Impulsive Traits and Unplanned Suicide Attempts Predict Exaggerated Prefrontal Response to Angry Faces in the Elderly

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Objective: Abnormal responses to social stimuli are seen in people vulnerable to suicidal behavior, indicating possible disruptions in the neural circuitry mediating the interpretation of socioemotional cues. These disruptions have not been empirically related to psychological and cognitive pathways to suicide. In the present study of older suicide attempters, we examined neural responses to emotional faces and their relationship to impulsivity, one of the components of the suicidal diathesis.

Methods: Using functional magnetic resonance imaging, we recorded neurobemodynamic responses to angry faces in a carefully characterized sample of 18 depressed elderly with history of suicide attempts, 13 depressed nonsuicidal patients, and 18 healthy individuals, all aged 60+. Impulsivity was assessed with the Social Problem Solving Inventory Impulsivity/Carelessness Style subscale and Barratt Impulsiveness Scale. The Suicide Intent Scale planning subscale was used to describe the degree of planning associated with the most lethal attempt. Results: Depression and history of attempted suicide were not associated with neural responses to angry faces, failing to replicate earlier studies. Higher impulsivity, however, predicted exaggerated responses to angry faces in fronto-opercular and dorsomedial prefrontal cortex (Pcorr < 0.05). Poorly planned suicide attempts also predicted increased fronto-opercular responses. Results were robust to effects of medication exposure, comorbid anxiety and addiction, severity of depression, burden of physical illness, and possible brain injury from suicide attempts. Conclusion: Impulsive traits and history of unplanned suicide attempts partly explain the heterogeneity in neural responses to angry faces in depressed elderly. Displays of social emotion command excessive cortical processing in impulsive suicide attempters. (Am J Geriatr Psychiatry 2015; - - e -)

Key Words: Aging, suicide, impulsivity, social threat, neuroimaging, prefrontal cortex
**INTRODUCTION**

Suicide among older adults remains common and evades efforts to predict and prevent it.\(^1\)\(^2\) Although pre-existing psychiatric disorders increase one’s liability, suicidal behavior does not appear to be simply an extreme expression of depression.\(^3\)\(^4\) The diversity of cognitive and psychosocial markers of suicide (e.g., cognitive deficits, interpersonal dysfunction, hopelessness, and impulsive-aggressive traits) attests to its highly heterogeneous nature and highlights the fact that it cannot be pinned down to a single neural substrate or mechanism. Instead, research examines different pathways to suicide, such as the stress-diathesis model. In this model, suicidal behavior arises from the interaction of depression, addiction, or psychosis with various neurobiologic and psychosocial vulnerability factors. The present study focuses on the coupling of two putative vulnerability factors: chronic interpersonal dysfunction\(^7\) associated with a maladaptive approach to social problems in older suicide attempters\(^6\)\(^–\)\(^9\) and impulsive aggressive traits.\(^10\) To uncover alterations in neural systems that underlie deficits in social functioning and trait impulsivity in elderly suicide attempters, we investigated neural processing of socioemotional stimuli (angry faces).

Accumulating evidence indicates that although depression may often be a necessary precondition for suicidal behavior, the risk architecture of suicidal behavior extends beyond depression. Depression is associated with frontostriatal alterations that parallel an altered encoding of rewards\(^11\)\(^–\)\(^14\) and a failure of cognitive control\(^15\)\(^,\)\(^16\) as well as with alterations in the paralimbic cortex (default-mode network) that may parallel abnormal self-referential processing.\(^17\) Although these features are present and even exaggerated in suicidal individuals,\(^6\)\(^,\)\(^18\)\(^–\)\(^20\) cognitive and neural correlates of suicidal behavior, beyond the features typical of depression, are closely associated with impulsive traits and poor decision-making. For example, depressed individuals express oversensitivity to punishment in reinforcement learning tasks, whereas suicide attempters pay excessive attention to superficial features of the task, like reward immediacy, indicating a nonstrategic, short-sighted approach to problem-solving and decision-making.\(^21\) These behaviors are mirrored by alterations in the ventromedial prefrontal cortex and in the basal ganglia, which are also related to impulsive traits.\(^11\)\(^,\)\(^21\)

Hence, to isolate neural alterations unique to suicidal behavior, the present study contrasts suicide attempters, depressed nonsuicidal patients, and healthy individuals, with a specific focus on impulsivity in social context.

