0.05/6=0.01; Go/No-go: 0.05/5=0.01; *n*-Back: 0.05/4=0.01).

3. Results

3.1. Demographics, empathy, and neurocognitive characteristics

Demographics and participant characteristics are presented in Table 2. On average, participants were in their eighth decade of life (mean age=79), average to high average intelligence (mean WRAT IQ=107), and married. Slightly greater than half were male and Caucasian. Affective empathy was not related to cognitive empathy ($r=-0.06$, $p=0.79$).

3.2. Neuropsychological performance and behavioral performance during emotional and cognitive tasks

The relationships between empathy measures and neuropsychological and behavioral performance during the cognitive and emotional fMRI tasks are presented in Table 3. Overall, there were no significant associations between empathy measures and either neuropsychological performance or behavioral performance during the fMRI tasks.

3.3. Task-related activation

3.3.1. Facial affect matching task

Voxel-wise whole brain *t*-tests revealed several regions that showed significant response (both increased and decreased activation) during processing of negative emotions relative to shapes (Fig. 2; Supplementary Table 1). These regions included structures in both limbic and paralimbic regions and included bilateral fusiform gyrus, bilateral middle frontal gyrus, midline precuneus, left inferior parietal lobule, left middle temporal gyrus, bilateral

Table 2
Demographic and participant characteristics ($N=30$).

Demographics			
	Range of scores	Mean or No.	S.D. or %
Age (years)	60–95	79.1	9.7
Education			
1–12 years or GED	–	1	3.4
13–15 years or vocational training	–	11	37.9
Bachelor's degree or above	–	17	58.6
Gender (% female)	–	12	41.4
Ethnicity (% Caucasian)	–	18	62.1
Marital status (% Married)	–	20	69.0
Empathy and compassion measures			
SCBCS	2.2–7.0	4.8	1.4
MET mental state recognition[a]	18–23	21	1.5
MET affective empathy composite[b]	−2.51–1.43	0.0	0.91
MET empathic concern	2.4–8.5	6.9	1.4
MET average arousal	1.7–7.5	5.1	1.3
Cognitive functioning			
WRAT IQ	88–134	107.4	10.8
MOCA	19–29	25	2.6
Neurocognitive composite[b]	−0.53–0.73	0.01	0.41
Attention composite[b]	−2.16–1.56	−0.00	0.96
Memory composite[b]	−2.47–1.55	−0.37	0.91
Working memory composite[b]	−1.15–1.22	0.09	0.61
Language composite[b]	−1.86–1.58	−0.36	0.78
Executive functioning composite[b]	−1.54–1.15	0.05	0.67
Motor speed composite[b]	−1.89–1.51	0.08	0.88
Processing speed composite[b]	−3.04–1.15	−0.05	0.82

Note: $^{*}p<0.05$; $^{**}p<0.01$. SCBCS=Santa Clara Brief Compassion Scale; MET=Multifaceted Empathy Test; WRAT=Wide-Range Achievement Test; MOCA=Montreal Cognitive Assessment.

[a] Cognitive empathy.
[b] *Z*-scores.

Table 3
Correlations between compassion and empathy measures, neurocognitive functioning, and behavioral performance on fMRI emotional processing and cognitive tasks.

	MET affective Empathy	MET cognitive Empathy
Neurocognitive data ($N=18$)		
Neurocognitive composite	−0.07	0.17
Attention composite	0.11	0.32
Memory composite	−0.29	0.10
Working memory composite	−0.15	−0.001
Language composite	0.13	0.19
Executive functioning composite	0.05	−0.03
Motor speed composite	0.15	−0.26
Processing speed composite	−0.33	0.25
Facial affect matching behavioral data ($N=27$)		
Shape accuracy	−0.09	−0.20
Angry accuracy	0.038	0.36
Fear accuracy	0.40	0.37
Go/No-go behavioral data ($N=28$)		
Go accuracy	0.18	0.20
No-go accuracy	−0.12	−0.02
***n*-Back behavioral data ($N=15$)**		
2-back minus 1-back hits	−0.33	−0.38

