HHS Public Access
Author manuscript
Biol Psychiatry Cogn Neurosci Neuroimaging. Author manuscript; available in PMC 2020 March 01.

Published in final edited form as:
Biol Psychiatry Cogn Neurosci Neuroimaging. 2019 March ; 4(3): 271–279. doi:10.1016/j.bpsc.2018.08.003.

Self-Generated Unconscious Processing of Loss Linked to Less Severe Grieving

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Abstract

Background: The intense loss processing that characterizes grieving may help people adapt to the loss. However, empirical studies show that more conscious loss-related thinking and greater reactivity to reminders of the deceased correspond to poorer adaptation. These findings raise the possibility that loss processing that is unconscious rather than conscious and self-generated rather than reactive may facilitate adaptation. Here, we used machine-learning to detect an fMRI signature of self-generated unconscious loss processing, which, we hypothesized to correlate with lower grief-severity.

Methods: 29 subjects bereaved within the past 14-months participated. Participants performed a modified-Stroop-fMRI-task using deceased-related words. A machine-learning-regression, trained on Stroop-fMRI data, learned a neural pattern for deceased-related-selective-attention (d-SA), the allocation of attention to the deceased. Expression of this pattern was tracked during a subsequent sustained-attention-fMRI-task interspersed with deceased-related thought probes (SART-PROBES). d-SA pattern expression during SART-PROBES blocks *without reported thoughts of*

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Financial Disclosures
Dr. Mann receives royalties for commercial use of the C-SSRS from the Research Foundation for Mental Hygiene. Dr. Sajda is the majority owner and Chairman of the Board of Neuromatters LLC, a brain computer interface neuromarketing and gaming company. Dr. Schneck, Dr. Shear, Dr. Bonnano, and Mr. Tu report no biomedical financial interests or potential conflicts of interests.

loss indicated self-generated unconscious loss processing. Grief severity was measured with the Inventory for Complicated Grief (ICG).

Results: d-SA expression during SART-PROBES blocks *without* conscious deceased-related thinking correlated negatively with ICG score (r_{25}=−0.711, p<0.001,95%CI: −.89 to −.42), accounting for 50% of variance. This relationship remained significant independently of demographic correlates of ICG (B_{25}=−30, t=−2.64, p=0.02, 95%CI=−56.2 to −4.6). Unconscious d-SA pattern expression also correlated with activity in dorsolateral prefrontal cortex and temporal parietal junction during the SART-PROBES (voxel-p<0.001, cluster-p<0.05).

Conclusions: Self-generated unconscious loss processing correlated with reduced grief-severity. This activity, supported by a cognitive-social neural architecture, may advance adaptation to the loss.

Keywords

Grieving; Unconscious; Mind-wandering; DLPFC; TPJ; Machine-Learning

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Early grieving is generally marked by increased mental engagement with the loss (1). This loss processing may help the bereaved reconstruct meaning, reformulate their relationship with the deceased and cope with the event of the death(2–6). Contrasting this view, empirical studies relate more loss processing with severe and unremitting grief (7–16). However, these studies identify loss processing through reactivity to reminders of the deceased or rumination. When loss processing manifests as reactivity or rumination it is perceptually-guided or conscious. Both of these attributes may account for the detrimental relationship with grieving observed in prior work.

When loss processing is perceptually-guided it occurs in reaction to explicitly presented reminders of the deceased (17–20). Such reactivity has been identified through attentional bias (12, 15, 21), neural responses (11), saccades (16) and approach-avoidance (22) and related to a poorer outcome. The content and timing of perceptually-guided loss processing depends on the external stimuli and may not reflect the elements of grieving that are relevant to the bereaved. Mental processing occurring independently of external stimulation can be described as self-generated rather than perceptually guided (17–20). Self-generated processing of the loss arises idiosyncratically and naturalistically and is therefore more likely to advance adaptation to the loss.

When loss processing gains conscious access, it is reportable, subjectively experienced, durable (23) and noticed as a thought or image related to the loss. Processing of the loss that is not subjectively experienced lacks conscious access and is therefore “unconscious”. Questionnaire studies relate more pronounced conscious loss processing with worse grief outcomes (7–10). Excessive thinking about the loss may represent rumination(8, 10, 16, 24, 25), which can detract from engagement in current life demands and future orientation (26). *Unconscious processing* may allow the bereaved to integrate the reality of the loss in parallel to engaging with current demands and without lapsing into ruminative cycles.

In summary, prior work has investigated manifestations of loss processing whose *content* and *context* may block or reverse its potential beneficial effects. When the *content* of loss processing is perceptually-guided it is dependent on external stimulation and may fail to incorporate the specific needs of the bereaved individual. When the *context* of loss processing is conscious it may lead to elaborative ruminative cycles, which detract from engagement in ongoing demands.

We therefore sought to identify loss processing as it occurred independently of ongoing stimulation, (i.e. self-generated), and without conscious access, (i.e. unconscious). To do this, we tracked self-generated unconscious processing of the loss in a sample grieving a recent death using a machine-learning based neural-decoding method. Neural decoding employs multivariate pattern analysis (MVPA) on a first set of fMRI data to learn a pattern of brain activity associated with a target mental process. This pattern serves as a decoder for a second set of data to track the occurrence of that mental process.

