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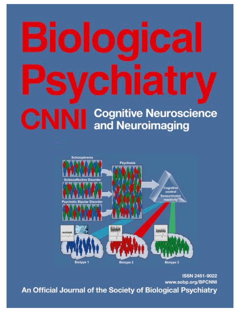

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PII: S2451-9022(24)00246-5

DOI: https://doi.org/10.1016/j.bpsc.2024.08.011

Reference: BPSC 1287

To appear in: *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*

Received Date: 12 April 2024

Revised Date: 16 July 2024

Accepted Date: 6 August 2024

Please cite this article as: Herzog S., Schneck N., Galfalvy H., Hwei-Choo T., Schmidt M., Michel C.A., Sublette M.E., Burke A., Ochsner K., Mann J.J., Oquendo M.A. & Stanley B.H., A Neural Signature for Reappraisal as an Emotion Regulation Strategy: Relationship to Stress-Related Suicidal Ideation and Negative Affect in Major Depression, *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (2024), doi: https://doi.org/10.1016/j.bpsc.2024.08.011.

A Neural Signature for Reappraisal as an Emotion Regulation Strategy: Relationship to Stress-Related Suicidal Ideation and Negative Affect in Major Depression

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Abstract

Background: Impaired emotion regulation (ER) contributes to major depression, and suicidal ideation (SI) and behavior. ER is typically studied by explicitly directing participants to regulate, but this may not capture depressed individuals' spontaneous tendencies to engage ER in daily life.

Methods: In *N*=82 participants with major depressive disorder (MDD), we examined the relationship of spontaneous engagement of ER to real-world responses to stress. We used a machine learning-derived neural signature reflecting neural systems underlying cognitive reappraisal (an ER strategy) to identify reappraisal-related activity while participants recalled negative autobiographical memories under the following conditions: 1) unstructured recall; 2) distanced recall, a form of reappraisal; and 3) immersed recall (comparison condition). Participants also completed a week of ecological momentary assessment (EMA) measuring daily stressors, suicidal ideation (SI), and negative affect.

Results: Higher reappraisal signature output for the unstructured period, a proxy for the spontaneous tendency to engage ER, was associated with greater increases in SI following stressors (b=0.083, p=0.041). Higher signature output for distanced recall, a proxy for the capacity to engage ER when directed, was associated with lower negative affect following stressors (b=-0.085, p=0.029). Output for the immerse period was not associated with EMA outcomes.

Conclusions: Findings suggest that, in MDD, the spontaneous tendency to react to negative memories with attempts to reappraise may indicate greater reactivity to negative cues; while intact capacity to use reappraisal when directed may be associated with more adaptive responses to stress. These data have implications for understanding stress-related increases in suicide risk in depression.

Introduction

Emotion regulation (ER), the process whereby emotional responses are modulated in order to meet situational demands and personal goals(1), contributes to psychological well-being. Impaired ER is implicated in mood- and anxiety-related psychiatric disorders including major depression(2, 3), and a growing body of literature suggests that suicidal ideation and behavior are likewise associated with ER deficits(4, 5). However, while the nature of ER deficits in depression are relatively well-characterized(6-9), research on suicide-related ER deficits lacks similar granularity. The preponderance of such studies employ self-report measures of global impairments in ER(10), and few empirical studies characterize the specific nature of ER deficits that lend vulnerability toward suicide risk.

Perhaps the most well-researched emotion regulation strategy is *cognitive reappraisal*, which involves changing one's interpretation of the meaning of a stimulus to alter its emotional impact(11). Cognitive reappraisal is effective at down-regulating negative affect(12, 13), and diminishes the relationship between mental pain and suicidal ideation (SI)(14). Notably, most behavioral studies of cognitive reappraisal in depressed and suicidal cohorts utilize structured tasks that explicitly prompt participants when and how to regulate emotions(15). Such tasks were developed for first-generation ER studies to ensure that observed changes in brain activity and behavior were related to engagement of self-regulatory mental processes(16-18). These studies usefully elucidated the behavioral consequences of various ER strategies and their underlying neural mechanisms(19). However, these directed behavioral tasks may not be informative about how ER is engaged in daily life, which usually occurs in an undirected, spontaneous fashion(20), without conscious goals to alter emotional reactions(21). Directed behavioral tasks can gauge an individual's *capacity* to engage ER when instructed, but may not reflect their natural spontaneous tendency to engage ER under ordinary circumstances.

Meaningful individual differences in the spontaneous tendency to engage ER may be of important clinical relevance to suicidal populations. Depressed participants with SI perform comparably to healthy volunteers when explicitly instructed to regulate(9), but report greater difficulty employing ER(4). This observation suggests that individuals with SI have the capacity to regulate emotions upon instruction in the laboratory, but may be less likely to engage these regulatory strategies in daily life(22). Consistent with this interpretation, less frequent use of cognitive reappraisal has been linked with higher levels of past-week SI in psychiatric inpatients with mood disorders(23). Conversely, a tendency toward greater reappraisal is associated with reduced risk of suicidal behavior(24). The literature also suggests that cognitive reappraisal is important to the regulation of emergent suicide risk in the context of stress in depressed individuals. A month-long ecological momentary assessment (EMA) study in depressed patients showed that greater use of cognitive reappraisal attenuated the relationship between daily stress levels and same-day SI(25). While cognitive reappraisal appears to be useful for mitigating suicide risk, no study has assessed–either behaviorally or neurally–whether the emergence of SI in depressed individuals is linked to their spontaneous tendency to use cognitive reappraisal.

