Title

Persistent Dissociation and Its Neural Correlates in Predicting Outcomes After Trauma Exposure.

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Persistent Dissociation and its Neural Correlates Uniquely Predict Worse Outcomes after Trauma Exposure

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Abstract

Objective: Dissociation, a disruption or discontinuity in psychological functioning, is often linked with worse psychiatric symptoms; however, the prognostic value of dissociation after trauma is inconsistent. Determining whether trauma-related dissociation is uniquely predictive of later outcomes would enable early identification of at-risk trauma populations. We completed the largest prospective, longitudinal, biomarker study of persistent dissociation to date to determine its predictive capacity for adverse psychiatric outcomes following acute trauma.

Methods: All data were part of the Freeze 2 data release from the AURORA study. Individuals provided self-report data about persistent derealization (*N*=1,464), a severe type of dissociation, and completed a functional magnetic resonance imaging (fMRI) emotion reactivity task and

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resting-state scan 2-weeks post-trauma (*N*=145). We collected 3-month follow-up reports of posttraumatic stress, depression, pain, anxiety symptoms and functional impairment.

Results: Derealization was associated with increased ventromedial prefrontal cortex (vmPFC) activation in the emotion reactivity task and decreased resting-state vmPFC connectivity with cerebellum and orbitofrontal cortex. Furthermore, in separate analyses, brain-based and self-report measures of persistent derealization at 2-weeks predicted worse 3-month posttraumatic stress symptoms, distinct from childhood maltreatment and current posttraumatic stress symptoms.

Conclusions: Our work suggests persistent derealization is both an early psychological and biological marker of worse later psychiatric outcomes. The neural correlates of trauma-related dissociation may serve as potential targets for treatment engagement to prevent PTSD. These results underscore dissociation assessment as crucial following trauma exposure to identify at-risk individuals and highlight an unmet clinical need for tailored early interventions.

Trauma-related pathological dissociation is a disruption or discontinuity in the typical integration of a person's psychological functioning in the aftermath of a traumatic event (1). It encompasses a range of symptoms including derealization – the focus of this study because it is a symptom that is, in particular, tied to impairment and disease severity (2, 3). Derealization is a feeling of detachment from people, places, or objects in one's environment (4). When experiencing derealization, individuals sometimes report feeling foggy or like they are in a movie or a dream. By providing some psychological distance from the traumatic experience, this type of dissociation may help people cope during experiences of overwhelming threat and in the aftermath of trauma (5).

Unfortunately, persistent dissociative coping responses come at a high cost for both the individual and society, as dissociative symptoms are often linked to a more severe psychiatric course and protracted treatment across disorders (6, 7). Furthermore, dissociation is often associated with worse symptoms of posttraumatic stress, depression, anxiety, pain, and greater functional impairment (7–10).

Still, evidence for the efficacy of leveraging dissociative symptoms to predict post-trauma psychiatric course is inconsistent. These inconsistencies are likely due to two interwoven issues: the duration of dissociation being measured (peritraumatic vs. persistent), and whether dissociation functions as an independent predictor of posttraumatic stress–that is, independent from variables like trauma history and current psychiatric symptoms. For example, peritraumatic dissociation that occurs during or in the immediate aftermath of a traumatic event predicts ongoing post-trauma stress, anxiety, depression, and pain, but this prediction is often removed or diminished when accounting for other variables (11, 12). Alternatively, a growing body of both cross-sectional and prospective work demonstrates persistent dissociation that lasts beyond the peritraumatic period is a much better indicator of long-term posttraumatic stress symptom severity compared to peritraumatic dissociation (13). Initial evidence also suggests persistent dissociation appears to maintain its predictive capacity for posttraumatic stress even when accounting for other variables such as trauma type and current PTSD symptoms (14). Notably, researchers have not yet tested whether persistent dissociation prospectively predicts post-trauma anxiety, depression, pain, and functional impairment while also accounting for other variables like trauma history and

current posttraumatic stress symptoms. Determining whether persistent dissociation is predictive of later outcomes would be enormously beneficial by enabling early identification of at-risk trauma populations and those in need of targeted, early mental health intervention.