We first used MVPA to delineate a neural pattern weighting-matrix (i.e. *W*) representing deceased-related selective attention (d-SA), i.e. the allocation of attention to the deceased, using a modified Stroop task(13, 27). In this task, words reminiscent of the deceased are presented in different colors and subjects report the color of the word as fast as possible. Attention to the meaning rather than the color of the word comprises a parallel process which slows down reaction time (RT) to report the color(27, 28). When the words presented are reminders of the deceased, slower RT indicates greater allocation of attention to the deceased. While other processes may also influence RT to deceased-related words such as sustained attention, semantic processing, arousal or motor processing we controlled for these processes using task regressors and alternate Stroop conditions.

Hence, the model learned a pattern of fMRI activity predictive of longer RTs to deceased-related words (Figure 1A). This selective attention to the deceased occurs in parallel to the main task, which is to name the color of the word(27). While d-SA occurring during the Stroop task is not necessarily unconscious or self-generated, this type of parallelized allocation of attention to off-task deceased-related information likely occurs during self-generated unconscious processing of loss as well, in which some degree of attention to the loss is siphoned away from ongoing conscious activities to allow for unconscious loss processing. For this reason, d-SA, as identified through a Stroop task, can serve to track loss processing occurring during a second task.

We next used the d-SA pattern to decode neural activity during a 10-minute neutral sustained attention to response task (SART-PROBES(29)) in which interspersed probes queried deceased-related thinking (Figure 1B). The SART task provides a relatively non-stimulating environment that is optimized to promote mindwandering while maintaining low-level on-task focus (29, 30). While the thought probes presented during the SART may cue deceased related processing, we collected brain data occurring after the probe was presented and thus deceased-related processing during this time period is self-generated rather than perceptually guided (17). As a result, engagement of d-SA during blocks of SART-PROBES in which no thoughts of loss were reported implies processing of the loss that is both *unconscious and self-generated* (Figure 1C), which we hypothesized to be correlated with less grief severity.

Data from both the Stroop and SART have been used previously. Data from the Stroop task alone was used for a manuscript investigating attentional bias to the deceased(13). Data from the SART task was used to test the ability of a separate neural decoder to predict conscious thoughts(31). The present manuscript does not investigate attentional bias or conscious thought prediction. Rather we report a Stroop based neural decoder to interpret brain activity occurring during the SART task in the absence of conscious thoughts as a measure of self-generated unconscious processing of the loss.

Methods

Subjects and recruitment

Twenty-nine people bereaved of a first-degree relative or partner within 14 months were enrolled. Twenty were bereaved by suicide and had been recruited as part of a suicide bereavement study. Subjects were 18-65 years old, had normal color vision and native English speakers. Recruitment was done through postings on social media websites. Subjects were medically healthy as determined by medical history, examination and standard blood/urine tests. Exclusion criteria were current bipolar disorder (i.e. manic episode within the past year), current substance use disorder (i.e. met criteria within past six months), current obsessive-compulsive disorder, lifetime schizophrenia or schizoaffective disorder assessed with the Structured Clinical Interview for DSM-IV Axis I (SCID I(32)). Subjects taking psychiatric medications were required to be on a stable dose for two weeks prior to scanning. Subjects taking benzodiazepines or sleep medications refrained from using these medications for 72 hours prior to scanning. The New York State Psychiatric Institute IRB approved this study and all subjects gave written informed consent.

Procedure

Between 3 and 14-months post-loss, subjects underwent a pre-scan interview, an MRI scan and then a post-scan interview. Both interviews occurred within one week of the scan. Grief severity was measured with the Inventory for Complicated Grief (ICG(33)). During the pre-scan interview, subjects provided words describing the deceased and a relationship matched living control for use in the Stroop task. During the post scan interview subjects completed all structured interviews and questionnaires.

MRI

Full details of MRI imaging and preprocessing are provided in Supplemental Information.

Tasks

Deceased-Related Selective Attention (d-SA) Task—A Stroop task was used to define the neural pattern corresponding to d-SA. Across four runs, each run consisted of four blocks of words: deceased, living, congruent and incongruent. In deceased and living blocks the words provided by the subject describing the deceased and living attachments were presented in red, green or blue. In congruent blocks the words “red”, “green” and “blue” were presented in the corresponding colors. During incongruent blocks, the color words were presented in a different color. Subjects were instructed to indicate the color of the word font as quickly as possible. Task training and presentation is described in full in our prior work(13).

Sustained Attention to Response Task (SART-PROBES)—In the SART-PROBES, subjects pressed a button every time a number came on screen except for the number "3". Numbers were presented for 1.5s with an inter-trial jitter averaging 2s. The number 3 was presented 11 % of the time to ensure subject engagement. Trials were presented in blocks ranging from 25 to 35 seconds. Following each block, binary thought probes assessed thoughts about the deceased, the living control and the self, occurring in the past block. Subjects completed 16 blocks. This task provides low-level attentional engagement in the context of which, processing of loss can be self-generated unconsciously (29, 34) and is described fully in our prior work(31).

Analyses—This study involved three broad goals. **1.** Identify a neural pattern for d-SA based on MVPA analyses of the Stroop fMRI tasks. **2.** Track the continuous expression of d-SA during the SART-PROBES. **3.** Relate d-SA expression during blocks of the SART-PROBES without loss related thoughts (i.e. self-generated unconscious processing of loss) to grief severity.

Identifying a Neural Pattern for d-SA—Prior to learning a multivariate d-SA neural pattern, we first used a univariate analysis to identify a mask of voxels involved in d-SA. In the Stroop task, longer RTs to deceased-related words serve as a proxy for attention to the deceased. To identify voxels associated with d-SA we therefore correlated voxel-wise BOLD signal with longer RTs to deceased-related words (Deceased-related (BOLD X RT)).