The aim of the current study was to quantify the tendency to engage an ER strategy of reappraisal in depressed adults, and assess how reappraisal is associated with real-world suicide-related responses to stress. To address this aim, we leveraged a neural signature for reappraisal that we developed and validated in a previous study(26). This signature was derived using a two-step multi-voxel pattern analysis (MVPA) trained on task-based fMRI data to identify a pattern of neural activity associated with directed attempts at cognitive reappraisal(26). The neural signature allows for quantification of cognitive reappraisal without the limitations of self-report measures, which are subject to incomplete/biased recall and constrained by level of insight into emotional experience(27); and without relying on indirect behavioral measures (e.g., reaction time or decision-making, assumed to be the products of successful regulation(28)). Another benefit of the neural signature is that it overcomes the need to explicitly instruct participants to regulate, and therefore allows assessment of the natural tendency to engage reappraisal.

In the present study, the signature was used to detect and quantify engagement of neural mechanisms supporting reappraisal while participants recalled negative autobiographical memories. Reappraisal was quantified 1) under unstructured recall conditions, as a proxy for the spontaneous tendency to engage reappraisal, 2) in response to explicit instruction to engage reappraisal using a distancing strategy, and 3) in response to explicit instruction to immerse in the memory. Participants completed a seven-day ecological momentary assessment (EMA) period in which they reported on stressors, SI, and negative affect up to six times daily. Based on prior work linking mood disorders to deficits in spontaneous ER(6, 29), we hypothesized that signature output during the unstructured recall period would be associated with lower stress-induced increases in SI and negative affect.

Methods and Materials

Sample

The sample consisted of 82 participants with major depressive disorder (MDD), 33 of whom were part of the training sample in which the neural signature was initially derived (see Schneck, et al 2022Schneck, Herzog (26) for a full description of the training sample). All participants were screened to confirm English reading fluency, normal or corrected-to-normal vision, and absence of conditions contraindicated for MRI. Study procedures were approved by the Institutional Review Board at the New York State Psychiatric Institute.

Clinical Assessment. Psychiatric diagnoses were established using the Structured Clinical Interview for DSM-IV(30), conducted by doctoral- or masters'-level psychologists. Depression severity was quantified with the 24-item Hamilton Depression Rating Scale (HDRS-24).

Inclusion/exclusion criteria. Depressed participants met criteria for a current major depressive episode, were between ages 18-65 years, and were medication-free for ≥21 days at the time of scan. The medication washout protocol, which was performed as part of participants' participation in a Positron Emission Tomography (PET) study of serotonin $(5\text{-HT})_{1A}$ autoreceptor binding, involved a one-week medication taper and three weeks off any medication that affects the serotonergic system. Exclusion criteria consisted of: 1) lifetime psychosis; 2) substance/alcohol abuse (past 2 months), or past-year substance/alcohol dependence; 3) past-year anorexia nervosa or bulimia nervosa; 4) lifetime intravenous (IV) drug use; 5) greater than 3 lifetime incidents of 3,4-methylenedioxy-methamphetamine (MDMA) use; 6) first-degree family member with schizophrenia (for participants under age 33); 7) significant active physical illness; 8) electroconvulsive therapy in the past 6 months (ECT); 9) previous head trauma with loss of consciousness or cognitive impairment.

Ecological Momentary Assessment (EMA)

The EMA period spanned seven consecutive days during which participants reported on SI, stressors, and negative affect six times daily (see Table S1 for prompts) on a personal device. Prompts were presented at random intervals within 2-hour epochs over a 12-hour wake period customized to each participant(31). This ensured that a participant's fixed schedule (e.g., sleep) did not interfere with data collection on a regular basis.

Total scores for EMA SI were computed by summing responses to the nine SI items within that same epoch, yielding a time-varying (lagged) total SI score. Change in SI at a given time *t* (e.g., epochs with stressors) was computed as the difference between the SI score at time *t* and the SI score at the previous epoch, (*t*-1), as long as both observations occurred on the same day. Change in negative affect was calculated in a similar manner. A time-varying stress indicator was also computed to identify epochs with vs. without stressors, denoted as "Yes/No." SI change following epochs with stressors was regarded as stress-reactive SI.

Neural Signature Development

To identify a neural signature reflecting engagement of reappraisal-related processes, we employed a multi-step procedure involving two separate fMRI tasks (see Figure 1 for a depiction of signature development). As reported in Schneck (2022)Schneck, Herzog (26), a linear classifier was trained on fMRI data collected during the course of a image-based reappraisal task(19). The classifier identifies a pattern of spatially distributed neural activity associated with trials for which participants were instructed to reappraise, versus a condition where participants were instructed to look at images and respond naturally. This image-based neural signature was validated within the same training sample in a separate "testing" dataset comprised of fMRI data collected during recall of negative autobiographical memories (task described below). This demonstrated that the signature was associated with reappraisal activity in a separate task, and that it was not overfit to the stimuli characteristics of the image-viewing task.