Given the potential predictive capacity of self-reported dissociation for various psychiatric outcomes and impairment, its biological correlates may also provide added value in identifying individuals at risk of worse outcomes. However, the biology of trauma-related dissociation has itself received limited attention, and its predictive capacity has not yet been studied. Work that has examined the biology of trauma-related dissociation demonstrates patterns of excessive corticolimbic inhibition for depersonalization/derealization in trauma spectrum disorders, suggesting this kind of dissociation is a type of emotion and arousal over-regulation (15, 16). In emotionally provocative contexts, individuals with high levels of dissociation exhibit hyperactivity in cortical regions related to emotion regulation (e.g., ventromedial prefrontal cortex, vmPFC) and hypoactivity in limbic regions related to salience detection and the visceral experience of one's body (e.g., amygdala, insula). Hyperactivity in medial prefrontal cortex, in particular, demonstrates the most prominent association with depersonalization/derealization symptoms of dissociation (17). Like self-report studies, longitudinal neurobiological studies of dissociation are limited, and none have used the neurobiology of dissociation to predict later outcomes.

To address these critical gaps, we conducted the largest prospective, longitudinal biomarker study of dissociation to date focused on a specific type of dissociation: persistent derealization. We focused specifically on derealization because recent evidence suggests this subtype of dissociation may, in particular, be associated with symptom and impairment severity in trauma spectrum disorders (2, 3). In a sample of adults who recently experienced trauma, we tested the unique predictive capacity of both self-report and neurobiological measures of persistent derealization.

Approximately 2-weeks after the traumatic event, participants reported on symptoms of persistent derealization, and a subset completed a functional magnetic resonance imaging (fMRI) scan including an emotion reactivity task (passive viewing of fearful faces) and a resting-state scan. Based on prior data, while viewing fearful faces, we expected derealization would be related to hyperactivity in vmPFC and hypoactivity in amygdala and insula – potentially reflecting overmodulation of affective responses. Additionally, given the strength of medial PFC findings with dissociation in prior work, we hypothesized both self-report derealization and vmPFC activity during the fearful faces task would predict 3-month follow-up reports of posttraumatic stress, depression, pain, anxiety symptoms and functional impairment, even when accounting for a history of childhood maltreatment and 2-week levels of posttraumatic stress symptoms.

Methods

Participants

Participants were a convenience sample recruited as part of a multisite study on adverse posttraumatic psychiatric outcomes from twenty-two different emergency departments across the United States (18). To be eligible for the study, participants had to be ages

18–75, fluent in English, alert and oriented at the time of enrollment, and possess an iOS or Android-compatible smartphone. Exclusion criteria included self-inflicted injury, occupational injury, prisoner status, individuals pregnant or breastfeeding, individuals in an ongoing domestic violence situation, and those with more severe physical injury. Additional exclusion criteria for the MRI session were contraindications to MRI (e.g., metal implants). MRI scans were completed approximately 2-weeks after the emergency department visit at one of four sites: McLean Hospital, Emory University, Temple University or Wayne State University. All data reported here were part of the Freeze 2 data release from the AURORA study which includes data collection from September 23, 2016, to July 31, 2019. All participants provided written informed consent. All data were collected in accordance with ethical guidelines pertaining to the use of human participants and procedures were approved by each data collection site's Institutional Review Board.

Measures

Participants completed surveys on their own at home or over the phone with an experimenter's assistance. We measured history of childhood maltreatment using an abbreviated version of the Childhood Trauma Questionnaire (19), and persistent derealization severity at 2-weeks post-trauma using a 2-item abbreviated version of the Brief Dissociative Experiences Scale (DES-B) (20). We measured posttraumatic stress symptom severity at 2-weeks and 3-months post-trauma using the PTSD checklist for DSM-5 (PCL-5) (21). At 3-months post-trauma, we also measured depression and anxiety symptom severity, pain extent, and functional impairment in work, family, and social life using the PROMIS Depression short form (22), an abbreviated version of the PROMIS Anxiety Bank (22), the Numeric Pain Rating Scale, and the Sheehan Disability Scale (23), respectively. Higher scores on all measures indicated more severe symptoms or impairment (see Supplement for further details).

Magnetic Resonance Imaging

Detailed information on sequence and task parameters, and preprocessing steps is discussed in the Supplement. Briefly, brain scans were completed approximately 2-weeks after the emergency department visit using Siemens 3 Tesla MRI systems with an MPRAGE T1-weighted image for structural scans and an EP2d-BOLD sequence for functional scans. The functional scans occurred in the following order: a 9.2 min resting-state scan, a 4.9 min emotion reactivity task, a 9.8 min go/no-go inhibition task (not reported here), and a 9.7 min monetary reward task (not reported here). The emotion reactivity task was designed to probe reactivity to social threat cues by having participants passively view fearful and neutral facial expressions (24). All data were preprocessed using a standardized pipeline via the FMRIPREP 1.2.2 software package.