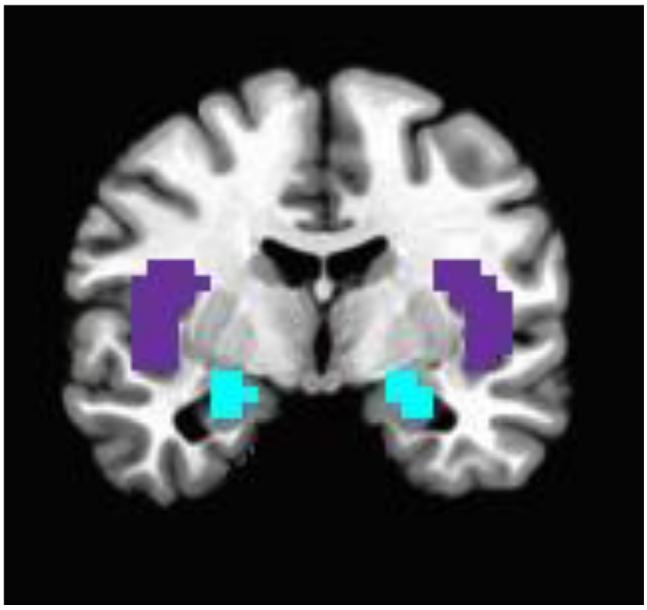

Fig. 1. Images demonstrating clusters of significant changes in BOLD activation during functional tasks. Regions of interest (ROIs) in green indicate regions of significant differential response (whole-brain $p < 0.05$) for angry and fearful faces versus shapes during the Facial Affect Matching task, ROIs in blue indicate regions of significant differential response for go versus no go trials during the Go/No-go Task, and ROIs in red demonstrate regions of significant differential response for 2-back versus 1-back during the *n*-Back Task. F1=left fusiform gyrus; F2=right frontal lobe; F3=left frontal lobe; F4=midline precuneus; F5=left middle temporal gyrus; F6=left inferior parietal gyrus. G1=left post-central gyrus; G2=left frontal lobe; G3=right frontal lobe; G4=right superior frontal gyrus; G5=right inferior parietal gyrus. N1=left inferior parietal gyrus; N2=right inferior parietal gyrus; N3=right frontal lobe; N4=left frontal lobe. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

ventral medial prefrontal, and bilateral dorsal medial prefrontal (all p's < 0.05). These areas of significant response are consistent with previous results using this task in healthy adults (for e.g., Paulus et al., 2012). Bilateral insula and bilateral amygdala response was also examined based on *a priori* hypotheses. Task-related mean response was significantly greater in the shape than in the face condition in the left insula only; there were no differences between the two conditions in the right insula or bilateral amygdala (R insula: $t(26) = -1.49$, $p = 0.15$; L insula: $t(26) = -2.21$, $p = 0.04$; R amygdala, $t(26) = -0.35$, $p = 0.73$; L amygdala, $t(26) = -1.49$, $p = 0.15$).

3.3.2. Go/No-go

Voxel-wise whole brain *t*-tests revealed several regions that were differentially active during Go versus No-go trials (Fig. 2; Supplementary Table 1). Left post-central gyrus was more active in Go compared to No-go trials. Many regions were more active in No-go than Go trials, including: bilateral superior frontal gyrus, right inferior frontal gyrus, right insula, midline superior frontal gyrus and right inferior parietal lobule. The insula and amygdala were included in analyses on an *a priori* basis. Task related mean response was significantly greater in the No-go condition in bilateral insula ROIs. There were no differences between the two conditions in the bilateral amygdala (R insula: $t(27) = -2.69$, $p = 0.01$; L insula: $t(27) = -2.53$, $p = 0.02$; R amygdala: $t(27) = -1.52$, $p = 0.14$; L amygdala: $t(27) = -1.06$, $p = 0.30$).

3.3.3. n-Back task

Voxel-wise whole brain single-sample *t*-tests revealed bilateral parietal and bilateral frontal regions as more active during the 2-back compared to 1-back condition in the *n*-Back task (Fig. 2; Supplementary Table 1). These regions included the left and right inferior parietal gyrus, and left and right frontal lobe. As with the Go/No-go task, the insula and amygdala were included in the analyses on an *a priori* basis. The group of older adults as a whole did not show significant task-related response in these ROIs; mean response was not significantly different from zero (R insula: $t(14) = -1.17$, $p = 0.26$; L insula: $t(14) = -0.56$, $p = 0.59$; R amygdala: $t(14) = 1.07$, $p = 0.30$; L amygdala: $t(14) = 0.67$, $p = 0.51$).