In the current study, the classifier, or neural signature, was applied to a larger sample of depressed participants who completed the both autobiographical memory task and a week-long ecological momentary assessment of stress, suicidal ideation, and negative affect.

fMRI Task

Autobiographical Memory Task. In a pre-scan interview, participants provided eight personal negative memories of events that had occurred within the last six months, and generated 2–4 words per event to be used as cues to elicit those memories. Before scanning, participants were tested to confirm that they could recall their memories with the cues provided. All trials began with a 10s presentation of a memory cue, and this comprised the unstructured recall period. After the initial 10s, and a brief jittered interstimulus interval, participants were directed to either "distance" or "immerse" while continuing to recall the memory for another 10s. On immerse trials, participants recalled their negative memories from a first-person perspective, allowing recollected events to unfold naturally ("as if re-living the event through your own eyes"). On distance trials, participants recalled their memories from a fact-focused, 3rd-person perspective ("as if watching events unfold from the viewpoint of a camera"). In prior work using this paradigm, distance trials were associated with lower negative affect relative to the immerse condition(26, 32, 33), supporting use of distancing as a reappraisal strategy that can be used to down-regulate negative emotion(34-36). See Figure 1 for a depiction of task structure. Participants were trained on the autobiographical memory task prior to scanning.

Each of 8 memories were recalled twice, once for distanced and once for immersed trials, in counterbalanced order across participants. After each distance or immerse trial, participants rated their negative affect and memory vividness. Trials were followed by a 26s active baseline task in which participants indicated the direction of arrows on the screen, to provide a perceptual baseline condition that was not emotion-focused and did not involve recall(37). The task was completed in 4 runs of 4 trials each, approximately 8.5 minutes total duration.

Image acquisition. fMRI scans were conducted with small variations in scanning protocols. See *Supplemental Methods* for details on image sequence parameters and MR preprocessing steps. For all participants, runs began with an 8-second fixation, and the corresponding four volumes were discarded. During functional scanning, task stimuli were viewed on an MR-compatible back-projection screen seen in a mirror mounted atop the headcoil. Stimuli were presented using E-prime software (Psychology Software Tools, Inc.) on a PC computer. Affect ratings were collected using a MR-compatible 5 button response box.

Application of Neural Signature

The neural signature was applied to the autobiographical memory task data within the same prespecified ventral-frontal mask used to train the signature (see *Supplement* for the description and rationale of the mask used). The classifier was applied to two distinct periods of all trials: 1) an unstructured 10s recall period at the beginning of each trial, and 2) the subsequent 10s during which participants were directed to use distanced recall or immersed recall (see Figure 1). Application of the neural signature entailed voxelwise multiplication of the weighted vector from the image-based task with the values for BOLD data collected during the autobiographical memory task, followed by a linear summation across voxels. Neural signature output is continuous and reflects the degree to which fMRI activity during the memory task is similar to the voxel pattern associated with reappraisal trials on the image-based task. See the *Supplemental Methods* section for a detailed explanation of how the signature was trained and validated.

Statistical Analyses

Auxiliary analyses. Condition-wise differences in signature output were probed with longitudinal mixed effects linear models. Models featured TR-by-TR signature output as the outcome variable, condition (unstructured/distance/immerse) as a categorical predictor, and participant-specific random intercepts. Models covaried for task run number (1-4), trial number (1-4), and average BOLD signal. A similar model was used to assess the relationship between affect ratings on TR-by-TR signature output, and included a main effect for affect rating (continuous) and a condition-by-affect rating interaction term.

Data preparation. Since EMA data are longitudinal (i.e., repeated), neural signature output values were reduced to participant-level averages for models examining associations between signature output and EMA outcome variables. First, to account for the potential influence of fluctuation in overall BOLD signal over time, signature output values were residualized on the average BOLD signal using a generalized least squares regression model featuring an AR(1) within-participant correlation structure. Participant-level mean values for the residualized signature output were calculated separately for unstructured recall, distance trials, and immerse trials.

Primary analyses. Three separate models examined the respective effects of participant-level average neural signature output for unstructured, distanced, and immersed recall on EMA-assessed change in suicidal ideation following epochs with vs. without stressors. The first of those models (unstructured recall) was the main analysis of interest, and the latter two were conducted for purposes of comparison. Longitudinal mixed effects linear regression models featured EMA-assessed SI change as the outcome variable and participant-specific random intercepts. Predictors included neural signature output (continuous) and the time-varying EMA stress indicator (stressor vs. non-stressor epochs) as main effects, and an interaction term for signature output-by-stress. In order to model change in ideation, the model included a time-lagged SI total score as a covariate, reflecting average ideation at the previous epoch.

We examined the effect of neural signature output on EMA-assessed change in negative affect in a similar manner to SI. The abovementioned three models were replicated while substituting the outcome variable for negative affect change. The time-lagged total SI score was replaced with a time-lagged negative affect score.

All aforementioned models included a binary covariate representing scanning protocol to account for differences in fMRI sequence and participation in the training sample. Standardized beta coefficients are reported for all models.

Results

Sample characteristics

Participants were recruited as part of a study on biomarkes of suicide risk in depression, and the sample was enriched for suicidal behavior. The sample (*N*=82) had a mean age of 30.2 years (SD=8.9), was largely female (64.6%), and most had higher education (91.5%). Participants self-identified as Asian (17.1%), Black/African American (22.0%), Hispanic (29.3%), and White (45.1%). Participants were moderately to severely depressed (mean BDI 25.6 ± 8.2), and 45.0% of the sample reported a prior suicide. See Table 1 for a description of sample demographic and clinical information.