We derived our vmPFC and insula ROI from previous dissociation-related results in motor vehicle accident samples completing an emotionally provocative task (25). Specifically, we used a 5mm sphere placed in left vmPFC (MNI coordinates −12, 50, 4) and right anterior insula (MNI coordinates 38, 20, 0). We derived our amygdala ROI from previous work using the fearful faces task in a traumatized civilian sample (24). Specifically, we used a 5mm sphere placed in right amygdala (MNI coordinates 20, 0, −16). We extracted the

average value of the ROIs from the first-level fearful>neutral face contrast in the emotion reactivity task. We also used the vmPFC ROI to extract the average value from subject-level resting-state data. We correlated the vmPFC ROI values with the whole brain voxel time courses for each subject, and computed Fisher Z transformations to generate subject-level connectivity maps.

Group-Level Statistical Analyses

Reported p-values are two-tailed. All hypothesis tests and confidence intervals based on linear regression models were calculated using type HC3 robust standard errors in SPSS version 28, which do not require assumptions of normality or constant variance for validity (26).

Neural Correlates of Derealization.—To test whether self-report persistent derealization was associated with ROI activity in vmPFC, amygdala, and insula during the emotion reactivity task we conducted three separate linear regressions controlling for MRI scanner (McLean Hospital, Emory University, Temple University or Wayne State University), sex assigned at birth (male, female), age, childhood maltreatment and 2-week posttraumatic stress symptoms. We applied a Hommel multiple testing correction (27) using R version 3.5.3 to account for our choice of three ROIs with derealization; corresponding p-values are designated “corrected” in the text of the results. No multiple testing correction was applied to results for control covariates. To test whether vmPFC connectivity was associated with derealization, we entered subject-level seed-based connectivity maps into a linear model using the AFNI 20.0.24 3dMVM program (28). Only results that survived multiple comparison correction are reported (see Supplement for further details).

Derealization self-report and 3-month outcomes.—We conducted Pearson correlation analyses to test associations between 2-week derealization and 3-month symptom outcomes. We then completed a series of multiple linear regression analyses to test whether derealization self-report data predicted 3-month symptom outcomes when controlling for sex, age, childhood maltreatment and 2-week posttraumatic stress symptoms. We applied a Hommel multiple testing correction (27) to account for our choice of five clinical associations of interest with derealization. No multiple testing correction was applied to results for control covariates.

vmPFC and 3-month outcomes.—We conducted Pearson correlation analyses to test associations between vmPFC activity and 3-month symptom outcomes. To test whether vmPFC activity during the emotion reactivity task also predicted 3-month outcomes that were found to be significant in the self-report sample, we then completed a series of linear regressions when controlling for MRI scanner, sex, age, childhood maltreatment and 2-week posttraumatic stress symptoms. We conducted 2 separate regressions (one for each significant 3-month outcome in the self-report sample). We applied a Hommel multiple testing correction (27) to account for our choice of two clinical associations of interest with vmPFC activity. No multiple testing correction was applied to results for control covariates.

Results

Sample Characteristics

Participants were 1,464 adults who presented in the emergency department within 72 hours after a trauma exposure. A subset of these individuals also completed an MRI scan approximately 2-weeks after their emergency department visit ($N = 145$). See Supplement for details on quality control exclusion. Participant demographics and acute trauma exposure types are summarized in Table 1. Approximately 55% of self-report participants ($N = 798$) and 50% of MRI participants ($N = 72$) endorsed some level of persistent derealization at 2-weeks. See the Supplement for details on demographic variables associated with derealization.

Neural Correlates of Persistent Derealization

Emotion Reactivity Task Activity.—A linear regression controlling for MRI scanner, sex, age, childhood maltreatment and 2-week posttraumatic stress symptoms revealed higher levels of derealization were associated with greater vmPFC ROI activity during fearful > neutral face conditions, $B = .03$, $SE = .01$, $t = 2.60$, $p_{corrected} = .030$, ($\eta_p^2 = .03$); Figure 1a, b). This relationship was robust to MRI scanner effects (see supplement). A second and third linear regression tested the same model, but now predicting amygdala and insula ROI activity during fearful > neutral face conditions, respectively. The relationship between derealization and amygdala, $B = -.01$, $SE = .03$, $t = -.35$, $p_{corrected} = .730$, ($\eta_p^2 = .00$), and insula activity, $B = -.01$, $SE = .02$, $t = .36$, $p_{corrected} = .730$, ($\eta_p^2 = .00$), in these models was not significant. Finally, we completed an exploratory whole-brain voxelwise correlation analysis with persistent derealization in the fearful > neutral contrast controlling for the same covariates as those in the ROI analyses; however, no activity survived multiple comparison correction.