3.4. Relationship of response within a priori ROIs and active clusters to individual differences in empathy

3.4.1. Affective empathy

Results are presented in Table 4. Significant correlations between degree of activation during the *n*-Back task in our *a priori* ROIs and individual differences in affective empathy were observed. Higher affective empathy was related to greater deactivation of the bilateral amygdala (right amygdala: $r = -0.52$, $p = 0.05$; left amygdala: $r = -0.53$, $p = 0.04$), and of the right insula ($r = -0.54$, $p = 0.04$) during the *n*-Back task (Fig. 3). That is, individuals with higher affective empathy had greater response of the amygdala and right insula during the 1-back than the 2-back condition. No associations with response in task-related functional regions for any task remained significant after correction for multiple comparisons.

3.4.2. Cognitive empathy

Significant correlations between degree of activation during the Go/No-go task and individual differences in cognitive empathy were observed. Specifically, when comparing brain response

Table 4
Correlations between brain activation and affective and cognitive empathy.

	Affective empathy	Cognitive empathy
Facial affect matching task (*N*=27)		
A priori right amygdala	−0.21	0.20
A priori left amygdala	−0.26	0.39
A priori right insula	−0.12	0.21
A priori left insula	−0.18	0.24
F1. Left fusiform gyrus	0.24	0.39
F2. Right frontal lobe	0.14	0.36
F3. Left frontal lobe	−0.05	0.33
F4. Midline precuneus	0.05	0.43
F5. Left middle temporal gyrus	0.45	0.10
F6. Left inferior parietal gyrus	0.04	0.24
Go/No-Go Task (*N*=28)		
A priori right amygdala	−0.21	0.26
A priori left amygdala	−0.04	0.34
A priori right insula	−0.13	0.57**
A priori left insula	−0.14	0.47*
G1. Left post-central gyrus	0.16	−0.20
G2. Left frontal lobe	−0.02	0.06
G3. Right frontal lobe	−0.03	0.55**+
G4. Right superior frontal gyrus	0.13	0.36
G5. Right inferior parietal	−0.11	0.19
***n*N-Back task (*N*=15)**		
A priori right amygdala	−0.52*	0.01
A priori left amygdala	−0.53*	0.08
A priori right insula	−0.54*	−0.01
A priori left insula	−0.07	−0.27
N1. Left inferior parietal gyrus	−0.09	−0.18
N2. Right inferior parietal gyrus	0.14	−0.12
N3. Right frontal lobe	0.42	0.02
N4. Left frontal lobe	0.36	−0.06

* $p < 0.05$.
** $p < 0.001$.
\+ When outlier removed, $r = 0.42$, $p < 0.05$, no longer passes Bonferroni-corrected threshold.

