WANTING WHAT IS ALREADY GONE:

FUNCTIONAL IMAGING DIFFERENTIATING REWARD COMPONENTS IN BEREAVEMENT

by

Mairead H. McConnell

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SIGNED: *Mairead H. McConnell*

APPROVAL BY THESIS DIRECTOR

This thesis has been approved on the date shown below:

Mary-Frances O'Connor
Assistant Professor of Psychology

March 6, 2017
Date

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Abstract

Complicated grief, or persistent complex bereavement disorder, is a condition that affects approximately 10% of bereaved individuals and is marked by intense longing and yearning for the deceased. Little is known about the neurocognitive mechanisms contributing to this syndrome, but previous research suggests that reward pathways in the brain may play a role. The present study was designed with this theory in mind, aiming to understand reward processing in those experiencing complicated and non-complicated grief as well as to differentiate the "wanting" and "liking" phases of reward processing in bereavement. Twenty-five older adults were categorized based on grief severity into one of three groups: complicated grief (CG), non-complicated grief (NCG) and non-bereaved married controls (NB). Neural activation was examined using fMRI while participants viewed a countdown on the screen (anticipation) followed by a photo of their (living or deceased) spouse. There was no significantly differential activation between the three groups for the spouse v. stranger photo contrast, nor for anticipation period v. spouse photo. However, these two contrasts were also run separately in the three groups. Each group produced significant activation, in similar and distinct regions, primarily associated with emotion and visual processing. In addition, post-hoc analyses were conducted using self-reported yearning scores as a regressor across all bereaved participants, which revealed that greater symptoms of yearning predicted greater activation in the subgenual anterior cingulate cortex (sgACC). This region of the brain has been previously linked to depression and suggests that symptoms of yearning may present an opportune place to intervene to improve outcomes in CG.

Introduction

Grief is a common human experience, yet represents one of life's greatest stressors. While many individuals successfully cope and adapt in response to loss, a subset of bereaved people do not seem to recover, and their grief is especially prolonged and intense. Complicated grief (CG), termed persistent complex bereavement disorder (PCBD) by the DSM-5, affects approximately 10% of all bereaved individuals (Lundorff et al., 2017). CG is characterized by recurrent and persistent painful emotions, accompanied by intense longing and yearning for the deceased. Individuals with CG may experience a host of symptoms, including difficulty accepting the reality of the loss, intense anger, bitterness, or complete emotional numbness, and often report that life feels meaningless and not worth living (Shear, 2012). These symptoms must persist for at least 12 months to confirm a diagnosis, but they may last for years after the death event (American Psychiatric Association, 2013).

Research within the past decade has distinguished CG from other psychopathologies, including depression. Simon et al. (2007) found that in a sample of 206 individuals with CG, 25% of cases did not meet criteria for any other DSM-IV diagnoses. Although this reflects the high rates of comorbidity among those with CG, it also demonstrates that CG is a distinct disorder and that the associated impairments are often unexplained by other diagnoses. Additional research has demonstrated that while CG symptoms are correlated with depressive symptoms, the two are distinct and distinguishable (Boelen, Reijntjes, J. Djelantik, & Smid, 2016). While this body of literature supports the existence of CG as a distinct disorder, the neurocognitive mechanisms contributing to CG remain far from understood.

Reward Systems

Research in the field of social neuroscience tells us that relationships with our attachment figures are very rewarding. This is well demonstrated in self-reports, but is also evident through activation of reward-related brain regions in individuals viewing a photograph of a long-term romantic partner and in mothers viewing photos of their children (Acevedo, Aron, Fisher & Brown, 2012).

However, there is evidence that these reward systems may operate differently in those who have not adjusted to the end of a rewarding relationship, whether due to the partner's death or to romantic rejection. O'Connor et al. (2008) found increased activity in the nucleus accumbens in participants with CG compared to bereaved participants that didn't meet CG criteria (or non-complicated grief: NCG) when viewing a photo of their deceased loved one. Subjective reports of yearning during an interview correlated with activation in this region, an area of the brain associated with reward. One interpretation of this finding is that the reward signal is an instantiation of the yearning and longing for the deceased experienced by those with CG. Subjectively, they desire to be reunited with their loved one in response to memories and cues associated with the deceased. Neurally, these cues and memories may be rewarding and therefore reinforce the longing, preventing extinction of the reward response.