More specifically, older suicide attempters often perceive life problems as threatening and unsolvable and exhibit an impulsive and avoidant approach to social problems.\(^7\) Altered processing of emotional expressions may influence how these individuals approach social conflict,\(^22\)\(^–\)\(^24\) because suicide attempters also make more errors in identifying emotional states from facial expressions.\(^9\) Until now, only two studies have examined the functioning of neural systems underlying the processing of emotional expressions in attempted suicide and found evidence of alterations. Angry faces elicited greater activity in the right lateral orbitofrontal cortex in adult male suicide attempters than in depressed individuals, although neither group was different from the healthy comparison group.\(^25\) In suicidal adolescents, response to angry faces elicited greater activity in the prefrontal, primary sensory, and temporal cortices.\(^26\) Additional evidence for association between impulsivity, abnormal perception of socioemotional cues, and disrupted neural dynamics during processing of emotional faces is seen in clinical populations that express extreme levels of trait impulsivity and high rates of suicidal behavior: patients with borderline personality disorder\(^27\)\(^,\)\(^28\) and intermittent explosive disorder.\(^29\)\(^,\)\(^30\) Overall, these findings indicate that socially threatening stimuli may command excessive processing resources in suicidal individuals. No study, however, has investigated these alterations in suicidal elderly; also, no study has examined the association between impulsivity, which, as noted earlier, plays an important role in suicide diathesis, and functional abnormalities in suicide attempters.

The present study targets suicidal elderly because the suicide rate is high in this population. Suicidal behavior tends to be more lethal in this group, with a much higher attempt to completion ratio than that of younger suicide attempters.\(^31\)\(^,\)\(^32\) In addition, clinically and demographically older suicide attempters may be more likely to resemble cases of death by suicide.
We investigate whether elderly suicide attempters process emotional faces differently from depressed nonsuicidal and nonpsychiatric comparison groups. Nonsuicidal depressed elderly were included in the study to detect an association between altered processing and suicidal behavior beyond the effects of depression.

We hypothesized that suicide attempters would have an exaggerated response in the orbitofrontal cortex in response to angry faces compared with nonsuicidal depressed and healthy comparison groups. This finding would replicate that of Jollant et al. and provide support for differential recruitment of cognitive resources in response to socially threatening stimuli in suicide attempters. We also hypothesized that trait impulsivity, probed by a variety of clinical measures, would predict disrupted processing of emotional stimuli in suicide attempters. Finally, we investigated whether executive function and interpersonal dysfunction were related to processing of angry faces.

**METHODS**

**Participants**

Forty-nine participants 60 years and older completed the study: 18 individuals with history of suicide attempts and major depression, 13 individuals with major depression but no history of suicide attempt, and 18 healthy individuals. Their demographic, clinical, and cognitive characteristics are described in Table 1.

Major depression was diagnosed by the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID) axis I disorders. We excluded individuals with a diagnosis of clinical dementia and/or a score of less than 24 on...
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the Mini-Mental State Exam. Further details on the recruitment of participants and exclusion criteria can be found in our previous study.11

All participants provided written informed consent. The University of Pittsburgh institutional review approved the study.

Suicide attempters engaged in self-injurious acts with an intent to die; six made their first suicide attempt before 50 years of age, four after 50 years of age, and eight after 60 years of age. The suicidal intent associated with suicide attempt was measured with Beck’s Suicide Intent Scale (SIS)37 (mean: 18.83; standard deviation: 5.46). The SIS-planning subscale38 was used to assess the degree of planning of suicide attempts (mean: 6.27; standard deviation: 2.61). A study psychiatrist (A.Y. D. or K. S.) verified a history of suicide attempts, based on the interview, medical records, and information from family members and friends. We excluded participants with significant discrepancies between these sources.