Resting-state Connectivity.—To further understand how the vmPFC ROI was related to derealization, we completed a whole-brain resting-state seed-based connectivity analysis with the same vmPFC ROI (25) as the seed. When controlling for MRI scanner, sex, age, childhood trauma, and 2-week posttraumatic stress symptom severity, derealization was associated with decreased connectivity between vmPFC and two regions: the right lobule VIIIa in the cerebellum, cluster volume = 92, Peak $t = -4.14$, MNI coordinates for the peak $t = 26, -63, -57$ (Figure 1c), and an area in right orbitofrontal cortex (OFC), Brodmann area 47, cluster volume = 74, Peak $t = -4.11$, MNI coordinates for the peak $t = 26, 26, -15$ (Figure 1d). In post-hoc analyses, this connectivity was not linked to levels of activity in vmPFC during the emotional reactivity task (see supplement).

Do Self-report and Neural Correlates of Persistent Derealization Predict 3-Month Outcomes?

Self-report Derealization.—Higher 2-week derealization was associated with higher levels of 3-month PTSD, anxiety, depression, pain extent, and impairment (Table 2). A series of multiple linear regressions revealed that 2-week derealization predicted 3-month PTSD

($p_{corrected}$=.040) and depression symptoms ($p_{corrected}$=.020) even when accounting for sex, age, childhood maltreatment and 2-week PTSD symptoms (Table 3).

vmPFC Activity.—More vmPFC activity in the fear > neutral face contrast during the emotion reactivity task was associated with higher 3-month PTSD and depression (Table 2). Given self-report derealization predicted 3-month PTSD and depression symptoms, we wanted to test if vmPFC would also predict these outcomes. A series of multiple linear regressions revealed that 2-week vmPFC activity predicted 3-month PTSD symptoms ($p_{corrected}$=.022) even when accounting for MRI scanner, sex, age, childhood maltreatment and 2-week posttraumatic stress symptoms (Table 4).

The prior results predict dimensional symptom outcomes. We also completed a post-hoc set of analyses to predict PTSD and depression diagnosis using self-report derealization and vmPFC activity (see supplement). Models with 2-week derealization alone as a predictor had adequate discrimination for both depression and PTSD diagnosis at three months. However, improvement in overall discrimination and in sensitivity and specificity were minimal when 2-week derealization score was combined with other clinical predictors. Discrimination for vmPFC activity alone was below acceptable levels for both depression and PTSD diagnosis, and addition of vmPFC to other clinical predictors only modestly improved overall discrimination, sensitivity, and specificity.

Discussion

Despite foundational work on the psychological and neural basis of dissociation, the field has yet to definitively determine whether dissociation is a unique predictor of worse post-trauma psychiatric course. We examined whether the psychological and neural correlates of a specific type of dissociation, derealization, predicted worse psychiatric symptoms in the largest prospective, longitudinal biomarker study of dissociation to date. Here, we demonstrated that self-report and the neural manifestations of persistent (2-week) derealization both predicted 3-month PTSD symptom severity, distinct from a history of childhood maltreatment history and 2-week posttraumatic stress symptoms. This suggests that persistent derealization, following acute trauma, is an early sign of individuals who will likely have worse mental health as time goes on.

In terms of the underlying neural markers, we found that persistent derealization was associated with increased vmPFC activity during an emotion reactivity task when controlling for the severity of childhood maltreatment and current posttraumatic stress symptoms. This finding partially replicates prior work demonstrating a pattern of increased medial PFC activity in the dissociative subtype of PTSD and dissociative identity disorder (15, 16), especially for consciously perceived fearful facial stimuli (29). The vmPFC is consistently involved in emotion regulation, and specifically emotion regulation that is automatic and outside awareness or conscious control (30). This neural activity in part, may underlie emotion over-regulation and the experience of feeling detached from surroundings in the aftermath of traumatic events.

Interestingly, we did not find an association between derealization and amygdala or insula activation in the emotion reactivity task. Models of dissociation implicate corticolimbic inhibition and decreased amygdala/insula activity in emotionally arousing contexts when individuals are feeling dissociative (15, 16). However, a recent systematic review found the direction and strength of amygdala and insula findings in relation to dissociation to be mixed (17). The relationship between dissociation and activity in these structures may be highly dependent on the task context and type of dissociation being studied. More work is necessary to understand the nuances of these potential neural markers of dissociation.