Consistent with these results, Fisher and colleagues (2010) found that for individuals who had been rejected by a romantic partner but were still in love, viewing a photo of that person produced greater activation in the nucleus accumbens than for happily-in-love participants viewing their partner (Fisher, Brown, Aron, Strong, & Mashek,

2010). Once again, this finding is interpreted as indicative of "craving" the rejecting or lost romantic partner.

Liking vs. Wanting

Delving deeper in the reward literature, previous research suggests that anticipation of rewards recruits distinct brain regions compared to the consumption of rewards (Diekhof, Kaps, Falkai & Gruber, 2012). Anticipatory reward can be considered akin to "wanting" something, while consummatory reward can be described as "liking" that which has been consumed or received. There is some disagreement as to whether these reward processes recruit distinct or overlapping brain regions. While the nucleus accumbens has been cited as a region of significant overlap for each phases of reward processing (Diekhof, Kaps, Falkai & Gruber, 2012; Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001), another group of studies found activation in the nucleus accumbens to be associated with anticipation of a reward, while consumption was more likely to recruit from the orbitofrontal cortex (OFC) (Diekhof, Kaps, Falkai & Gruber, 2012; Knutson, Fong, Adams, Varner, & Hommer, 2001).

Many of these studies assess anticipation and consumption of rewards through tasks that involve monetary gains and losses. However, this differentiation between wanting and liking is relevant beyond such decision-making paradigms and may be implicated in the experience of complicated grief. In CG, the "consumption" or experience of that rewarding relationship is no longer possible due to the nature of the loss, yet the "craving" or "yearning" remains and is one of the most intense symptoms reported in this disorder. Therefore, for those with CG, similar to those who have experienced romantic rejection, this activation of reward circuitry may be more associated with the anticipatory

reward, or 'wanting' the loved one. The present study was designed to test this theory using a novel photo-viewing paradigm designed to differentiate anticipation and consumption of rewards in bereavement. For these reasons, we hypothesized:

1) Individuals with CG, compared to those with NCG, will show increased activity in the nucleus accumbens while viewing a photo of the spouse compared to a stranger. We expect both the non-bereaved and CG groups to show this similar pattern of activation, because of the reward signal generated by the spouse among those currently married, and the failure to extinguish this signal among those with CG.

In addition to reward processing, O'Connor and colleagues (2008) also found that among all bereaved participants, viewing a photo of the deceased recruited brain regions known to be involved in the experience of emotion, such as the dorsal and rostral anterior cingulate, and the interior insula. This is consistent with the idea that a photo of a deceased loved one acts as an emotionally charged stimulus. It is possible that within the anticipation vs. consumption paradigm, bereaved individuals, regardless of their CG or NCG status, will experience greater emotion as they anticipate the upcoming photo. Therefore, our second hypothesis was:

2) Anticipation will activate emotion-related regions such as dorsal anterior cingulate, rostral anterior cingulate, and insula in both bereaved groups (CG and NCG) compared to non-bereaved individuals.

Method

Participants

Twenty-nine older adults were recruited from the community to participate in an fMRI experiment at the University of California, Los Angeles. The final sample consisted of

twenty-five older adults who were between 64 and 79 years of age (M= 71.4), were predominantly female (84%) and were predominantly Caucasian (77%) (See Table 1).

Participants had either experienced the death of a spouse in the past three years (time since loss M= 21.19 months) or were non-bereaved, married controls. After reviewing the fMRI data, two participants were removed for structural brain abnormalities and two were removed for motion artifacts in the neuroimaging data. Two of these participants belonged to the NCG group, one belonged to the CG group and one was non-bereaved. This left a total sample of 25 participants. Among the 16 bereaved participants, 9 met the criteria for CG. The non-bereaved group consisted of 9 married individuals that had not experienced the loss of any first-degree relative in the past three years.

Individuals were not eligible to participate in the study if they endorsed (1) the presence of a current psychiatric disorder, (2) the use of psychotropic medications initiated since the death event, (3) immunosuppressive medication, (4) or current major medical illness. All participants scored at least a 25 on the Mini-Mental Status Examination (MMSE). Due to the fMRI component of the study, participants were also screened for any ferromagnetic material and fear of small, enclosed spaces.

Procedure

All bereaved participants completed a 19-item Inventory of Complicated Grief, a well-validated measure for determining grief severity and differentiating complicated from non-complicated grief (ICG; Prigerson et al., 1995). A score of 30 or higher (out of 76) is the standard criteria for CG and was the cut-off used for this study.

Each participant provided five photos of their deceased or living spouse, which were matched with five photos of a stranger on age, sex, race, and indoor/outdoor setting.