Nonsuicidal depressed had no current or lifetime history of suicide attempts or suicidal ideation as established by clinical interview, review of medical records, SCID, and the Scale for Suicidal Ideation39 (lifetime). Participants were excluded from this group if they had a current passive death wish or a history of indirect self-destructive behaviors.

Nondepressed individuals were included as the benchmark group. They had no lifetime history of any psychiatric disorder as determined by SCID. Clinical and cognitive assessments used to characterize the study groups are described in detail in the Supplement.

Impulsivity, Executive Function, Chronic Interpersonal Difficulties, and Attempt-Related Impulsivity

Impulsivity is a multifaceted construct.40 We selected two widely used self-report measures of impulsivity with the intent to interpret shared features of neural activity. The Impulsive/Careless Style subscale of the Social Problem-Solving Inventory (SPSI-ICS)7,41 measures a narrow and hurried approach to social problem-solving situations. The Nonplanning and Attention/Cognitive subscales of the Barratt Impulsiveness Scale (BIS-nonplanning)42 have been associated with suicide attempts in previous studies.43 High values on the BIS-nonplanning subscale correspond to acting without consideration of consequences and with a focus on immediate rather than long-term outcomes. The two self-report measures of impulsivity are moderately correlated with each other and with the measure of chronic interpersonal difficulties, measured by the 15-item version of the Inventory of Interpersonal Problems (IIP-15).44 Statistics for these and other intercorrelations are reported in the Supplement.

The degree to which suicide attempts were planned (SIS-planning) captures preparation, premeditation, isolation, timing, and precautions against discovery. Our past research indicated that the planning of suicide attempts in the elderly is inversely related to the willingness to wait for larger rewards on a delay discounting task45 and to paralimbic expected value signals.11 The SIS-planning subscale was only modestly and nonsignificantly correlated with the self-report measures of impulsivity.

Faces and Shapes Task

The faces and shapes functional magnetic resonance imaging task (Fig. 1) has been used extensively to investigate the neural circuitry of processing facial emotions.46 On a single trial participants are simultaneously presented with two stimuli and a target stimulus. During the faces condition, they choose a match to a target stimulus from two facial expressions (angry or afraid). Twelve different images derived from a standard set of pictures of facial affect are used,47 six per block and three of each gender. During the control shapes condition, participants choose a match from two geometric shapes. Participants complete five blocks of matching shapes alternating with four blocks of matching faces. Each block lasts 30 seconds (six trials that last 5 seconds each).
**Data Acquisition**

Imaging data were collected with a 3-T Trio Tim scanner (Siemens, Malvern, PA) located in the MR Research Center at the University of Pittsburgh. For functional image alignment we used T2*-weighted image-depicting blood oxygenation level–dependent (BOLD) contrast (TR: 2000 msec, TE: 29 msec, field of view: 20 cm, flip: 75, 28 3-mm slices). Stimulus presentation and response recording was controlled using the E-Prime software package.48

**Image Preprocessing**

Functional images were preprocessed using tools from AFNI49 and the FMRIB software library (FSL).50 Functional volumes were aligned to the mean functional image using the FSL MCFLIRT program with sinc interpolation, and head motion parameters were estimated. Scans with scan-to-scan movement over 0.7 mm in any dimension were censored from analyses (<2%). Next, slice-timing correction was performed using FSL slicetimer. Nonbrain voxels were removed from functional images by masking voxels with extremely low intensities and by a brain-extraction algorithm implemented in FSL’s BET. Anatomic scans were registered to the MNI152 template51 using both affine transformation (FSL FLIRT) and nonlinear deformation (FSL FNIRT). The alignment of functional images to each subject’s anatomic scan was computed using the white matter segmentation of each image and a boundary-based registration algorithm.52 Functional scans were then resampled into 3-mm isocubic voxels and warped into the MNI152 template’s space using the concatenation of the functional-structural and structural-MNI152 transforms. Images were spatially smoothed using a 5-mm full-width at half-maximum kernel (FSL SUSAN). A 0.008-Hz temporal high-pass filter was then applied to remove slow-frequency signal changes. Finally, images were normalized to a global-median intensity to allow for comparability of parameter estimates across subjects.