This feature selection allowed us to control for button pressing, sustained attention and motor processing subtracted voxels correlation with reaction time to congruent words (Deceased-related (BOLD X RT)-Congruent (BOLD X RT)). To ensure that neural response to RT reflected attentional processing rather than neural reaction to the substantial semantic differences between deceased-related and color-congruent words, a trial level on/off regressor was included. We have previously shown that the process of d-SA likely comprises a subset within a broader process of attachment related attention(13, 35). As a result, the contrast of deceased-related *vs.* congruent, rather than deceased-related vs. living words was used. For this analysis we employed a threshold of voxel-$p<0.01$ and cluster corrected $p<0.05$. This lenient threshold was used for this preparatory analysis because in order to incorporate more information into the subsequent MVPA.

Pattern Learning—To develop the d-SA neural pattern, MVPA predicted RT to deceased-related words based on Stroop fMRI activity within the pre-specified mask. A spatial filter, represented by a weighting vector W, was developed to optimally predict d-SA by exploiting the relations between voxels within the pattern. This spatial filter W is optimized across multiple iterations of the prediction of RT. The W that best predicts RT is then selected as the pattern decoder. Full details of the MVPA are provided in supplemental information.

Tracking of d-SA Pattern Expression during the SART-PROBES—The decoder identified in the pattern-learning step was next applied to the SART-PROBES dataset. 4D time-series of SART-PROBES data were registered to standard space and motion effects were regressed out using 6-degree motion regressors. Each time series was standardized by its own mean and standard deviation. Blocks of SART-PROBES with errors (i.e. omission or commission) were excluded from subsequent analyses because of the potential effects of errors on metacognitive processes occurring during this task.

Pattern expression was estimated by applying the d-SA pattern decoder (i.e. *W*) to the SART-PROBES fMRI data. Model application entails voxel-wise multiplication of the *W* in the preselected feature masks with the values for the new BOLD data, followed by a linear summation across voxels. This produces TR-by-TR d-SA pattern expression. Greater d-SA pattern expression at a given time-point indicates higher neural similarity to slower Stroop trials and therefore higher likelihood that d-SA is occurring.

Unconscious Pattern Expression—We next calculated block-wise averages of d-SA pattern expression for each of the 16 SART-PROBES blocks. Each block was labeled as an intrusion or non-intrusion block based on whether or not the subject reported thinking about the deceased over the course of that block. Subject level averages of d-SA output were calculated for intrusion (i.e. conscious processing of loss) and non-intrusion (i.e. unconscious processing of loss) blocks separately. To account for the hemodynamic response delay we applied the model starting at the fourth TR following each probes period and into the second TR into the next probes period. Average d-SA expression taken from non-intrusion blocks was correlated with ICG score, a measure of grieving severity.

We refer to d-SA expression occurring during blocks of SART-PROBES with no reported thoughts of loss as “unconscious”. This delineation of unconscious is entirely based on the lack of conscious access which is identified by subjective report(23); and not rooted in the training or application of the d-SA pattern itself. While the d-SA pattern was trained during a conscious time period (i.e. the Stroop), its occurrence in the absence of subjectively experienced thoughts of loss denotes an unconscious processing of the loss.

Because the neural pattern was derived during the Stroop task which is conscious. It is possible that the derived pattern corresponds to conscious processing of the loss, which may be inherently related to ICG. To preclude this possibility we also calculated *conscious* d-SA expression from d-SA output during SART-PROBES blocks *with* reported thoughts of loss. A control analysis was conducted estimating the relationship between *conscious* d-SA and ICG. If d-SA were biased to be related to ICG than this analysis would yield a significant correlation as well.

Functional Neuroanatomy of Self-Generated Unconscious Processing of Loss—Finally, we sought to identify the functional neuroanatomy of self-generated unconscious processing of loss. We computed individual general linear models for each subject’s SART-PROBES fMRI data on residualized data that removed the effect of responding to SART trials and errors. Each model included a regressor for d-SA pattern expression, block label (i.e. intrusion/non-intrusion) and the interaction between the two (i.e. d-SA X intrusion/non-intrusion). A fixed effects analysis calculated average voxel activity associated with the interaction of d-SA and intrusion/non-intrusion label (voxel-p=0.001, cluster-p<0.05).

Results

Table 1 describes the sample demographics. The ICG mean score of 26.14 (SD=12.84) indicates generally severe grief, although scores had a wide range (1-50). Axis I disorders included, major depressive disorder and the following anxiety disorders: generalized anxiety disorder, post-traumatic stress disorder, and specific phobia. 10 subjects met criteria for CG on the basis of an ICG score of 30 or above and six months elapsed since loss(1). ICG score correlated with time since loss, income, a current diagnosis of major depressive disorder, number of previous depressive episodes, length of lifetime depression diagnosis, current psychiatric medication use, and PRN benzodiazepine/sleep medication use (not used for 72 hours before scan; Table 1).

d-SA Feature Selection and Pattern Learning

In the Stroop task, BOLD activation in lateral occipital cortex, temporal fusiform gyrus, subgenual cingulate, orbital frontal cortex, anterior insula among other regions correlated with slower deceased-related trial RT. Engagement of these regions in slower responses to deceased-related trials indicates involvement in d-SA. Subsequently, the d-SA pattern-learning algorithm predicted RT from the neural data within this mask ($p=10^{-3}$). This p-value may be artificially decreased due to the preselection provided by the univariate analysis. We only present this p-value to demonstrate that the MVPA was successful and therefore the derived W matrix can be relied upon. This analysis provided a spatially distributed neural pattern (i.e. W; Supplement Figure S1, Table S1) to be used for decoding the SART-PROBES data.