Ecological momentary assessment (EMA)

The mean number of epochs with responses per participant was 31.8 (*SD*=10.2), reflecting a completion rate of 75.7%. On average, participants reported experiencing stressors during 45.7% of EMA epochs. The occurrence of stressors (binary) was associated with increases in SI relative to ideation level during the previous epoch, b=0.331, SE=0.05, p<0.001. A similar pattern was evident for the impact of stressors on negative affect, b=0.720, SE=0.05, p<0.001. See Figures S3 and S4 in the Supplement for a graphical depiction of SI, negative affect, and stress reported across the EMA period.

Autobiographical memory task

Mixed linear models with random subject-level intercepts indicated that neural signature output was greater on distance compared with immerse trials in the memory task (b=0.006, SE=0.002, p<.001). Output did not differ on distance trials compared with the unstructured recall period (b=0.002, SE=0.001, p=.118; see Table S2 for descriptive statistics). Participant-level average output on distance and immerse trials were positively correlated, Pearson's r=.265, *p*=.016. Average output from the unstructured period was not correlated with distanced recall output (*r*=-.127, *p*=.256) but was negatively correlated with immersed recall output (*r*=-.319, *p*=.003).

Memory task affect ratings. Participants reported greater negative affect on post-trial affect ratings for immerse trials compared with distance trials (*b*=0.671, *SE*=0.02, *p*<.001). Higher negative affect ratings were associated with lower ER signature output (*b*=-0.002, *SE*=0.001, *p*=.002) regardless of condition (*b*=0.000, *SE*=0.000, *p*=.839).

Neural signature output and EMA

Unstructured recall. Results of the mixed linear model indicated no main effect for ER signature output for the unstructured recall period on change in EMA SI (*b*=0.040, *SE*=0.12, *p*=.736, 95% CI -0.196; 0.276). There was an interaction between signature output and the EMA stress indicator, wherein greater ER signature output during the unstructured period was associated with greater increases in SI in the context of stressors, *b*=0.083, *SE*=0.04, *p*=.041, 95% CI 0.003; 0.162.

There was no main effect of ER signature output during unstructured recall on EMA negative affect change (*b*=-0.049, *SE*=0.10, *p*=.638, 95% CI -0.254; 0.157), and no interaction for ER signature relationship to negative affect change by presence or absence of EMA stress (*b*=0.019, *SE*=04, *p*=.625, 95% CI -0.056; 0.093).

Distanced recall. There was no relationship between ER signature output during distance trials and EMA SI change (*b*=-0.004 *SE*=0.12, *p*=.976, 95% CI -0.240; 0.247), and no interaction between signature output and SI change due to presence or absence of EMA stress (*b*=0.028, *SE*=0.04, *p*=.491, 95% CI -0.053; 0.109).

There was no main effect of signature output during distance trials on EMA negative affect change (*b*=-0.163, *SE*=0.11, *p*=.127, 95% CI -0.373; 0.047). There was an interaction between signature output and EMA stress on negative affect change such that higher ER signature output was associated with attenuated increases in negative affect in the context of stress (*b*=-0.085, *SE*=0.04, *p*=.029, 95% CI -0.009; -0.161).

Immersed recall. There was no main effect of signature output during immerse trials on EMA SI change (*b*=-0.122, *SE*=0.13, *p*=.340, 95% CI -0.376; 0.131), and no interaction based on presence or absence of EMA stress regarding the relationship between signature output and SI change (*b*=0.016, *SE*=0.06, *p*=.764, 95% CI -0.091; 0.124).

There was also no main effect of signature output during immerse trials on EMA negative affect change (*b*=-0.094, *SE*=0.11, *p*=.403, 95% CI -0.316; 0.128), and no interaction for signature output by EMA stress on negative affect change (*b*=0.013, *SE*=0.05, *p*=.796, 95% CI -0.065; 0.137).

Discussion

We aimed to understand whether engagement of an ER strategy of cognitive reppraisal by depressed individuals was related to the emergence of SI and negative affect in response to real-world stressors. We found that reappraisal neural signature output for the unstructured period was associated with *greater* increases in SI following stressors, and was not associated with negative affect. Conversely, signature output for the distanced recall period was associated with *lower* negative affect following stressors, and not associated with SI. Thus, the spontaneous tendency to reappraise during exposure to negative memories was related to more pronounced SI in response to stressors, while greater use of reappraisal when directed was associated with less acute negative affective responses to stress. Since the unstructured recall period consisted of the first 10 seconds of exposure to the memory cue, the positive association between signature output during unstructured recall and more acute SI following stressors might imply that stress-sensitive individuals attempt to dampen initial emotional responses to upsetting cues. This could perhaps be due to depressed individuals' difficulty managing negative reactions. Indeed, vulnerability to SI in depressed individuals is associated with non-acceptance of negative emotions(38) and frequent use of ineffective or detrimental emotion regulation strategies(23, 39, 40). Reduced confidence in the ability to effectively cope with negative emotions may result in attempts to regulate emotional reactions even in instances when the stakes are relatively low, as is the case in the current study; or when regulation may not be advantageous or functional(13, 29).