Photos were presented in an event-related design, in a randomized order for a total of 60 trials. Photos remained on the screen for three seconds and were each proceeded by a countdown of the numbers 4 through 1, which lasted two seconds (Figure 1). Participants were blind to the condition of the upcoming photo, thus creating anticipation on every trial. In between trials, a fixation point was displayed on the screen. The presentation order of the photo and fixation conditions was optimized for rapid event-related fMRI using optseq2. The inter-stimulus interval varied between 0-10 seconds. Stimuli were presented to participants in the scanner using MacStim software.

All participants completed the photo-viewing task in the fMRI scanner. They were told they would see a countdown followed by photos they had provided of their spouse in addition to photos of someone they did not know. Participants were instructed to focus on the thoughts, feeling and memories elicited by viewing the photographs, without trying to alter them. As a manipulation check, participants completed a post-scan questionnaire in which they were asked to write about the experience of viewing the photos of their (living or deceased) spouse.

fMRI Data Acquisition

Scanning took place in a Siemens Trio 3T scanner at UCLA Ahmanson-Lovelace Brain Mapping Center. A high-resolution structural T1 weighted image was (MPRAGE, TR = 2200ms; TE = 3.4ms, TI = 900ms, flip angle= 10°, FOV = 256mm, 176 continuous 1mm slices, 1.0 x 1.0 x 1.0 mm) was collected for each participant for anatomical reference. T2 weighted functional scans (TR – 2500ms; TE = 25ms, flip angle = 90°, FOV = 200mm, 36 3mm slices, 3.1 x 3.1 x 3.0 mm) were collected during the task.

Data Analysis

Image processing and statistical analyses were completed using Statistical Parametric Mapping (SPM12, Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK, http://www.fil.ion.ucl.ac.uk/spm). Raw functional images were manually reoriented with the origin set to the anterior commissure. Functional images were then realigned, unwarped, and co-registered to the participant's anatomical image using the default algorithms in SPM12. Images were normalized to the MNI template and smoothed with an 8mm Gaussian kernel, and were resliced to 2 x 2 x 2mm voxels. Artifact Detection Tools (ART) was used to identify outliers with global intensity >3 standard deviation and scan-to-scan motion >1mm. These outliers were included as nuisance regressor in the design matrix.

First level analyses at the single subject level involved contrasts for the different phases of the task. This included a contrast for photo condition (spouse v. stranger) as well as for phase of task (anticipation v. photo viewing). Each condition was also compared to a "null" condition, during which the participant was asked to fixate on a cross displayed in the middle of the screen.

Second level analyses were at the group level and used F-tests to test for differences between CG, NCG and non-bereaved at different phases of the task. Where the F-tests were significant, these analyses were followed by planned comparisons t-tests to determine which groups were significantly different. All group level analyses were thresholded at an uncorrected p-value of .001, with a cluster size of 20. All coordinates are reported in MNI format.

Region of Interest Analyses

Region of interest (ROI) analyses were conducted on *a priori* ROIs using the Marsbar toolbox for SPM12. This involved calculating parameter estimates of the hemodynamic response in each region. All ROIs were created based on coordinates from neuroimaging studies in the literature, which involved building a 10mm sphere around the coordinates.

The ROI seed region for the nucleus accumbens (x=10, y=20, z=−6) was drawn from previous work by O'Connor et al. (2008) which found greater activation in this area for participants with CG compared to those with NCG while viewing a photo of the deceased versus a stranger.

The second ROI (x= -10, y= 10, z= -2) modeled the ventral striatum, which includes the nucleus accumbens, caudate and putamen. This seed region, along with coordinates for the anterior insula (x= -46, y= 16, z= -6) were drawn from work by Diekhof et al. (2012), which found these regions to be associated with reward anticipation in a meta-analysis.

ROI seed regions also included the rostral anterior cingulate (rACC, x= -10, y= 36, z= 2), the dorsal ACC (x= 8, y= 22, z= 28), and the orbitofrontal cortex (OFC, x= 6, y= 54, z= -10). Coordinates for these regions were taken from a different scan in this same sample using the eStroop task (Arizmendi, Kazniak & O'Connor, 2016).

Results

The three groups did not differ on any demographic variables, levels of depression or measures of cognitive function (Table 1). Regional activation across all participants for the two main contrasts, (1) spouse versus stranger photo and (2) anticipation versus spouse photo conditions, are displayed in Tables 2 & 3. Contrary to our hypothesis, the three groups showed no differential activation for the spouse v. stranger contrast, or for

the anticipation v. spouse photo contrast. Tables 4-7 display significant regional activation for each individual group (CG, NCG and NB) for each contrast.