Moreover, we found that at rest, derealization was associated with decreased resting-state connectivity between vmPFC and the posterior lobe of the cerebellum (lobule VIIIa). This region of the cerebellum is largely involved in sensorimotor function and includes a secondary somatotopic representation of the human body (31). Lobule VIII typically demonstrates functional connectivity with anterior prefrontal cortex and primary motor cortex (32). Recent work on the dissociative subtype of PTSD found decreased connectivity in other sensorimotor regions of the cerebellum and cortical regions involved in multisensory integration (33). Contemporary theories of cerebellar function hypothesize that the cerebellum is a master regulator across sensorimotor, cognitive, and affective domains, helping to maintain allostasis (34). Given this, we speculate that decreased synchronization between vmPFC and this region of the cerebellum may contribute to perceptual and affective distortions experienced during derealization (e.g., feelings that surroundings are fading away, unreal, strange). Taken together, the cerebellum is emerging as a key region that has been understudied in trauma-related dissociation.

Additionally, we observed an association between derealization and decreased resting-state connectivity between vmPFC and OFC. Both regions have recently been identified as potential biomarkers of pathological dissociation, though their functional connectivity remains understudied in relation to dissociation (17). The OFC receives a wide array of sensory and visceral input and may serve as a major integration area for this information (35). It has also been implicated in decision making, emotional processing and assigning a reward value and valence to experience (35). It has also been linked to individual differences in anxiety through its role in amygdala regulation (36, 37). The vmPFC is a hub of the default network involved in emotion processing and self-related thinking (38). Typically, OFC has strong connections with cingulate regions, and vmPFC receives inputs from both OFC and cingulate regions (39). This communication is thought to facilitate an assessment of a stimulus' value and can influence goal directed action (39). Moreover, altered communication between OFC and cingulate regions can impact the output of all medial PFC regions (39). Given this, we hypothesize that decreased synchronization between OFC and vmPFC may also be connected to the increased vmPFC activity during derealization. Furthermore, we hypothesize these altered networks may also contribute to perceptual and affective distortions experienced during derealization (e.g., feelings that familiar surroundings are unreal, unfamiliar, strange, puzzling).

Concerning the relationship between persistent derealization and later symptoms, we found that more severe persistent derealization was associated with increased PTSD, anxiety, and depression symptom severity, pain extent, and functional impairment 3 months after

trauma exposure. However, when accounting for sex assigned at birth, age, childhood maltreatment and concurrent posttraumatic stress symptom severity, persistent derealization only predicted later PTSD and depression symptoms. PTSD and depression often co-occur in the aftermath of trauma (40). There is both evidence that co-occurring PTSD and depression may represent a more general traumatic stress factor, and in contrast, that these disorders can be separate constructs with unique predictors and outcomes (41). It is yet unclear whether derealization predicts PTSD and depression as separate entities or whether it predicts a more general traumatic stress reaction in this population, which we hope can be further addressed in future studies. Nonetheless, these results suggest that knowing someone's levels of derealization in the weeks following trauma exposure will help predict their future depression and PTSD symptoms, distinct from knowing their sex, age, childhood maltreatment history and current posttraumatic stress symptoms. This highlights the importance of assessing for dissociation in the aftermath of traumatic events to identify individuals who are at risk of a worse psychiatric course.

Similarly, brain activity associated with persistent derealization was related to more severe PTSD and depression symptoms later on (i.e., increased vmPFC activity in an emotionally provocative context). When accounting for MRI scanner, sex, age, childhood maltreatment and concurrent posttraumatic stress symptom severity, vmPFC activity still significantly predicted future PTSD symptoms. This suggests that after acute trauma, increased vmPFC activity during an emotionally provocative task may be a signal of worse PTSD symptoms to come.

This result is consistent with other recent findings implicating vmPFC as a central node in prolonged posttraumatic psychopathology. For example, less vmPFC activation during an emotionally provocative task before a difficult combat training was linked to more PTSD symptoms after training (42). A "Goldilocks" level of vmPFC activity during emotionally charged contexts may exist (43). This optimal level of activity may be representative of successful emotion regulation that protects against future PTSD symptoms. In contrast, either an excess or a deficiency in this activity may lead to worse PTSD later on. Alternatively, the vmPFC may be comprised of subregions, some of which are associated with persistent dissociative symptoms (and later worse PTSD) while others are associated with successful emotion regulation (and fewer PTSD symptoms later on).

Several limitations constrain the interpretations of our findings. We have demonstrated that the neural correlates and self-report measures of derealization predict later psychiatric outcomes; however, we have not tested whether they cause these outcomes directly. Moreover, it could be that some derealization preceded the specific traumatic event that brought individuals to the emergency department in this study. Future work is needed to test the causal relationship between trauma-related persistent dissociation and later psychiatric outcomes. Pathological dissociation is a multidimensional construct encompassing a wide range of experiences; however, we focused solely on derealization given its link to impairment severity (2, 3). The AURORA study prioritized measuring many posttraumatic sequalae, which limited the depth of assessment into any one construct. Therefore, our findings may not be generalizable to other types of dissociation. Also, our measure of persistent derealization was limited to a self-report 2-weeks from the acute trauma.