This study is one of the first to neurally quantify both the spontaneous tendency of depressed adults to engage cognitive reappraisal, as well as the capacity to reappraise when directed. The tendency vs. capacity to regulate is a distinction that has only more recently entered the discourse on ER(41, 42). The importance of this distinction to clinical outcomes is underscored by evidence suggesting that the tendency to regulate more closely captures individual variation in ER than capacity to regulate(22). In the current study, neural signature output for unstructured and distanced recall periods were not correlated, supporting their distinction as separate constructs. Our findings suggest that the capacity of depressed individuals to engage reappraisal when instructed may be a positive prognostic indicator of their ability to cope with stress in daily life, while the spontaneous tendency to engage reappraisal under conditions of benign risk (as in the autobiographical memory task) may reflect a general tendency toward experiencing negative cues with a greater sense of threat. That is to say, greater sensitivity to a relatively benign negative stimulus may provoke both increased efforts at regulation and greater increases in SI in response to daily stress. Relatedly, our finding that spontaneous engagement of ER was associated only with stress-related SI but not negative affect may be reflect to a general tendency toward engaging maladaptive methods of coping. Suicidal ideation has been understood by clinical theorists as an attempt at coping with psychological pain or problem-solving difficult circumstances(43). This understanding is central to the theoretical approach of prominent evidence-based interventions for suicide risk(44). It is possible that individuals who spontaneously regulate their emotional reactions may be more likely to cope with stress through suicidal ideation, but do not necessarily experience stress with heightened negative emotion.

The distinction between tendency vs. capacity for reappraisal may help to bridge seemingly divergent findings in the literature on ER in depressed populations. Depressed individuals report higher daily stress and negative emotion compared with non-depressed individuals(45, 46) and exhibit difficulty with the cognitive inhibition of negative emotion(2), but demonstrate comparable performance with healthy individuals on directed tasks of ER(26). There is also evidence to suggest that depression-related deficits in inhibitory control are associated with a lower tendency to use cognitive reappraisal(2). Potentially, depressed individuals have the capacity to compensate for inhibitory control deficits when reappraising in the laboratory, but such deficits may discourage spontaneous use of reappraisal in daily life. Another explanation for divergence between self-reported difficulties in ER and lab-based measures of ER in depression is that lab-based tasks may not be sufficiently potent (as compared with real-world stressors) to distinguish between depressed versus healthy individuals.

We note that the neural signature for reappraisal used here was limited to ventrolateral prefrontal regions involved in general cognitive control (see Supplement), and therefore the signature may capture processes that are not uniquely involved in reappraisal *per se*, but related to other forms of cognitive effort governed by this brain region. Some such forms of cognitive effort include selective attention, or the effortful selection between competing mental representations. However, prior literature suggests that many cognitive forms of emotion regulation, like reappraisal, do not depend on processes entirely distinct from those involved in the cognitive control of attention or memory, but rather reflect cognitive control exerted in the context of emotional distress(19, 47). In addition to reappraisal, another coping mechanism that involves applying cognitive effort in the context of distress is rumination, which is a maldaptive regulation strategy implicated in the maintanence of depression(48). In the current study, signature output for the immerse period, which approximates ruminative activity, was unrelated to EMA-assessed suicidal ideation and negative affect. This may lend further support to the neural signature as an indicator of reappraisal.

A potential limitation of the current study is that the neural signature was developed using a task wherein participants were explicitly prompted to reappraise, and it can therefore be argued that signature output better reflects neural systems associated with explicit regulation, i.e., consciously engaged or controlled reappraisal. However, whether participants deployed reappraisal during the unstructured memory period in an explicit or implicit manner (i.e., consciously aware of a goal to regulate or without awareness of such a goal(21)) cannot be confirmed from the current data. Spontaneous or implicit attempts at reappraisal can be applied with or without a conscious goal to regulate emotions(34, 49), and can be deployed with controlled effort or relatively automatically(21). Additionally, since explicit and implicit regulation exist on a continuum, they are unlikely to engage entirely dissimilar neural systems. In fact, neural systems engaged by explicit and implicit regulation are overlapping, and include areas such as the ventrolateral PFC, dorsal anterior cingulate cortex, and medial prefrontal cortex (PFC)(19, 50). Similarly, both implicit and explicit regulation, when engaged without direct instruction, involve engagement of the ventromedial PFC(51, 52). Another potential limitation of this study concerns the lack of affect ratings immediately following the unstructured period. This prevents examination of whether unprompted downregulation of negative affect is associated with real-world responses to stress.

Conclusions

We used an innovative machine learning-based method to identify neural activity underlying reappraisal. Our findings link spontanenous reappraisal to increases in SI following real-world stressors. Results suggest that the spontaneous tendency to reappraise negative memories in depressed individuals may indicate lower tolerance of negative affective cues rather than reflecting adaptive efforts at coping. Future research might apply the signature to the study of real-time temporal patterns in emotional responses to dynamic stimuli, in order to characterize dynamic fluctuation in the process of regulation in depressed populations. The neural signature approach might also be extended to characterize a broader range of emotion regulatory strategies, which might then be applied to the monitoring of medication and psychotherapy treatment outcomes.

Acknowledgements

This research was supported in part by grants from the National Institute of Mental Health: R01 MH109326 (MPIs: B. Stanley, M. Oquendo), P50 MH090964 (PI: J. Mann), and K23 MH114021 (PI: N. Schneck).