**Statistical Analysis**

For the purposes of the analyses the design was mixed, with condition (faces versus shapes) as a block and trials as events. Events were defined as the period between stimulus presentation and response (response times), convolved with condition (faces versus shapes)53 and with motor response (right versus left). Each resulting regressor was convolved with the canonical SPM5 double-gamma hemodynamic response function. Voxelwise BOLD signal was regressed on these estimates in the single-subject analyses using AFNI’s 3dDeconvolve.39 Regressors included condition (faces versus shapes) as the regressor of interest (aligned to stimulus onset and with a duration equal to the response time) as well as response time, motor responses (right versus left), and the six motion parameters as nuisance regressors. Group differences in neural activation for faces versus shapes were estimated using AFNI’s 3dRegAna by regressing the beta weights against predictors that included depression, history of suicide attempts, and age. Analyses of individual differences included the measure of interest (impulsivity, executive function, chronic interpersonal difficulties) in addition to depression and age in AFNI’s 3dRegAna.

To control Type I error, we used a voxelwise threshold of p < 0.001. The cluster threshold for whole-brain analysis was set with Monte Carlo simulations based on the residual spatial smoothness of the derived maps using AFNI’s 3dFWHM and 3dAlphaSim49,54 (17 voxels, yielding p <0.05, corrected). Data from significant clusters in each map (task contrast, BIS, and SPSI-ICS) were extracted for further region of interest analyses. In contrast to the whole-brain approach used with BIS and SPSI-ICS measures, we used an unbiased task-based region of interest to test the association of the suicide attempt planning measure (SIS-planning) with the activity in the frontal operculum. Because the SIS-planning subscale is only applicable to suicide attempters, the reduced sample size afforded insufficient power for whole-brain analysis.

**RESULTS**

**Main Effect of Task: Faces Versus Shapes**

Figure 2 and Table 2 describe the network of regions activated by the task. At the conservative threshold of p_{voxelwise} <0.001, p_{corr} <0.05, viewing of angry faces positively modulated the BOLD signal in the visual areas (bilateral occipital cortex, Brodmann areas [BAs] 17 and 18) and bilateral frontal
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FIGURE 2. Task contrast (faces > shapes) positively modulated the BOLD signal in the prefrontal cortex ([1–3], right and left inferior frontal gyri; BAs 44 and 45), occipital cortex ([5], BAs 17 and 18), and limbic regions ([6], right amygdala), shown in warm colors. The 20-voxel cluster in the right amygdala ($p_{\text{voxel}} = 0.001$) and the 15-voxel cluster in the left amygdala ($p_{\text{voxel}} = 0.002$, not shown) did not pass the whole-brain cluster threshold. Signal was negatively modulated in somatosensory areas, shown in cold colors ([4], postcentral cortex; BA 2). Activity detected at $P_{\text{corr}} < 0.05$, voxelwise threshold $P_{0.001}$ is shown in contrasting color over the activity detected at voxelwise $P_{0.005}$.