SART-PROBES

Two subjects did not complete the SART-PROBES due to time limit in the scanner. Of the 27 subjects who completed the SART-PROBES, 25 produced at least one block with no-intrusions or errors (Mean=7.6, Range=1-13, SD=3.39). One outlier value for d-SA fell outside of the interquartile range and was censored down to the next closest value. As previously reported, there was no significant relationship between intrusions and errors(31).

Self-Generated Unconscious Processing of Loss and Grief Severity

Higher average d-SA output during non-intrusion blocks i.e. self-generated unconscious processing of loss, correlated with lower ICG score, accounting for 50% of variance (Figure 2, $r_{25} = -0.711$, $p<0.001$, 95%CI: −.89 to −.42). By contrast, d-SA output during conscious intrusion blocks did not correlate with ICG scores ($r_{19}=-0.195$, $p=0.43$, 95%CI: −.61 to .34).

d-SA output during non-intrusion blocks accounted for 30% of the variance in ICG score when controlling for current diagnosis of major depressive disorder, number of previous depressive episodes, length of lifetime depression diagnosis, time since loss, psychiatric medication use, and household income ($B_{25}=-27$, $t=-2.44$, $p=0.02$, 95%CI=−50 to −3, Supplemental Table S2). To investigate potential effects of medication type we computed this regression while controlling for SSRI use as well as PRN usage of benzodiazepines or sleep medications (although subjects in this latter category had not used these medications for 72 hours), d-SA accounted for 55% of variability in ICG when controlling for these factors (B_{25}=−37, t=−4.56, p<0.001,95%CI=−55 to −20).

Within the suicide-bereaved sample alone, d-SA expression during non-intrusion blocks accounted for 53% of variance in ICG score (r_{18}=−0.73, p<0.001, 95%CI: −.91 to −.41, Figure S2). Nevertheless, the findings in the whole sample were not entirely driven by suicide bereavement as d-SA expression accounted for 44% of variance in ICG score when controlling for loss-type (B_{25}= −29.68, t=−4.29, p<0.001, 95%CI: −44.02 to −15.34, Supplement Table S3). These findings also remained when employing only the original 23 subjects whose data contributed to the training models (Figure S3).

Control Analyses

It is possible that the relationship between unconscious d-SA expression and ICG score was a function of directed *vs.* non-directed thinking rather than deceased-related processing. Control analyses accounted for directed thinking in the pattern training and expression steps respectively.

Directed thinking in the pattern-training step was identified by general selective attention (g-SA). In the Stroop task, g-SA is the difference in reaction time to incongruent vs. congruent color words(36). Responding to incongruent words involves more directed thinking and focus than responding to congruent words and therefore this pattern can delineate mental processing relating to effort and directed thinking. Hence an identical analysis was performed replacing deceased-related words for color incongruent words in the pattern-learning step. The derived g-SA pattern was next applied to SART-PROBES data and the resulting output from non-intrusion SART-PROBES blocks was calculated. g-SA pattern expression during non-intrusion blocks of the SART-PROBES did not correlate significantly with ICG score (r_{25}=0.26, p=0.20, 95%CI: −.16 to .61).

To control for directed thinking in the pattern expression step we extracted d-SA output during the SART-PROBES based on whether or not subjects had reported a *self*-related thought during a given block. Thoughts of the self, comprise a form of directed thinking occurring during the SART-PROBES aside from deceased-related thinking. d-SA output from SART-PROBES blocks with no reported *self-related* thoughts did not significantly correlate with ICG (r_{25}=−0.28, p=0.17, 95%CI: −.6 to .11).

Validation of d-SA Expression

In order to validate d-SA pattern expression during the SART-PROBES as a measure of deceased-related processing we calculated a paired samples t-test, comparing d-SA expression during blocks with and without conscious thoughts of loss. While a significant amount of processing may occur unconsciously it remains likely that, as a measure of deceased-related thinking, d-SA would be higher during blocks with conscious thoughts of loss. As expected, d-SA expression was higher during blocks with conscious thoughts of loss (M(SD)= −.09(.21)) than without (M(SD)=−.28(.21); Paired Samples t_{16}=−2.55, p=.02, 95%CI=−.32 to −.04).

Functional Neuroanatomy of Self-generated Unconscious Processing of Loss

During the SART-PROBES, greater d-SA activation during non-intrusion blocks correlated with BOLD signal in superior frontal gyrus (SFG), dorsolateral prefrontal cortex (DLPFC), superior parietal lobe (SPL) and temporal parietal junction (TPJ) amongst other regions (Figure 3, Table 2).

Discussion

We identified self-generated unconscious loss processing, by measuring ongoing fluctuations in a neural proxy of deceased-related selective attention (d-SA) during a neutral task. Engagement of d-SA during this task, in the absence of a conscious thought of the deceased, correlated with less severe grieving. These findings shed light on some of the unconscious and self-generated processes involved in grieving.