Future work may wish to explore dissociation that persists beyond 2-weeks with clinician-administered measures. In addition, the requirement of smartphone ownership may limit the generalizability of this sample. Moreover, we excluded individuals in ongoing domestic violence situations and those with self-inflicted injuries. Interpersonal trauma is associated with more dissociative symptoms and self-harm (44). Additionally, dissociative disorder diagnosis is strongly associated with measures of self-harm, suicidality, and numbers of suicide attempts (45). Therefore, our findings may suffer from a restriction of range in level of participant acuity. Specifically, the prevalence of derealization may have been even higher if individuals in domestic violence situations and those with self-inflicted injuries were eligible for enrollment. We recommend future work include these individuals to both better understand the full range of dissociative symptomatology and to also better aid those with more severe pathology down the line.

Conclusions and Clinical Implications

In the largest prospective, longitudinal biomarker study of dissociation to date, our work suggests persistent derealization is both a psychological and biological marker of worse later psychiatric outcomes. Additionally, we have replicated previous neurobiological work and introduced novel findings demarcating the neural correlates of trauma-related dissociation. Importantly, the activity and connectivity of these regions may serve as potential neural targets for treatment engagement to prevent PTSD.

Prior work suggests that dissociation may undermine seeking treatment for PTSD, highlighting that there may be a need to screen for and treat individuals with prominent dissociative symptoms differently (7). Our work lends urgency to these claims, as persistent derealization is associated with more severe depression, anxiety, pain and posttraumatic stress and greater functional impairment at 3 months following trauma. Clinicians may wish to screen for dissociation in the weeks following trauma, and perhaps in other contexts (e.g., primary care) to identify individuals potentially at risk of a chronic, more severe psychiatric course. Ultimately, we hope this would, in turn, address a presently unmet clinical need for early intervention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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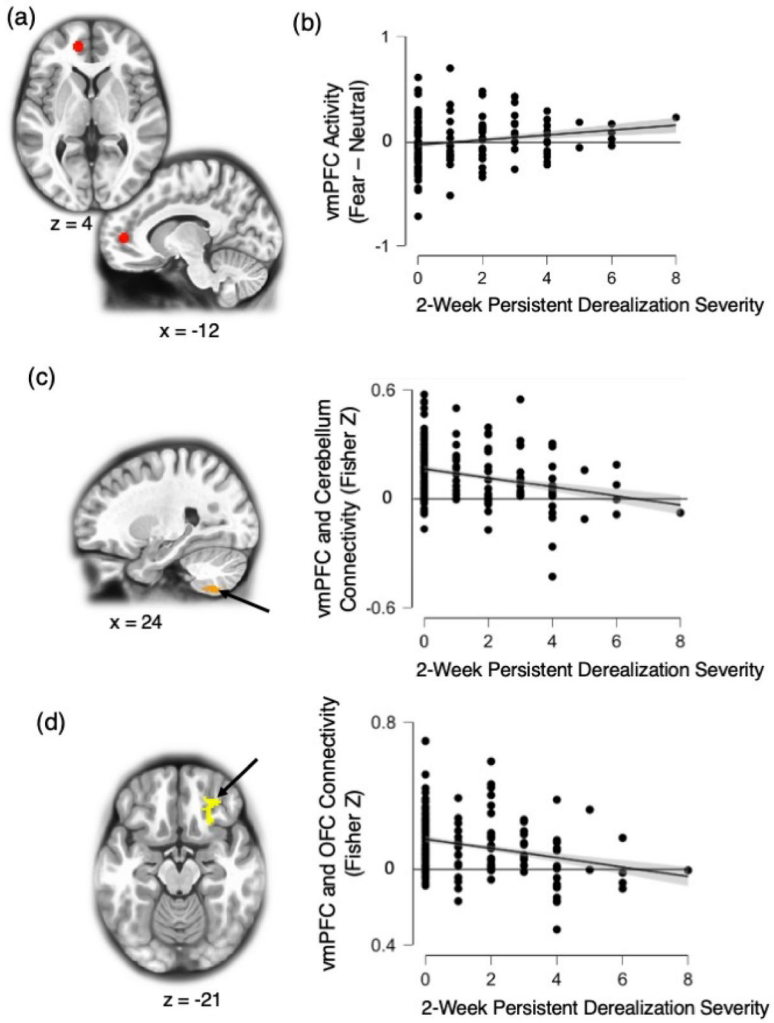

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Figure 1.