TABLE 2. Functional Magnetic Resonance Imaging Activation for the Task Contrast (Angry Faces versus Shapes) in the Entire Sample

<table>
<thead>
<tr>
<th>Region</th>
<th>MNI Coordinates</th>
<th>Peak ($t(47)$)</th>
<th>Cluster Size (mm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[1] Right inferior frontal gyrus (BA 45)</td>
<td>49, 33, 24</td>
<td>4.78</td>
<td>918</td>
</tr>
<tr>
<td>[2] Right inferior frontal gyrus (BA 44)</td>
<td>41, 14, 36</td>
<td>6.07</td>
<td>1,107</td>
</tr>
<tr>
<td>[3] Left inferior frontal gyrus (BAs 45, 44)</td>
<td>48, 19, 51</td>
<td>6.09</td>
<td>2,484</td>
</tr>
<tr>
<td>[5] Occipital cortex (BAs 17 and 18)</td>
<td>2, –85, –6</td>
<td>10.70</td>
<td>86,157</td>
</tr>
</tbody>
</table>

Notes: MNI: Montreal Neurological Institute.

operculum (BAs 44 and 45) and negatively modulated the signal in the right somatosensory cortex (BA 2). Figure 2 also shows positively modulated activity in the amygdala that did not pass cluster-forming threshold (shown: 20 voxels at $p_{\text{voxelwise}} < 0.005$) but was observed within the Montreal Neurological Institute (MNI) amygdala anatomic region of interest (right: $p_{\text{voxelwise}} = 0.001$, left: $p_{\text{voxelwise}} = 0.002$, $P_{\text{corr}} < 0.05$ using a small volume correction for the amygdala).

Comparison of Responses with Angry Faces in Suicide Attempters Versus Depressed Versus Nonpsychiatric Comparison Group

Our first hypothesis was not supported: Responses to angry faces were not related to the history of attempted suicide or to major depression, even at the more liberal threshold of $p_{\text{voxelwise}} = 0.005$. Analyses using severity of depression measured by the 16-item
Hamilton Rating Scale for Depression (without suicide item) were similarly negative, controlling for age.

**Responses to Angry Faces and Impulsivity**

Consistent with our second hypothesis, impulsivity was positively associated with prefrontal responses to angry faces, particularly in the left frontal operculum (Table 3 and Fig. 3), controlling for age. Furthermore, among suicide attempters, activity in the frontal operculum (independently defined by the task contrast) was related to the attempt planning (SIS) (Fig. 4). Exaggerated response was associated with poor attempt planning (in the right BA 45: F[1,16] = 8.12, p < 0.05, \( \eta_p^2 = 0.34 \); marginally significant in the right BA 44: F[1, 16] = 4.42, p < 0.06, \( \eta_p^2 = 0.22 \); but did not reach significance in the left operculum: F[1,16] = 2.68, p < 0.13, \( \eta_p^2 = 0.14 \)). The effect sizes were reduced, but effects were still present when we covaried for age (BA 44: \( \eta_p^2 = 0.13 \), BA 45: \( \eta_p^2 = 0.28 \), and left operculum: \( \eta_p^2 = 0.08 \)). Associations between the measures of impulsivity (self-reports and SIS-planning) and the frontal operculum are more fully illustrated in the Supplement.

**Exploratory Analyses: Responses to Angry Faces, Executive Function, and Interpersonal Dysfunction**

Executive dysfunction, measured by the Executive Interview-25,55 and chronic interpersonal difficulties, measured by the IIP-15, were not related to responses to angry faces.

**Sensitivity Analyses**

The relationship between fronto-opercular responses to angry faces and impulsivity remained
after controlling for lifetime substance use and anxiety disorders, severity of depression, burden of physical illness, cumulative antidepressant exposure in the current episode, and possible brain injury from suicide attempts (see Supplement for the statistics).

**DISCUSSION**

We found impulsivity-related individual differences in prefrontal responses to angry faces. However, we did not find evidence that processing of angry faces was altered in elderly suicide attempters as a group. Lending further credence to the association between impulsivity and prefrontal responses, individuals with more poorly planned attempts also tended to have an exaggerated response in functionally similar prefrontal regions as identified by the task contrast. Our combined-sample analyses indicate a robust distributed response to angry faces consistent with the canonical pattern of activation (for a review see Fusar-Poli et al.). Specifically, we observed increased activation to angry faces versus shapes in the visual (occipital cortex), prefrontal (bilateral inferior frontal gyri), and limbic system regions (amgydala, parahippocampal gyrus, posterior cingulate), although the latter did not withstand the more conservative thresholding in the reported sample.