A central question in the bereavement field has been the role of “grief-work,” i.e. the painful experiences of grief and engagement with reminders of the deceased, in adaptation to the loss (2, 37). These experiences are thought to contribute to acceptance and adaptation to the reality of loss(2–6). At the same time, empirical work shows that greater reactivity to deceased-related stimuli and conscious thinking about the loss correspond with worse grief outcomes (7–12, 15, 21, 22). Self-generated unconscious processing of the loss may allow the bereaved to adapt to the reality of the loss, in a way that emphasizes their specific individual needs without becoming overwhelmed by loss-related thinking and rumination. This is the first study to date to assess this type of loss processing and consequently, one of the first studies to identify a relationship between loss processing and adaptation to the loss.

This interpretation posits self-generated unconscious loss processing as a dynamic element of the grief trajectory. This interpretation is made with the caveat that these findings are cross-sectional. Hence, self-generated unconscious processing may not influence the course of grieving at all but may simply be a trait of people with less severe grief. For example, prior episodes of depression which correlate to ICG score may also be a feature that plays a role in loss processing. Future longitudinal studies are needed to address the nature of self-generated unconscious loss processing as a trait or state characteristic.

The brain regions associated with self-generated unconscious processing of the loss are consistent with the roles of updating and modifying representations of the deceased. Regions involved in social processing and mental abstraction such as the TPJ, LOC and SPL might modify and update the representation of the deceased(38–40), while DLPFC might exclude this grief processing from consciousness(41). Nevertheless, these regions may simply reflect neural reaction to and regulation of representations of the deceased.

Unconscious and Self-Generated

During the SART-PROBES, thought probes occurred every 25-35 seconds. Hence, thoughts occurring early in the block may have been forgotten later on. As a result, pattern expression during a block labeled as a non-intrusion block may have occurred during a conscious intrusion. Nevertheless, the average of pattern expression was extracted for each block. Even if people forgot some of their conscious thoughts it is likely the case that, on average, non-intrusion blocks had fewer conscious thoughts than intrusion blocks. Pattern expression during non-intrusion blocks is thus *more likely to be unconscious* than pattern expression during intrusion blocks.

The SART combined with experience sampling, or thought probes, serves to assay self-generated processing(29, 30, 34). This type of processing occurs independently of the external environment (17). However, the label "self-generated" remains agnostic to the source of mental activity. While thought probes presented during the SART may have cued deceased related thinking, d-SA occurring in parallel to the SART trials was decoupled from the current perceptual environment and therefore self-generated.

Limitations

This study was conducted in a relatively small sample that used a cross-sectional design and findings require replication and validation in a larger longitudinal sample. Grieving is a dynamic process and a post-loss time-range of 3-14 months may have introduced heterogeneity into our sample that could be eliminated with a more constrained sample. While we controlled for mental processes potentially contributing to RT by contrasting with color-congruent words in the univariate analysis and incorporating a semantic regressor, a better control would be a non-attachment control person condition. We did not include formal measures of rumination, which would have allowed the parsing of the relationship between unconscious processing, and general and grief-related rumination.

Future Studies

This study presents an initial demonstration of how the d-SA pattern can be used to identify unconscious loss-processing in the absence of conscious thoughts of loss. Nevertheless, the relationship of this pattern to actual thoughts of loss remains unclear. Future studies should assess how well this pattern predicts thoughts of loss at the individual level in a real-time fMRI setting. This would further validate the d-SA pattern as a component of the conscious or unconscious processing of loss.

The univariate approach used for feature selection was chosen due to the lack of a strong body of knowledge regarding neural correlates of deceased-related attention. Nevertheless, this approach raises concerns of circularity as the MVPA repeats the univariate analysis. This is a limitation in the present study. A more rigorous approach would be to adopt a leave-one-out training procedure for both the univariate and multivariate analyses. Given the small size of the sample and the lack of preexisting knowledge about deceased-related attentional processes we adopted the current approach. Future studies in larger samples can use a more hypothesis driven approach by adopting the weighting matrix presented here in a directed fashion or employing leave-one-out procedures throughout all training steps.

Conclusions

This study identified self-generated unconscious loss processing through expression of a neural pattern for deceased-related attention during a neutral task in the absence of reported thoughts of loss. Greater self-generated unconscious processing of loss correlated with less grieving severity; and concurrent neural activity in TPJ and DLPFC indicating a combination of social processing and conscious control. A longitudinal study can test whether such processing facilitates more successful adaptation to the loss.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was funded by a Distinguished Investigator Grant (DIG-0-163-12) (JJM) and a Young Investigator Grant (YIG-0-215-13) (NS) from the American Foundation for Suicide Prevention. NS was supported by a National Institute of Mental Health T32 Training Grant in Anxiety and Related Disorders (T32-MH020004-16). Dr. Shear receives funding from the Department of Defense and the New York Life Foundation.