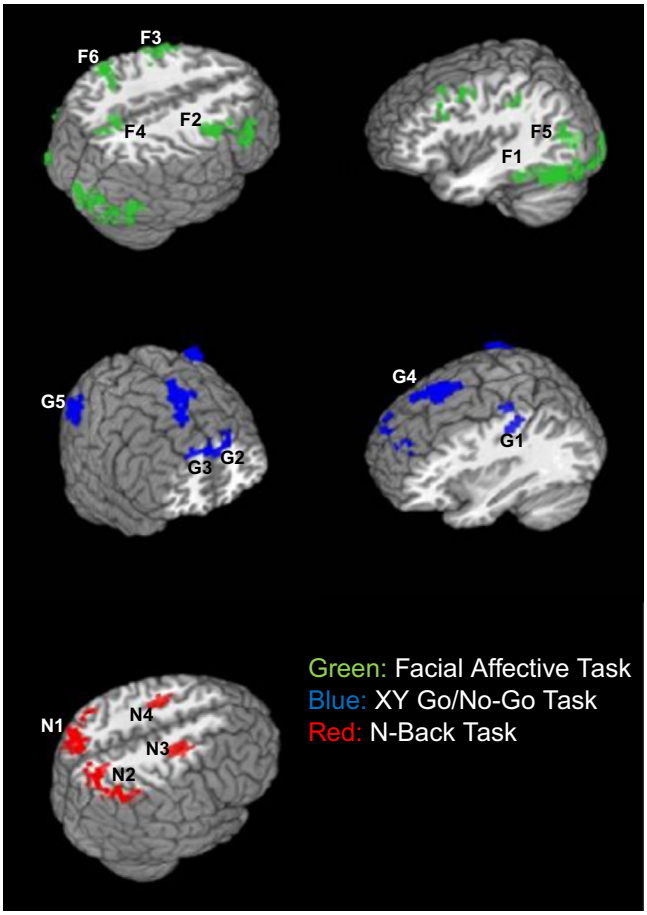

Fig. 2. Bilateral amygdala and insula *a priori* regions of interest. Image is presented in radiological convention (right=left). Bilateral amygdala (cyan) and insula (purple) a priori regions of interest defined in standard space using AFNI's Talairach Atlas daemon. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

during Go and No-go trials, higher cognitive empathy was related to greater No-go compared to Go response in the *a priori* bilateral insula region (right insula: $r=0.57$, $p<0.01$; left insula: $r=0.47$, $p=0.02$). There was also a relationship between cognitive empathy and greater No-go than Go response in the task-related right insula/inferior frontal gyrus region ($r=0.55$, $p<0.01$). However, after removing an outlier from this analysis, the correlation was weakened (to $r=0.42$, $p<0.05$), and therefore no longer survived Bonferroni correction for multiple comparisons. No other associations with response in task-related functional regions remained significant after correction for multiple comparisons.

4. Discussion

This study examined the neural substrates related to cognitive and affective empathy that are revealed during recognition of emotion in others, response inhibition, and working memory in older adults. Overall, several brain–behavior relationships emerged, and the preliminary findings begin to address our questions about differential relationships for cognitive and affective empathy in old age. We found higher affective empathy was associated with bilateral amygdala and right insula deactivation during the high versus low load condition of a working memory task. The amygdala and insula were examined as *a priori* regions of interest during the working memory task, and were not differentially activated between the two load conditions during whole-brain analysis of this task or in the ROI analysis. Interestingly, no differences in working memory task performance were found based on levels empathy. Therefore, the relationship between empathy and brain response does not appear to be mediated by task performance. Our results suggest that there is a possibility that the insula and amygdala served different roles than emotion regulation during purely cognitive tasks such that when higher empathic older adults are not engaged in an emotion regulation task their amygdala and insula produce less spontaneous activation. While classically viewed as a structure primarily related to emotional functions, some evidence exists for the role of the amygdala in higher-order cognitive processes such as working memory and cognitive control. Across two unique samples of younger adults, Schaefer et al. (2006) reported better performance in individuals with higher amygdala BOLD activation during the most demanding condition of the *n*-Back task (3-back). This study also found that the left amygdala was a better predictor of working memory performance than the right amygdala, implicating some sensitivity of the left amygdala. Our results indicating that older adults with greater affective empathy had less activation in the bilateral amygdala during higher loads of a working memory task may imply that highly empathic individuals recruit more efficient emotion regulation processes in brain regions also implicated in working memory.

Consistent with this theory, several studies have found age-related decreases in amygdala activation in response to negative stimuli; and these studies largely support the cognitive-control model which argues that prefrontal emotion regulation processes reduce amygdala response to negative stimuli (e.g., Mather, 2012; Nashiro et al., 2012). Our own work has previously shown greater optimism was related to reduced activation of emotion regulation regions among an independent sample of older adults (Bangen et al., 2013). Together, this previous study and our current findings show that there is less activation with negative stimuli in optimistic as well as empathic older adults, which may be indicative of conserving "emotional energy". This pattern of activation is opposite of the association of cognitive performance with greater activation in "successful" agers (Eyler et al., 2011). Thus, the nature of compensation appears to be different for cognitive versus emotional tasks among successful agers.