We detected no differences in neural responses to angry faces between older suicide attempters and the comparison groups, thus failing to replicate the earlier findings of exaggerated lateral orbitofrontal (BA 47) responses to angry faces in younger suicide attempters. Our findings of increased fronto-opercular responses (BAs 44 and 45) raise the possibility that impulsivity may have mediated the group differences observed by Jollant et al. Impulsivity measures were not reported for that sample; however, it is likely that suicide attempters (adult men with a mean age of 32) were more impulsive than the patient control subjects. The region mapped in our study is more dorsal, although it still lies in the granular lateral prefrontal “frontoinsular cortex,” architectonically and functionally similar to the region identified by Jollant.
et al. Our more detailed model for single-subject analyses included reaction-time-convolved regressors for condition and stimulus presentation and motor response, whereas Jollant et al. included a block condition regressor only. The question remains whether the elderly in our study process emotional faces differently from younger adult males in the Jollant et al. study.

We identified the frontal operculum as the primary locus of individual differences in self-reported trait impulsivity, social problem-solving, and planning of suicide attempts. This region implicates the cingulo-opercular network, thought to maintain stable control of goal-directed behavior and to allocate cognitive resources as information is processed downstream. Another influential account of cingulo-opercular function focuses on the stimuli’s salience or informational value. In this context, our finding suggests that high impulsivity in the task context corresponds to greater salience of angry faces, resulting in excessive recruitment of cognitive resources (indexed by cortical processing).

Our results parallel those with the probabilistic reversal learning and delayed reward-discounting tasks. Suicide attempts, particularly poorly planned ones, were related to blunted expected value signals in a paralimbic network centered around the ventromedial prefrontal cortex. This blunting was extreme in highly impulsive individuals and was paralleled by a tendency to neglect decision-relevant information on the probabilistic reversal and Cambridge Gamble tasks. Further, individuals with a history of unplanned suicide attempts showed an exaggerated preference for immediate versus delayed rewards and alterations in the gray matter of the basal ganglia. Although the regions implicated in each of these studies differ, neural alterations are invariably associated with facets of impulsivity. These alterations may underlie a failure to consider deterrents to suicide. In contrast, older adults who engage in premeditated suicidal behavior appear more intact in this regard, while displaying distinct cognitive and decision-making deficits.

Limitations

Our failure to replicate earlier findings may be due to a relatively small sample size. In addition, the discrepancy in the findings across studies may be partly explained by the use of subtly different emotional faces tasks that may therefore target different neural mechanisms. At least one study offers evidence that the same psychopathology can reveal contrasting (and abnormal) patterns of functional activations depending on whether affected participants paid attention to emotional faces implicitly, by identifying the gender of faces, or explicitly, by matching facial expressions. Altogether, although emotional faces tasks may broadly probe the processing of the socioemotional cues, there is a need to more carefully consider how task features may modulate the contribution of relevant neural mechanisms.

In summary, the present study did not find evidence of alterations during explicit processing of socioemotional cues in older suicide attempters as a group. Instead, impulsivity and unplanned suicide attempts were associated with an exaggerated fronto-opercular response. This pattern may be indicative of disruptions at the fundamental level of socioemotional processing, which may also contribute to the social problem-solving deficits experienced by the more impulsive suicide attempters. Taken together with prior research, these findings suggest that impulsive suicidal individuals may be neurobiologically distinct from other people with depression. In addition to depression treatment, these patients may benefit from pharmacologic and learning-based interventions targeting faulty decision processes subserved by corticolimbic loops. A combination of trait impulsivity, behavioral indices of disadvantageous decision-making, and planning of suicide attempts may help define a subgroup of patients for future trials. Psychologically, impulsivity and impaired decision-making should be seen as a focus of treatment rather than a mere “character” flaw.

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