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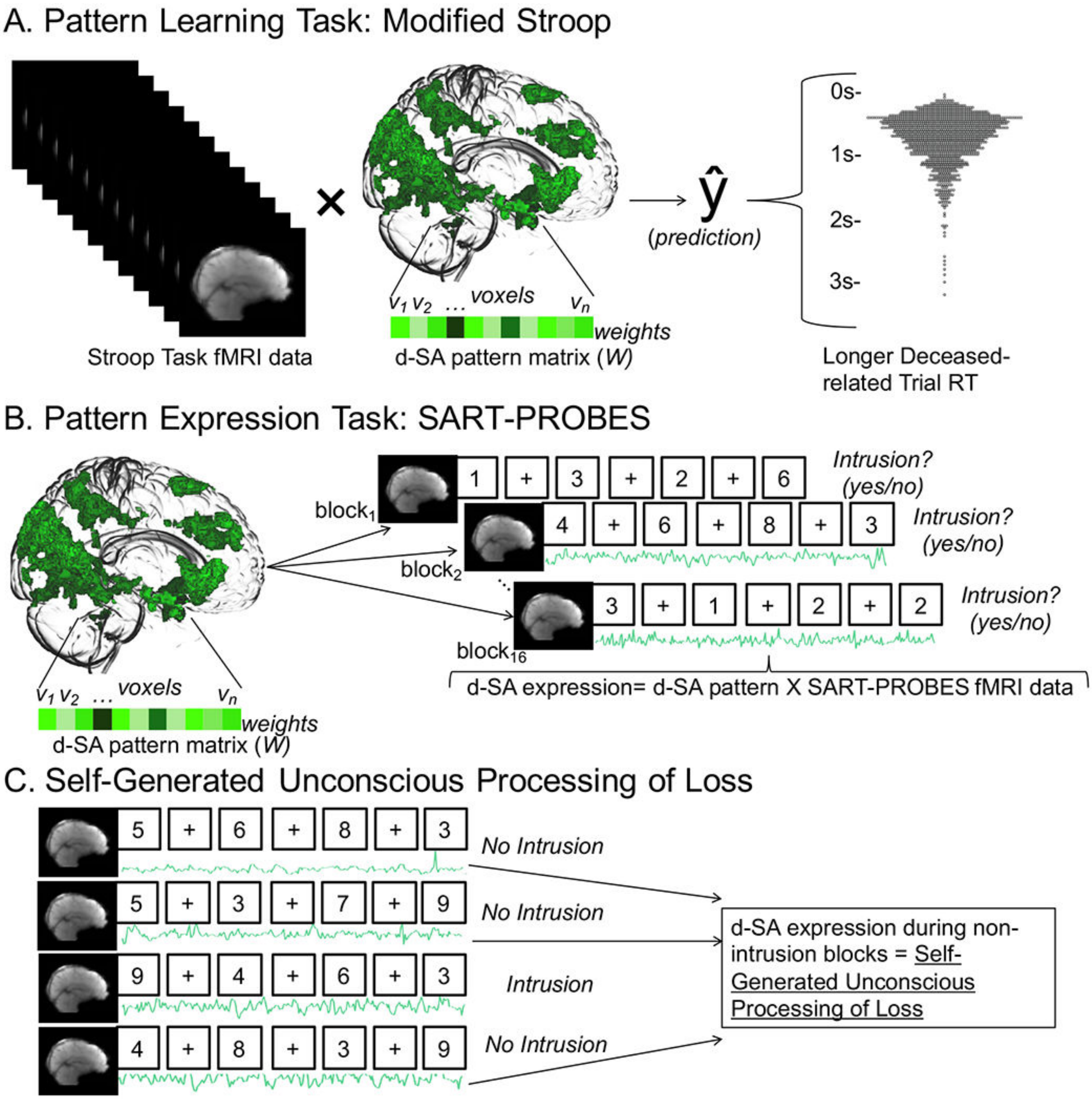

Figure 1. Identifying Self-Generated Unconscious Processing of Loss.

A. A modified Stroop fMRI task was used to learn a neural pattern corresponding to deceased-related selective attention (d-SA). To do this, a machine learning regression delineated a voxelwise d-SA weighting matrix (green) that optimized the prediction of longer reaction times to deceased-related words from trial level Stroop fMRI data. **B.** Subjects completed 16 blocks of an extended neutral sustained attention task (SART-PROBES). During this task they were instructed to push a button everytime they saw a number except for the number "3", intermittent probes assessed the occurrence of a thought about the deceased, i.e. an intrusion. The d-SA weighting matrix identified in the prior step was applied to fMRI data produced during the SART-PROBES. Expression of the d-SA neural pattern indicated the similarity between SART-PROBES neural data at each time point and the neural pattern associated with slower Stroop trials (green oscillations). This served as an ongoing measure of d-SA transpiring during the SART-PROBES. **C.** Expression of the d-SA neural pattern during SART-PROBES blocks without reported thoughts of loss was taken as a measure of self-generated unconscious processing of the loss.