Region of Interest Analyses

The three groups showed no differential activation on any of the hypothesized regions of interest, which included the nucleus accumbens, ventral striatum, rostral and dorsal ACC, insula, and OFC, on either the spouse v. stranger or anticipation v. photo contrast.

Post-hoc Analysis

Due to the hypothesized link between the CG symptom of yearning and reward processes, the single yearning item was extracted from the ICG scale. This item asks participants to rate the extent to which they yearn for the deceased on a scale from 1 to 4. A regression analysis revealed that among all bereaved participants, regardless of CG diagnosis, a higher self-reported yearning score predicted activation in the subgenual anterior cingulate (sgACC, x = -4, y = 28, z= -6) during the anticipation period compared to viewing a photo of one's spouse (z= 3.11, p <.005, cluster size =25)(Figure 2).

Discussion

The present study investigated neural activity associated with anticipation and experience of a rewarding stimulus in bereavement. Informed by the previous literature on reward and CG, we hypothesized that those with CG would show greater activation in the nucleus accumbens in response to a photo of the deceased compared to those with NCG. However, this pattern of activation was not observed and that finding from O'Connor et al. (2008) was not replicated.

Although there were not hypothesized group differences in the regional activation to the task, there is evidence of reward processing in the analysis of the overall sample, and in the groups when analyzed separately. In the anticipation > spouse contrast across all participants (Table 3), the OFC, insula, and putamen are all activated, as seen in previous reward tasks. In addition, the midbrain is activated, as seen in reward learning (Kable & Glimcher, 2009). The putamen activation is seen in the analyses of the anticipation > spouse contrast for NCG (Table 6) and for NB (Table 7). The midbrain activation is also seen in the anticipation > spouse contrast for CG (Table 5).

The activation of the ACC was seen in the overall sample in the spouse > stranger contrast, as seen in O'Connor et al. (2008). It was also activated in the spouse > stranger contrast for the CG group and the NB group (Table 4). Although the ACC is activated in many different mental functions, it is strongly associated with emotion and pain processing, including social pain (Eisenberger & Lieberman, 2004).

Subgenual ACC and depression

Post-hoc analyses revealed a link between yearning score and activity in the sgACC. Interestingly, this area has been previously associated with depressive symptoms. Kross, Davidson, Weber and Ochsner (2008) found sgACC activity to be associated with higher self-reported negative affect when participants were cued to "feel" the emotions elicited by autobiographical memories. Cooney, Joormann, Eugene, Dennis and Gotlib (2010) found that participants with depression, relative to controls, exhibited greater activation in the sgACC during a rumination task compared to distraction.

One interpretation of this finding is that yearning and depressive rumination may share important qualities. For one, both rumination and yearning, especially in the context

of grief, are maladaptive repetitive thoughts. However, sgACC activity may represent more than merely repetitive thoughts. Rumination and yearning are not uncommon psychological events—everyone experiences thoughts, even maladaptive and repetitive thoughts, to some degree. Yet these events are experienced more often and to a greater degree in major depressive disorder (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008) and CG (Eisma et al., 2015) and become a source of distress and dysfunction in those psychopathologies. The fact that we see this activation in these two populations, but not in control groups, may indicate that the sgACC reflects the degree, or uncontrollability, of the emotional response elicited by these psychological events within each population.

More research will be necessary to support this theory and to determine if there is one specific emotion tapped by both rumination and yearning, such as sadness, loneliness, or emotional pain, that is processed in the sgACC. Finally, this finding may help to expand the understanding of the role of the sgACC transdiagnostically, not merely within depression.

Importantly, self-reported yearning predicted sgACC activity regardless of CG or NCG diagnosis. Some participants with NCG scored high on the yearning item, and some participants with CG scored low on this particular item. This begs the question of whether certain symptoms within CG are more important than others or whether some symptoms are represented neurobiologically while others contribute to functioning in behavioral patterns not assessed at this level.

Limitations

There are several possible explanations for the failure to replicate the nucleus accumbens activation in the spouse > stranger contrast, some of which reflect limitations of

the present study and others that simply represent notable differences between the two studies and samples. First, the sample characteristics in O'Connor et al. (2008) are somewhat different than those in the present study. Mean age is the present study was 71.4 years, while the prior study sample had a mean age of 44. Furthermore, CG was assessed using different metrics—through a structured interview in the prior study, and through use of the self-reported ICG in the present sample. This means that grief severity between the two samples is not easily comparable, so it is possible that the earlier study sample may have captured a group of participants experiencing greater CG symptoms.