Variability in cognitive empathy was related to differences among older adults in response to cognitive tasks; a positive relationship was found between cognitive empathy and insula activation during the response inhibition task. The anterior insula has consistently been found to be involved in both the affective and cognitive components of empathy (Fan et al., 2011), and our findings with a small sample of older adults support previous research. Similar to the current findings, Masten et al. (2011) examined neural activity for social pain (i.e., observing a stranger being excluded from an activity) in a sample of young adults (mean age=20 years) and found additional activity in the anterior insula in the higher empathic individuals, but not in the lower empathic individuals.

There are several limitations to this study. The correlations between empathy and brain were only moderate in size, and we tested our *a priori* regions of interest without an adjustment for multiple comparisons. The results will need to be replicated in another sample to rule out Type I error. On the other hand, our power to detect relationships with functional response may have been limited by small sample size and lower than desired reliability of the fMRI tasks for the contrasts used. Some studies indicate that the insula is comprised of sub-regions with distinct functional and anatomical boundaries, suggesting that anterior regions are involved in processing emotion, empathy and some cognitive functions while posterior regions are largely responsible for interoception, somatosensation and pain (Craig, 2002; Menon and Uddin, 2010; Taylor et al., 2009). In our sample however,

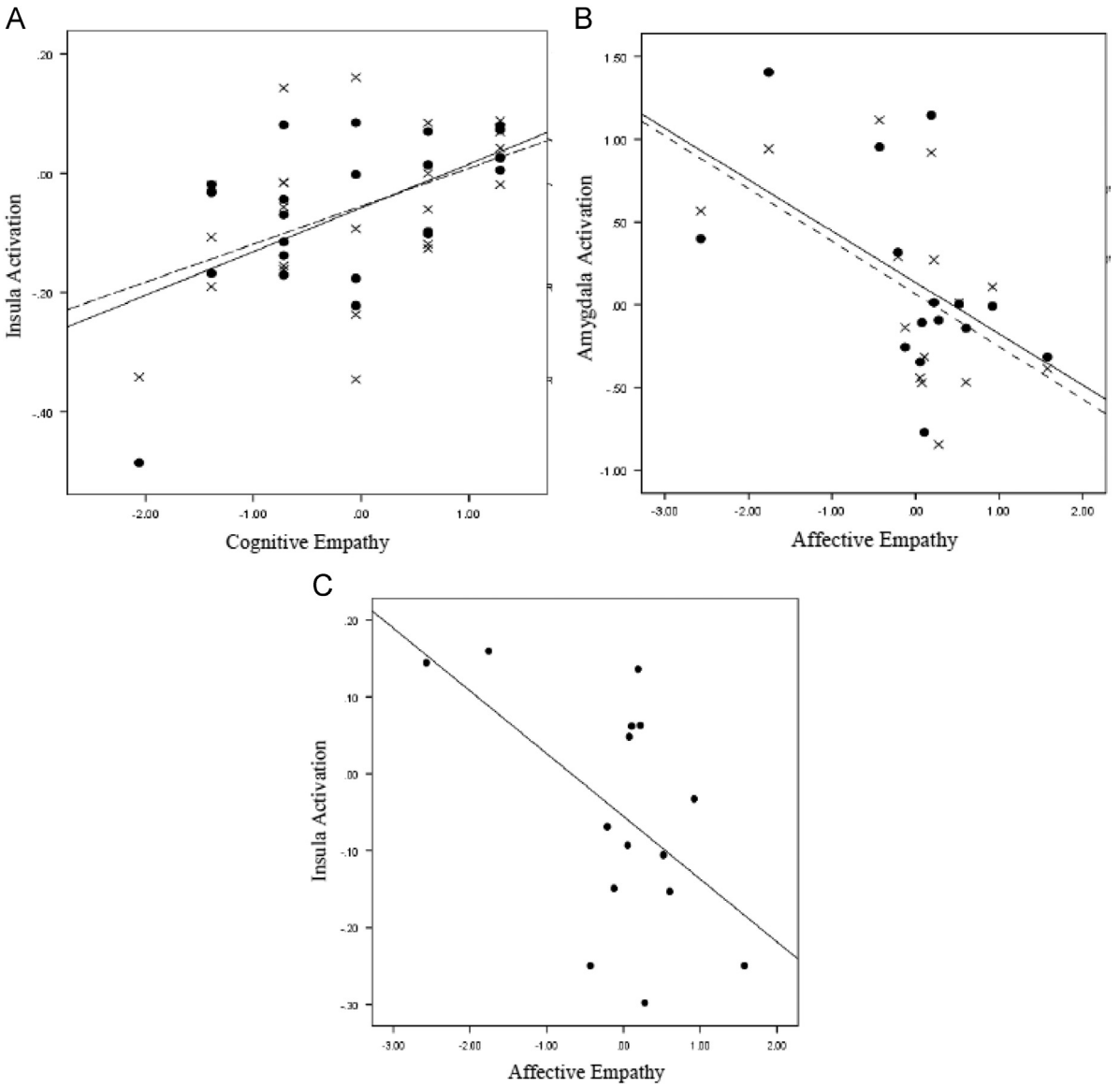

Fig. 3. Scatterplot of correlations between brain response (*y*-axis = mean beta weight for contrast of interest) and cognitive or affective empathy scores from the Multifaceted Empathy Test for all significant associations. *Note*: (A) x = left insula activation and • = right insula activation; (B) x = left amygdala activation and • = right amygdala activation (C) • = right insula activation.

neither a cluster analysis nor anatomically defined anterior and posterior insula masks (Saze et al., 2007) indicated a differential relationship between anterior and posterior insula activation during any task and cognitive and affective empathy (data not shown). Thus, our results support a global association between insula response in cognitive tasks and measures of empathy, and future work will be needed to determine if more localized associations exist. Furthermore, there was no younger comparison group which limits the generalizability of the results. Additionally, due to the older age of our sample (mean age 79 years old) and subsequent physical problems that accompany older age (e.g., limited mobility; discomfort lying on back; vision problems), many participants took longer than anticipated to get in the scanner and/or had to end the imaging protocol prematurely. Therefore, despite scanning 30 participants, our usable data per fMRI task was less than 30. Still, these findings provide preliminary support for the notion that older adults may have enhanced emotional responding and/or a qualitatively