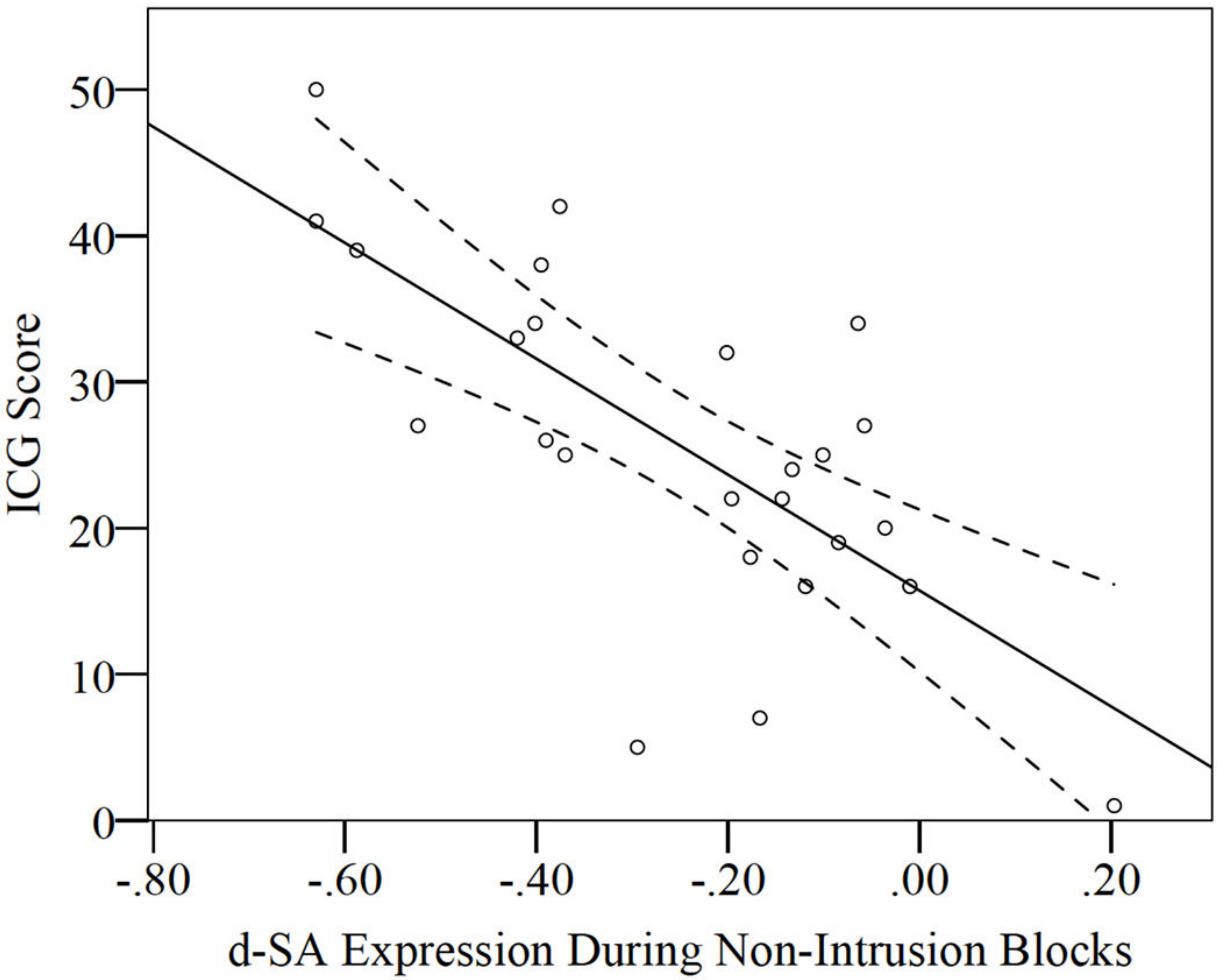

Figure 2. Grief Severity and Self-Generated Unconscious Processing of Loss.

d-SA expression during non-intrusion blocks of the SART-PROBES task (i.e. self-generated unconscious processing of loss) correlated inversely with grief severity as measured by the Inventory for Complicated Grief. Dotted lines display 95%CIs.