Failure to replicate previous findings may also be accounted for by the fact that the task in the present study was not a direct replication of the previously used task. The present task was distinct from that utilized by O'Connor (2008) such that in the present study, each trial was preceded by an anticipation countdown. In addition, the previous study had grief-related and neutral words embedded in the photos, creating a 2 (word) x 2 (photo) design. The nucleus accumbens finding was strongest in the word condition (grief-related > neutral) in the previous study, which did not appear in the current study. Finally, because of concerns about habituation in the prior study, there were more images of the deceased in the present study. The introduction of this variability may have affected processing of the stimuli, focusing the participants more on the range of visual stimuli, rather than the semantic category of the spouse. This might explain the large activations in the visual cortex.

Failure to replicate previous findings may also be the result of power limations. Given that the smallest subgroup contained only seven participants, this study may have been underpowered to reliably detect activations.

There are several additional limitations to this study, related to the task design. First, the task did not require participants to make a response or exhibit a behavior other than the instructions to focus on their thoughts and feelings. Other than anecdotal evidence about what the participants were "doing" during the task, we have no objective measure of whether, or the extent to which, participants were attending to the task. It is possible that during the anticipation phase, participants were imagining the most recent photo of the spouse, which may explain the large amount of activation in brain areas associated with visual processing during the anticipation phase of the task.

Anectdotal evidence collected after the scans suggests that participants were attending to the photos. In fact, several participants reported that the experience of vieweing a photo of their deceased spouse was pleasurable, stating "it was so nice to see him again", or that it elicited positive memories. There was also evidence that the photo of the stranger may have been aversive to some participants, either because they preferred to see the spouse or due to an assumption that the photo represented someone else's deceased spouse, which elicited sadness and/or empathy. These responses should be considered and potentially explored further in later analyses and in future studies.

Another possible limitation is that the inter-trial-interval between the photo viewing phase of the task and the anticipation phase of the following trial may have been too short to allow for attenuation of the reward response. ITIs are intended to allow the neural response to return to baseline before the following trial, otherwise, in this case, the anticipation phase may be capturing the reward response from the previous trial, essentially "bleeding over" into the next trial. One possible way to control for this in future analyses is to only examine anticipation trials that are preceded by non-reward trials (the

stranger photo), in order to rule out the possibility of capturing the reward signal. This design is possible with the current data and will be considered for further analyses in order to better understand the outcomes of this study.

Finally, it is also possible that the resolution and alignment of the fMRI images may have been too poor to allow for accurate mapping of brain regions as precise as the nucleus accumbens. Future research can and should employ the most advanced technology to ensure better spatial resolution and accuracy.

Future directions

Given that the preliminary analyses in this study failed to replicate prior findings, future research should aim to address these discrepancies and determine whether, and to what extent, the reward system is implicated in CG. It is also possible that in bereavement, and in social relationships in general, constructs like reward and anticipation are inherently different than rewards with monetary value. The task in the present study was based on those used in monetary reward tasks; future tasks should consider tasks that are based on social reward.

Further research should also focus on the role of the sgACC in emotional experiences within psychopathologies such as depression and CG. This should include an investigation of whether sgACC activity reflects mental functions such as ruminative thought or if it better represents specific aspects of emotions such as loneliness, social isolation, or sadness.

Summary

Complicated grief is a disorder characterized by an inability to adapt to the death of a loved one, accompanied by intense yearning for the deceased and other symptoms, which

result in significant impairment. Previous research has linked CG to neural reward processes, suggesting that the reward system might play an important role in the maintenance of, and potentially the treatment of, this disorder. The present study attempted to replicate these findings and extend the understanding of reward processes in CG by distinguishing between anticipation, or "wanting" and consumption, or "liking", rewards associated with an attachment figure.

Although the present study did not replicate previous findings regarding between group differences, the overall results are consistent with the theory that reward processes are implicated in bereavement. Post-hoc analyses revealed that self-reported yearning scores significantly predicted neural activity in the subgenual anterior cingulate cortex (sgACC), an area of the brain previously associated with depression and symptoms of rumination. This finding suggests that yearning and depressive rumination may share similar characteristics and that yearning, like depressive rumination, may represent an opportunity for behavioral interventions.

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Tables.

Table 1.