Neural Correlates of Derealization. (a) The red 5mm sphere represents the Hopper et al. (2007) left ventromedial prefrontal cortex (vmPFC) region of interest used in the emotion reactivity (fearful faces) task and resting-state connectivity analysis. (b) vmPFC activity during the emotion reactivity task was positively correlated with 2-week self-report derealization severity, $r(143) = .18$, $p = .030$ (c) Connectivity between left vmPFC and right cerebellar lobule VIIIa (orange) was negatively correlated with 2-week derealization scores, $r(143) = -.26$, $p = .001$ (d) Connectivity between left vmPFC and right orbitofrontal cortex (yellow) was negatively correlated with 2-week derealization scores, $r(143) = -.27$, $p < .001$. Scatterplots and correlation values are for zero-order correlations. Scatterplot dots represent individual participants scores for activity/connectivity and derealization severity. Lines represent the linear line of best fit. Shaded error bars represent +/− 1 standard error of the mean. vmPFC = ventromedial prefrontal cortex. OFC = orbitofrontal cortex.

Table 1.

Demographics and Acute Trauma Exposure Type

	Self-report Sample (*n*=1464)		MRI Sample (*n*=145)	
	n	***%***	***n***	***%***
Sex assigned at birth				
Female	954	65.2	97	66.9
Male	510	34.8	48	33.1
Race/Ethnicity				
Hispanic/Latino	174	11.9	26	17.9
White	472	32.2	54	37.2
Black/African American	765	52.3	59	40.7
Asian, Hawaiian, American Indian, Other	49	3.3	6	4.1
missing	4	0.3	0	0
Education				
Less than high school	171	11.7	5	3.4
High school diploma / GED	369	25.2	37	25.5
Some college	412	28.1	50	34.5
Associate	213	14.5	14	9.7
Bachelors	192	13.1	25	17.2
Masters	79	5.4	11	7.6
Professional / Doctorate	22	1.5	2	1.3
missing	6	.4	0	0
Yearly Family Income				
<$19,000	497	33.9	37	25.5
19,001–35,000	434	29.6	43	29.7
35,001–50,000	194	13.3	25	17.2
50,001–75,000	114	7.8	13	9.0
75,001–100,000	84	5.7	10	6.9
> 100,000	88	6.0	16	11.0
missing	53	3.6	1	0.7
Trauma type				
Motor vehicle collision	1138	77.7	107	73.8
Physical assault	139	9.5	16	11.0
Sexual assault	12	0.8	2	1.4
Fall >10’	16	1.1	1	0.7
Incident causing traumatic stress exposure to many people	5	0.3	1	0.7
Non-motorized collision (e.g., bike, skateboard)	17	1.2	5	3.4
Fall < 10’	48	3.3	4	2.8
Burns	7	0.5	1	0.7

	Self-report Sample (*n*=1464)		**MRI Sample (*n*=145)**	
	n	***%***	***n***	***%***
Animal-related	29	2.0	3	2.1
Other	53	3.6	5	3.4
	M	***SD***	***M***	***SD***
Age	35.39	12.94	34.66	12.62

Table 2.

Correlations with 3-Month Outcomes

2-week Derealization Self-report and 3-Month outcomes

	Mean	(SD)	1.	2.	3.	4.	5.	6.
1. Derealization 2-weeks	1.73	(2.12)	-					
2. PTSD 3-Months	25.13	(19.13)	.53**	-				
3. Pain Extent 3-Months	7.54	(6.50)	.32**	.55**	-			
4. Impairment 3-Months	11.87	(9.37)	.29**	.66**	.52**	-		
5. Anxiety 3-Months	6.63	(4.70)	.42**	.83**	.45**	.62**	-	
6. Depression 3-Months	53.34	(11.09)	.42**	.67**	.31**	.48**	.63**	-

Ventromedial Prefrontal Cortex Activity and 3-Month outcomes

	Mean	(SD)	1.	2.	3.	4.	5.	6.
1. vmPFC Fear > Neutral	−.01	(.23)	-					
2. PTSD 3-Months	23.40	(16.86)	.23*	-				
3. Pain Extent 3-Months	7.10	(6.08)	.14	.63**	-			
4. Impairment 3-Months	11.93	(10.06)	.05	.65**	.57**	-		
5. Anxiety 3-Months	6.46	(4.58)	.11	.84**	.52**	.64**	-	
6. Depression 3-Months	53.31	(10.66)	.19*	.78**	.49**	.62**	.82**	-

** p<.001,

* p<.05, vmPFC = ventromedial prefrontal cortex

Table 3.