Disclosures

Drs. Mann and Oquendo receive royalties for commercial use of the Columbia Suicide Severity Rating Scale from the Research Foundation for Mental Hygiene. Dr. Mann received royalties from Columbia University for the Columbia Pathways App. Dr. Oquendo serves as an advisor to Alkermes, Mind Medicine, Sage Therapeutics, St. George's University and Fundacion Jimenez Diaz. Her family owns stock in Bristol Myers Squibb. All other co-authors declare no biomedical financial interests or potential conflicts of interest.

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Table 1. Sample Demographic and Clinical Information

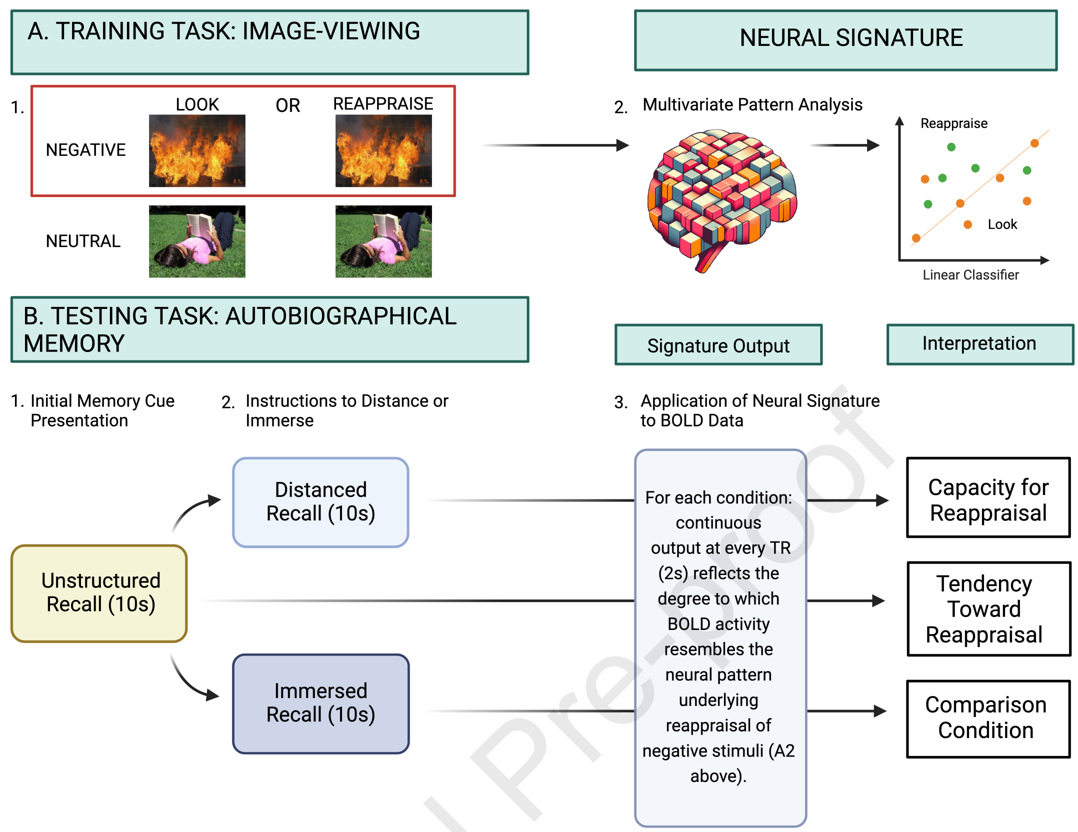
	Depressed Patients	
Variables	Total Sample (*N*=82)	
	Mean or Frequency	SD or %
Demographic Information		
Age (years)	30.2	8.9
Gender: Female	53	64.6%
Male	29	35.4%
Education: Some Higher Educ	75	91.5%
Race: African Amer/ Black	18	22.0%
Asian	14	17.1%
Multiracial/Unknown	13	15.8%
White	37	45.1%
Ethnicity: Hispanic	24	29.3%
Duration of current episode (weeks)	210.8	276.6
Psychiatric medication (3 months): Yes	23	28.0%
Non-psychiatric medication (3 months): Yes	32	39.0%
Comorbid Psychopathology		
Borderline Personality Disorder	17	20.7%
Other Personality Disorder	20	24.4%
Past Substance Disorder	25	30.5%
Clinical Rating Scale		
Beck Depression Inventory	25.6	8.2
Hamilton 24 Depression Scale	25.0	7.7
Suicidal Ideation and Behavior		
Scale for Suicidal Ideation: Past 2 weeks	6.6	8.2

	Mean or Frequency	SD or %
Prior Suicide Attempt (Yes)	37	45.0%
Ecological-Momentary Assessment		
Epochs with Responses	31.8	10.2
Epochs with Stressors	13.8	9.8
Proportion of Epochs with Stressors	45.7	27.9
Suicidal Ideation Total	7.0	4.5
Negative Affect Total	45.1	14.1