Sample Characteristics

		Non-bereaved (n=9)	Non-Complicated Grief (n=7)	Complicated Grief (n=9)	F/Fisher's Exact	p value
Age *M* (SD)		70.3 (4.7)	73.7 (4.7)	70.6 (3.1)	1.54	NS
Gender	Male	2	1	1	0.65	NS
	Female	7	6	8		
Ethnicity	Caucasian	5	7	7	3.94	NS
	Non-Caucasian	4	0	2		
Employment	Employed	4	0	2		
	Retired	4	7	7	6.63	NS
	Unemployed	0	0	0		
Education	High school	2	1	0		
	AA or BA	3	4	5	4.78	NS
	Post graduate	4	2	4		
Years married *M* (SD)		41.6 (13.4)	27.1 (17.8)	33.1 (16.4)	1.70	NS
Alcohol (drinks per week) *M* (SD)		0.2 (0.4)	1.1 (1.8)	2.9 (4.9)	1.70	NS
MMSE *M* (SD)		28.6 (1.3)	29 (1.5)	28.5 (1.8)	0.20	NS
ICG Total Score *M* (SD)		n/a	12.1 (4.5)	26.8 (4.4)	40.71	<.0001
ICG Yearn Score *M* (SD)		n/a	2.1 (.89)	2.9 (.64)	3.40	NS
BDI *M* (SD)		1.8 (3.5)	3.8 (6.0)	5.3 (5.3)	0.67	NS

Note. F scores apply to continuous variables, Fisher's Exact applies to categorical variables with cell sizes of <5. N/A = not applicable, NS = nonsignificant. MMSE = Mini-Mental State Examination, ICG = Inventory of Complicated Grief, BDI = Beck Depression Inventory.

Table 2.

Regional Activation for Spouse > Stranger, all subjects

Anatomical Region	**Z score**	**MNI coordinates**			**Voxels**
		x	*y*	*z*	
L Middle Occipital Gyrus	5.01	-22	-96	14	1259
R Middle Occipital Gyrus	4.28	46	-82	-2	48
Lingual Gyrus	4.02	-8	-90	-18	21
Anterior Cingulate Cortex	3.92	-6	44	4	165
L Cerebellum	3.8	-18	-64	-22	62
R Cerebellum	3.73	24	-62	-30	26
R Cerebellum	3.6	6	-62	-22	56
L Cerebellum	3.51	-38	-60	-34	21
R Cerebellum	3.44	16	-72	-26	20

Table 3.

Regional Activation for Anticipation > Spouse, all subjects

Anatomical Region	**Z score**	**MNI coordinates**			**Voxels**
		x	*y*	*z*	
R Occipital Cortex	6.8	34	-68	-8	15196
Posterior Cerebellum	4.1	-22	-68	-50	110
R Posterior Cingulate Cortex	4.07	6	-56	22	285
Orbitofrontal Cortex	4.03	-4	36	-16	59
Inferior Frontal Gyrus	3.89	50	36	0	33
R Insula	3.86	32	14	6	24
Midbrain	3.85	6	-16	-6	39
L Putamen	3.65	-24	0	8	32
R Putamen	3.59	22	0	4	35

Table 4.

Regional Activation for Spouse >Stranger

	Anatomical Region	**Z score**	**MNI Coordinates**			**Voxels**
			x	*y*	*z*	
CG only	Anterior cerebellum	4.18	-22	-54	-32	34
	Anterior Cingulate Cortex	3.4	0	52	2	58
NCG only	Vermis	3.68	4	-52	-6	30
NB only	Anterior Cingulate Cortex	3.75	-10	52	2	41
	Middle Occipital Gyrus	3.52	-16	-94	14	20

Table 5.

Regional Activation for Ant>Spouse, ***CG ONLY***

Anatomical Region	**Z score**	**MNI Coordinates**			**Voxels**
		x	*y*	*z*	
R Anterior Fusiform Gyrus	5.01	32	-46	-10	747
Thalamus	4.98	-18	-30	-4	208
L Anterior Fusiform Gyrus	4.7	-24	-68	-10	1059
R Posterior Cerebellum	4.65	26	-64	-38	52
R Cuneus	4.45	14	-92	2	239
L Cuneus	4.27	-22	-80	18	253
Superior Occipital Gyrus	3.98	32	-84	24	83
L Posterior Cerebellum	3.82	-28	-70	-28	31
Inferior Occipital Gyrus	3.79	-40	-86	-6	38
Midbrain	3.65	8	-34	-6	23

Table 6.