Derealization Self-report Predicting 3-Month Outcomes

	B	Robust SE	t	p	η^2_p	Adj. R^2	Model without Derealization Adj. R^2	F	df	p
PTSD 3-Months										
Overall Model						519	.515	222.71	5, 1022	<.001
Sex	.47	.89	.52	.601	.00					
Age	.09	.03	3.25	.001	.01					
Childhood Maltreatment	.13	.05	2.64	.009	.01					
PTSD 2-weeks	.62	.03	19.86	<.001	.28					
Derealization 2-weeks	.82	.32	2.58	.010*	.01					
Pain Extent 3-Months										
Overall Model						.223	.220	58.69	5, 1000	<.001
Sex	−.77	.39	.92	.355	.00					
Age	.36	.01	5.79	<.001	.03					
Childhood Maltreatment	.08	.02	3.68	<.001	.01					
PTSD 2-weeks	.11	.01	8.06	<.001	.06					
Derealization 2-weeks	.27	.13	2.08	.038^	.00					
Impairment 3-Months										
Overall Model						.246	.246	68.59	5, 1029	<.001
Sex	.75	.54	1.39	.165	.00					
Age	.10	.02	5.22	<.001	.03					
Childhood Maltreatment	.11	.03	3.92	<.001	.02					
PTSD 2-weeks	.23	.02	11.97	<.001	.12					
Derealization 2-weeks	−.22	.17	−1.28	.202	.00					
Anxiety 3-Months										
Overall Model						.372	.373	125.64	5, 1046	<.001
Sex	.25	.24	1.06	.291	.00					
Age	.02	.01	2.32	.020	.01					
Childhood Maltreatment	.04	.01	3.01	.003	.01					
PTSD 2-weeks	.14	.01	16.16	<.001	.20					
Derealization 2-weeks	.05	.08	.59	.557	.00					
Depression 3-Months										
Overall Model						.394	.389	138.32	5, 1050	<.001
Sex	−.77	.58	−1.33	.183	.01					
Age	.02	.02	1.20	.231	.00					
Childhood Maltreatment	.14	.03	4.87	<.001	.02					
PTSD 2-weeks	.29	.02	14.36	<.001	.16					
Derealization 2-weeks	.56	.19	2.88	.004*	.01					

Note. P-values reported in the table are uncorrected values, derealization p-values corrected for multiple comparison are reported in the text.

* = derealization p-value that survived multiple comparison correction;

^ = derealization p-value that did not survive multiple comparison correction. B = unstandardized estimates. η^2_p = partial eta squared. Adj R^2 = adjusted R^2 value

Table 4.

Ventromedial Prefrontal Cortex Activity in Fear > Neutral Face Contrast Predicting 3-Month Outcomes

	B	Robust SE	t	p	η^2_p	Adj. R^2	Model without Derealization Adj. R^2	F	df	p
PTSD 3-Months										
Overall Model						390	.366	10.34	8, 109	<.001
MRI Scanner										
1 vs. 4	4.93	3.31	1.49	.139	.02					
2 vs. 4	1.53	5.89	.26	.795	.00					
3 vs. 4	1.16	3.21	.36	.719	.00					
Sex	−2.26	2.82	−.80	.425	.01					
Age	.01	.11	.07	.943	.00					
Childhood Maltreatment	<.001	.14	0.003	.998	.00					
PTSD 2-weeks	.61	.09	7.10	<.001	.32					
vmPFC Activity	12.55	4.88	2.57	.011*	.06					
Depression 3-Months										
Overall Model						.298	.288	7.20	8, 109	<.001
MRI Scanner										
1 vs. 4	.09	2.45	.04	.971	.00					
2 vs. 4	.12	5.00	.02	.981	.00					
3 vs. 4	−1.13	2.10	−.54	.593	.00					
Sex	.19	1.93	.10	.920	.00					
Age	−.01	.07	−.15	.882	.00					
Childhood Maltreatment	.11	.11	1.06	.290	.01					
PTSD 2-Weeks	.32	.07	4.93	<.001	.18					
vmPFC Activity	5.80	2.28	1.77	.080	.03					

Note. P-values reported in the table are uncorrected values, vmPFC activity p-values corrected for multiple comparison are reported in the text.

* = vmPFC activity p-value that survived multiple comparison correction. B = unstandardized estimates. η^2_p = partial eta squared. Adj R^2 = adjusted R^2 value. vmPFC = ventromedial prefrontal cortex