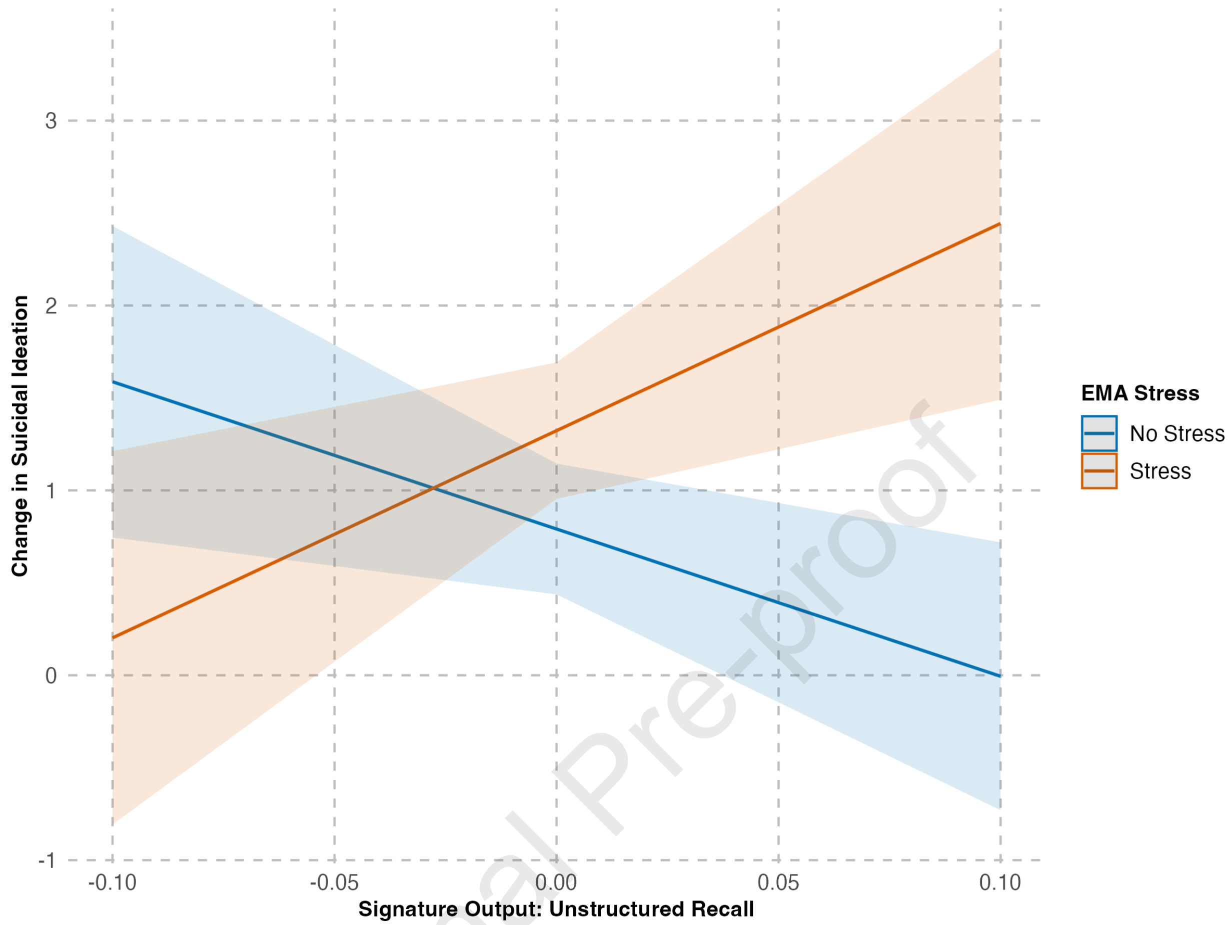
Figure 1. *Schematic depiction of the development and application of the neural signature for reappraisal.* **Panel A (top)**: The signature for reappraisal was trained on BOLD activity from an image-viewing task (**A1**). A linear classifier (**A2**) was trained to distinguish a pattern of neural activity within a prespecified ventromedial mask, that predicts reappraisal vs. "look" trials for negative images. **Panel B (bottom)**: Participants completed a negative autobiographical memory task in which they were cued to remember personal memories with brief phrases (e.g., "broke up with boyfriend"). Following a 10s unstructured recall period (**B1**), participants were prompted to either distance or immerse while continuing to recall the memory (**B2**). The neural classifier was applied to BOLD activity from the memory task, within the same prespecified ventromedial mask used to develop the signature. This yielded continuous output at each two-second TR (repetition time) reflecting the degree to which BOLD activity resembled the neural pattern underlying reappraisal of negative images (**B3**). Signature output during the distanced recall period was regarded as a proxy for the capacity to reappraise, while output for the unstructured recall period was regarded as a proxy for the tendency to reappraise.