Regional Activation for Ant>Spouse, ***NCG ONLY***

Anatomical Region	**Z score**	**MNI Coordinates**			**Voxels**
		x	*y*	*z*	
L Posterior Fusiform Gyrus	4.77	-30	-70	-10	645
L Anterior Fusiform Gyrus	4.29	-40	-46	-18	113
R Anterior Fusiform Gyrus	4.28	32	-40	-14	189
R Hippocampus	4.26	20	-8	-16	20
R Lingual Gyrus	4.03	14	-84	-6	195
Putamen	3.96	30	-14	-2	33
Middle Frontal Gyrus	3.84	40	30	20	49
R Posterior Fusiform Gyrus	3.77	34	-72	-10	38
L Lingual Gyrus	3.56	-16	-86	-10	20
R Cuneus	3.49	14	-94	14	25

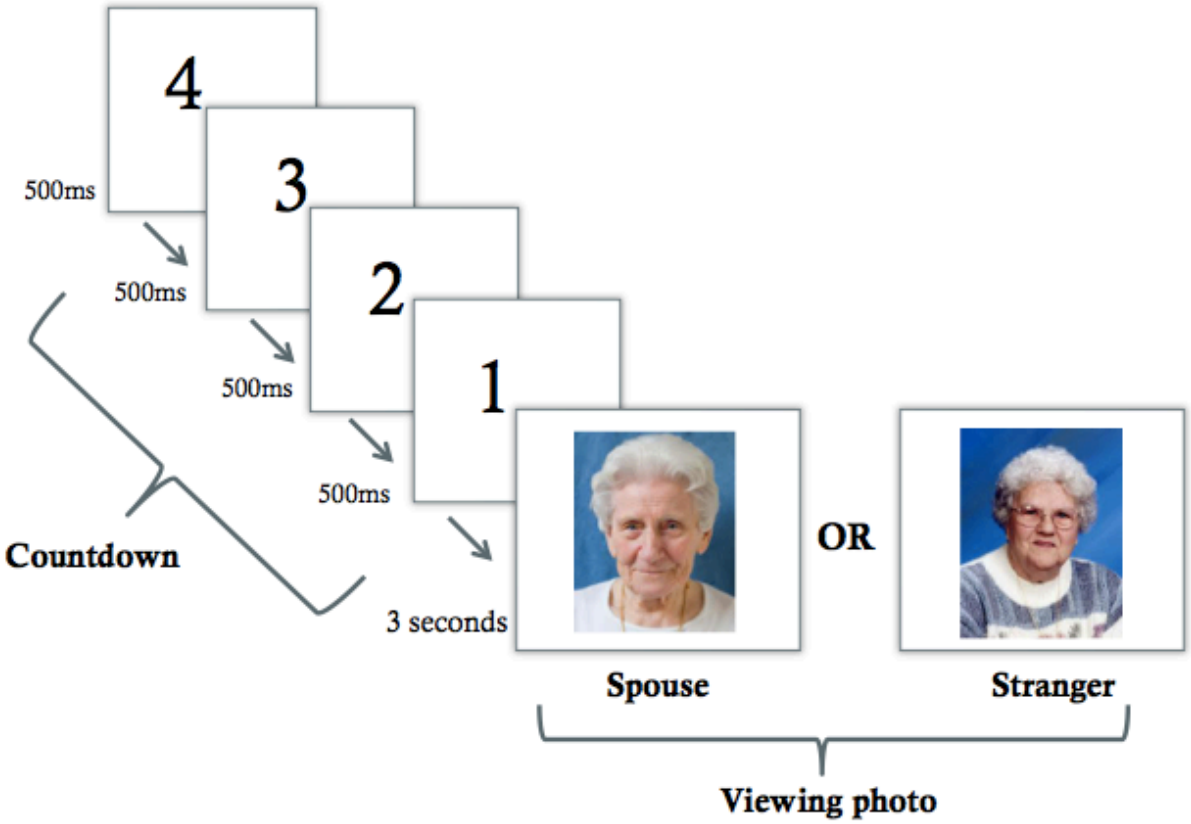
Table 7.

Regional Activation for Ant>Spouse, ***NB ONLY***

Anatomical Region	**Z score**	**MNI Coordinates**			**Voxels**
		x	*y*	*z*	
R Anterior Fusiform Gyrus	5.36	42	-52	-20	5176
L Thalamus	5.22	-12	-10	0	592
R Posterior Cingulate Cortex	4.79	18	-52	14	193
Putamen	4.66	20	0	4	254
Posterior Cerebellum	4.29	-22	-60	-46	44
Superior Frontal Gyrus	4	10	14	56	37
L Posterior Cingulate Cortex	3.98	-14	-54	12	55
R Thalamus	3.91	12	-24	0	23
Middle Occipital Gyrus	3.87	40	-74	26	36
Precuneus	3.8	8	-84	42	20
Precuneus	3.64	26	-82	42	22

Figure 1.