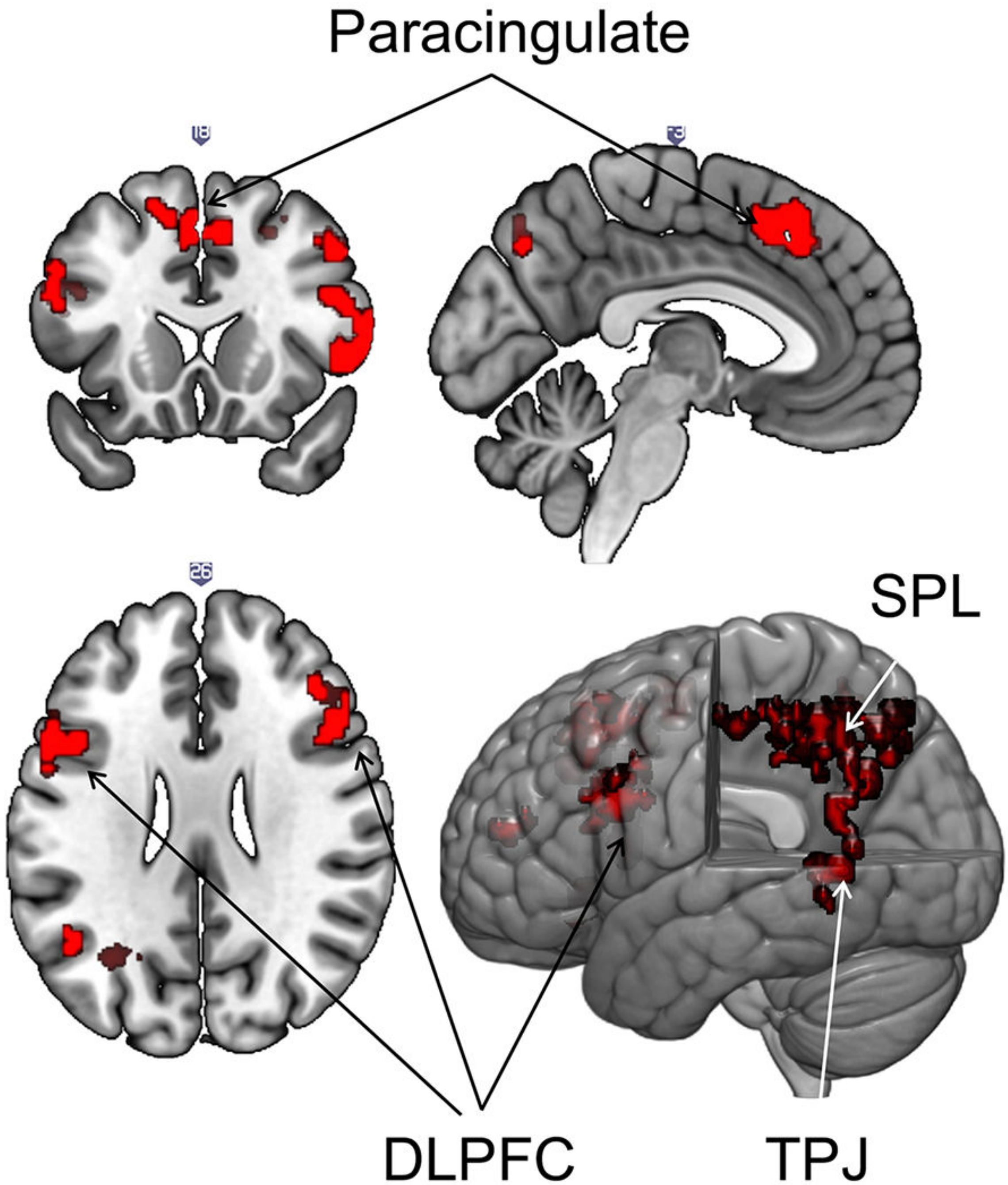

Figure 3. Clusters Engaged by Self-Generated Unconscious Processing of Loss.

Voxel clusters whose BOLD activity during non-intrusion blocks of the SART-PROBES correlated with greater d-SA pattern expression (i.e. self-generated unconscious processing; voxel-p <0.001, cluster-p<0.05). Multi axial image centered on mm coordinates (XYZ)=16, −3, 26. SPL=superior parietal lobe, DLPFC=dorsolateral prefrontal cortex, TPJ= temporal parietal junction.

Table 1.

Sample Description (N=29)

	M	SD	Correlation with ICG
Age	44	13	−.26
Months Since Loss	8.06	3.79	.64**
Education years	16.44	1.9	.05
	N	%	
Household Income			−.39*
>$70,000	18	62.1	
$60,000-$69,000	6	20.7	
$50,000-$59,000	1	3.4	
$30,000-$39,000	4	13.8	
Single	11	37.9	.19
Males	6	20.7	−.25
Current Major Depressive Disorder	10	34.5	.63**
Years Since First Diagnosis, range	1-36		.49*
Prior Depressive Episodes			.45*
0 Episodes	14	48.3	
1 Episode	7	24.1	
2 Episodes	4	13.8	
3 Episodes	2	6.9	
5 Episodes	2	6.9	
Current Anxiety Disorder	5	17	.17
Current Psychiatric Medication Use	10	34.5	.51**
SSRI	6	20	.14
Atypical Antipsychotic	2	6	n/a
Bupropion	1	3	n/a
Anticonvulsant	1	3	n/a
SSNRI	1	3	n/a
PRN usage of Benzodiazepines or Sleep Medications+	7	24	.51**

* p<.05

** p<.01

ICG= Inventory for Complicated Grief, Household income was coded with five interval levels of >$70,000, $60-$69,000, $50-$59,000, $40,000-$49,000, and $30-$39,000. Psychiatric medication use was coded as a binary variable corresponding to whether or not a subject was currently using a psychiatric medication. SSRI= Selective Serotonin Reuptake Inhibitor, SSNRI= Selective Serotonin Norepinephrine Reuptake Inhibitor.

+.Subjects with a PRN prescription of benzodiazepines or sleep medications refrained from using these medications for 72 hours prior to scanning

Table 2.

Clusters Associated with Self-generated Unconscious of Loss

	Cluster Center (XYZ)			Voxel #	Average Z-Score
Angular Gyrus	44.13	36.18	55.88	272	3.48
Frontal Operculum	20.82	71.82	36.18	11	3.42
Frontal Orbital Cortex	20.67	78.25	29.19	64	3.48
Frontal Pole	49.90	85.59	43.75	108	3.38
Inferior Frontal Gyrus	36.21	71.55	44.48	368	3.45
Lateral Occipital Cortex	53.80	29.54	57.19	406	3.67
Middle Frontal Gyrus (DLPFC)	26.14	71.09	56.78	772	3.56
Middle Temporal Gyrus (TPJ)	75.55	35.60	38.77	110	3.47
Paracingulate Gyrus	44.84	73.77	58.56	261	3.52
Postcentral Gyrus	67.45	48.29	62.33	82	3.36
Precentral Gyrus	51.38	64.51	55.65	130	3.30
Precuneous	46.36	27.02	57.90	91	3.36
Superior Frontal Gyrus	44.47	74.50	61.35	273	3.54
Superior Parietal Lobule	62.63	37.52	60.96	245	3.73
Supramarginal Gyrus	53.96	41.35	59.19	214	3.49

Clusters whose BOLD activity during non-intrusion blocks of the SART-PROBES task correlated with d-SA pattern expression (voxel-$p<0.001$, cluster-$p<0.05$). This analysis controlled for the main effects of both d-SA expression and reported thoughts of loss. These results reflect the interaction of d-SA expression with reported thoughts of loss. Specifically, these clusters were engaged by higher d-SA expression when no thoughts of loss were reported.