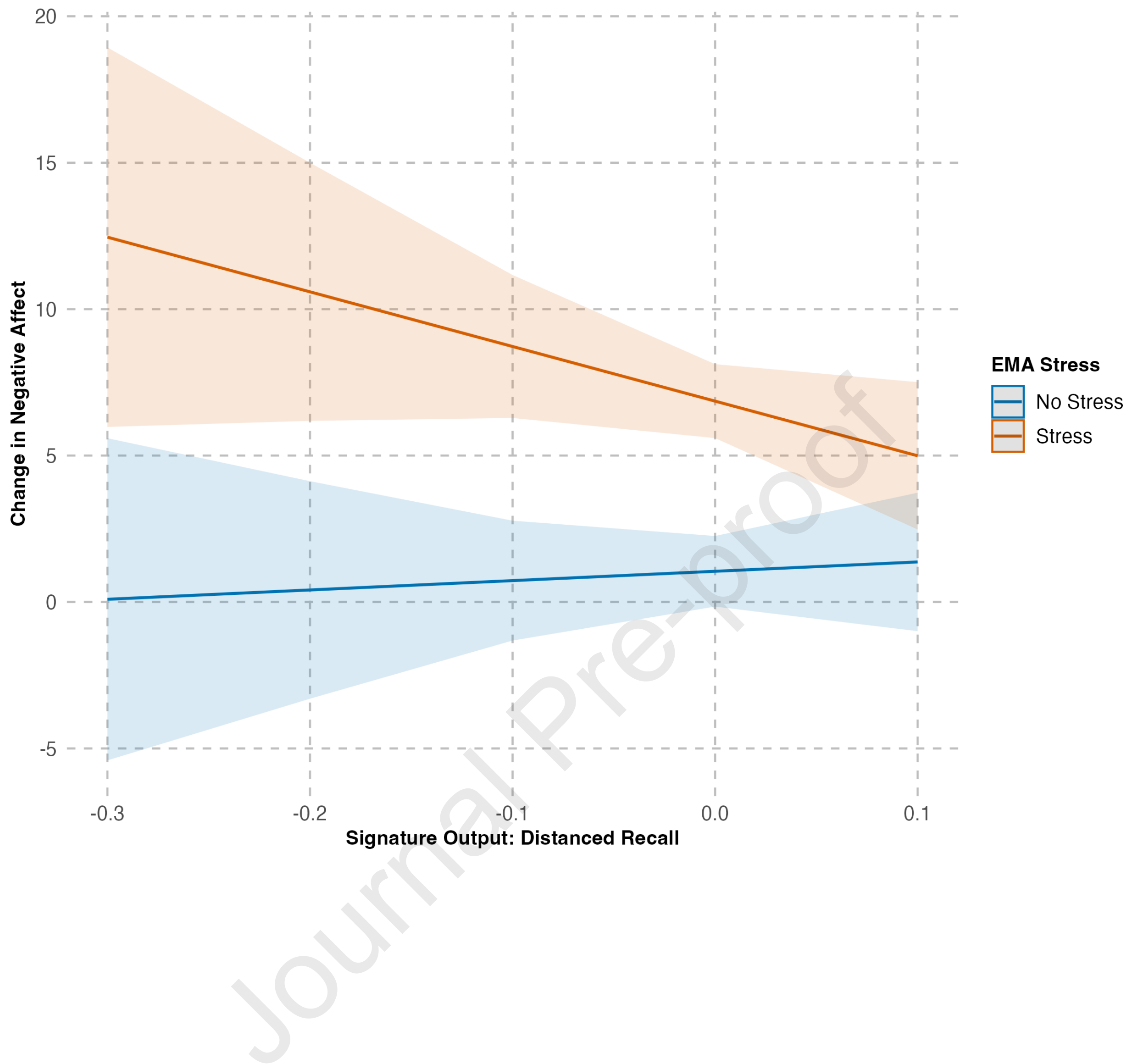
Figure 2. Interaction of signature output for unstructured recall and EMA stress change in suicidal ideation (SI): The plot depicts the estimated marginal means of the interaction model. There was a significant interaction between reappraisal signature output for the unstructured recall period and EMA stress on epoch-to-epoch change in suicidal ideation (SI). Greater reappraisal signature output during the unstructured recall period, a proxy for the *tendency* to engage reappraisal, was associated with greater increases in SI following epochs with stressors.

Figure 3. **Interaction of signature output for distanced recall and EMA stress on change in negative affect:** The plot depicts the estimated marginal means of the interaction model. There was a significant interaction between reappraisal signature output for the directed recall period and EMA stress on epoch-to-epoch change in negative affect. Greater reappraisal signature output during the directed reappraisal, a proxy for the *capacity* to engage reappraisal, was associated with lower negative affect change following epochs with stressors.



A. TRAINING TASK: IMAGE-VIEWING
1.
LOOK
OR
REAPPRAISE
NEGATIVE
NEUTRAL
NEURAL SIGNATURE
2. Multivariate Pattern Analysis
Reappraise
Look
Linear Classifier
B. TESTING TASK: AUTOBIOGRAPHICAL MEMORY
Signature Output
Interpretation
1. Initial Memory Cue Presentation
2. Instructions to Distance or Immerse
3. Application of Neural Signature to BOLD Data
Distanced Recall (10s)
Unstructured Recall (10s)
Immersed Recall (10s)
For each condition: continuous output at every TR (2s) reflects the degree to which BOLD activity resembles the neural pattern underlying reappraisal of negative stimuli (A2 above).
Capacity for Reappraisal
Tendency Toward Reappraisal
Comparison Condition


EMA Stress
No Stress
Stress
Change in Suicidal Ideation
3
2
1
0
-1
-0.10
-0.05
0.00
0.05
0.10
Signature Output: Unstructured Recall


20
15
10
5
0
-5
Change in Negative Affect
-0.3
-0.2
-0.1
0.0
0.1
Signature Output: Distanced Recall
EMA Stress
No Stress
Stress
Journal Pre-proof