Reward Task



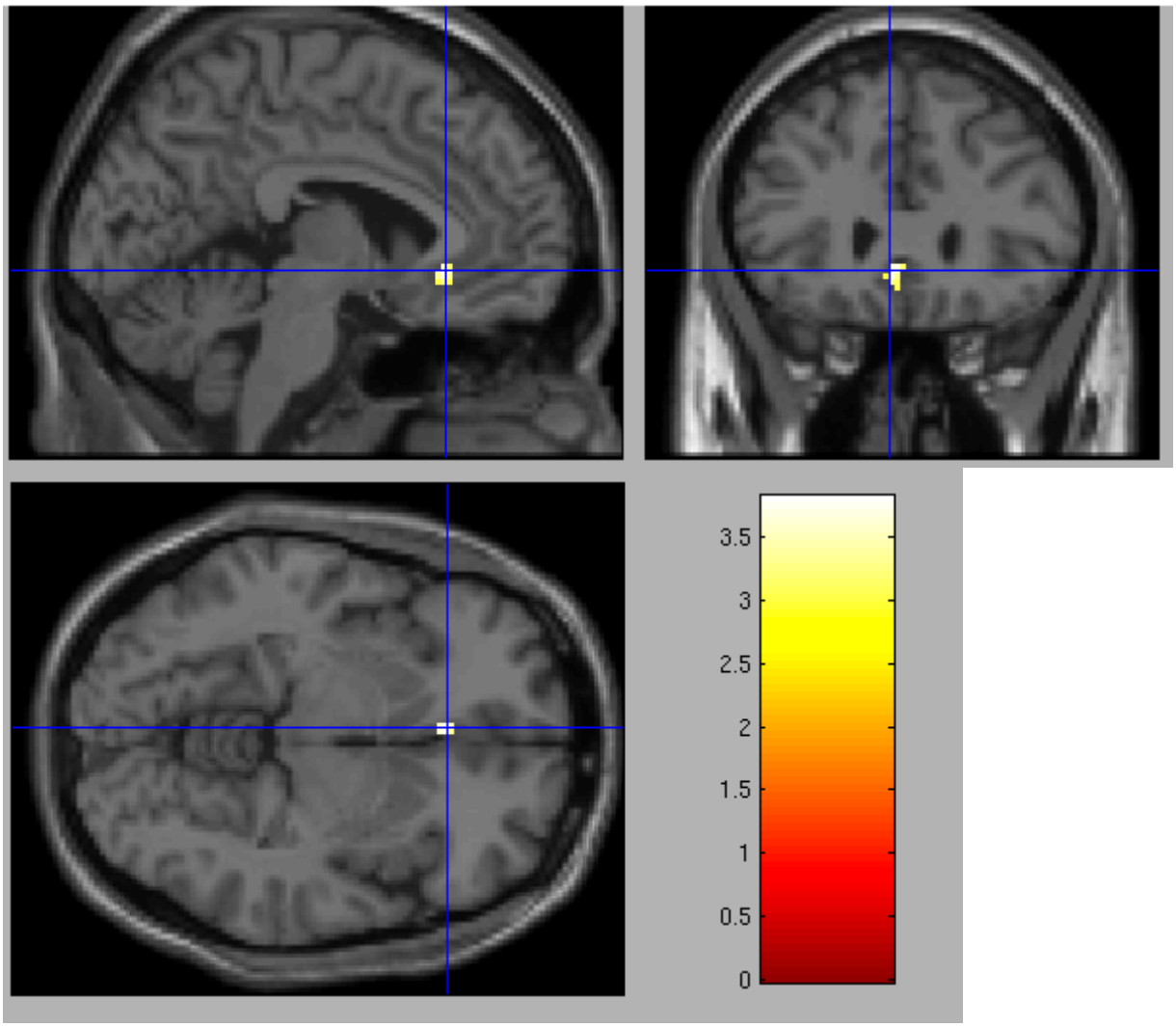


Figure 2.

Greater self-reported yearning associated with greater neural activity in the subgenual anterior cingulate cortex (sgACC, x = -4, y = 28, z= -6) across all bereaved participants (Z= 3.11, p <.005, cluster size = 25).