different brain–behavior relationship for affective empathy compared to younger adults, yet inferences about changes with age are currently speculative. Empathy related tasks were not used, so brain activity while engaged in empathic thought could not be directly measured. Tasks that have historically been used to measure empathy usually involve watching others suffer physical pain, which may not garner the same response from older adults as from younger individuals. Future work would benefit from developing empathy-invoking tasks tailored for older adults. Despite the fact that the functional imaging tasks we used were not designed to evoke empathy, nor the empathic network brain regions directly, significant relationships with established emotion processing and empathy brain regions were found, independent of task performance.

In summary, taking a localizationist approach to understanding empathy raises interesting questions about the responsiveness of the brain regions related to these constructs. Across the lifespan, difficulties with emotion processing are known to be related to a myriad of psychosocial and socioemotional problems, including reduced social competence and interest, poor interpersonal functioning and communication, reduced quality of life, and inappropriate social behavior (Ruffman et al., 2008). In turn, these

psychosocial problems can lead to increased social isolation and loneliness, which are significant contributors to poor mental well-being as well as morbidity and mortality in late life (Steptoe et al., 2013). There is also some evidence for the relationship between empathy and depression in late life. For example, one study found that caregivers with high cognitive empathy reported better appraisals of their caregiving sitatuation and were less depressed than caregivers with low cognitive empathy (Lee et al., 2001). From a neuro-behavioral approach, there is preliminary support for the idea that changes in the oxytocin system with age may have putative effects on socioemotional functioning, including decreased empathy and increased depression (Ebner et al., 2013).

Our preliminary findings raise the question as to whether interventions aimed at increasing affective empathy or compassion may also have benefits on the use of emotion regulation and processing. One study found increases in inferior frontal gyrus and dorsomedial prefrontal cortex after a cognitive-based compassion training among a group of younger adults, demonstrating the feasability of compassion training on altering neural processes (Mascaro et al., 2013). Conversely, the question also remains as to whether interventions focused on improving task performance would drive improvements in empathy. In turn, these improvements might have a positive impact on health related quality of life among older adults. Lastly, the evidence is still mixed regarding the state or trait-like nature of empathy. Our work has found preliminary cross-sectional evidence that compassion/empathy are cultivated through life experiences (Moore et al., in press), yet longitudinal studies are needed.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.pscychresns.2014.10.016.

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