

Affective Visual Circuit Dysfunction in Trauma and Stress-Related Disorders

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ABSTRACT

Posttraumatic stress disorder (PTSD) is widely recognized as involving disruption of core neurocircuitry that underlies processing, regulation, and response to threat. In particular, the prefrontal cortex–hippocampal–amygdala circuit is a major contributor to posttraumatic dysfunction. However, the functioning of core threat neurocircuitry is partially dependent on sensorial inputs, and previous research has demonstrated that dense, reciprocal connections exist between threat circuits and the ventral visual stream. Furthermore, emergent evidence suggests that trauma exposure and resultant PTSD symptoms are associated with altered structure and function of the ventral visual stream. In the current review, we discuss evidence that both threat and visual circuitry together are an integral part of PTSD pathogenesis. An overview of the relevance of visual processing to PTSD is discussed in the context of both basic and translational research, highlighting the impact of stress on affective visual circuitry. This review further synthesizes emergent literature to suggest potential timing-dependent effects of traumatic stress on threat and visual circuits that may contribute to PTSD development. We conclude with recommendations for future research to move the field toward a more complete understanding of PTSD neurobiology.

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Traumatic events can lead to debilitating cognitive and affective dysfunction that significantly impairs an individual's normal daily functioning. A subset of people exposed to trauma will go on to develop posttraumatic stress disorder (PTSD), which is characterized by intrusive thoughts and memories, avoidance behaviors, negative feelings about oneself and the world, and heightened physiological arousal (1). Furthermore, although posttraumatic reactions may initially be tied to stimuli directly related to the context and events of a trauma, they can become generalized to previously innocuous stimuli over time (2,3). Thus, PTSD is often thought to involve disruptions in the formation, consolidation, and retrieval of trauma-related threat memories. However, most individuals exposed to trauma do not develop PTSD or long-term psychiatric dysfunction. Thus, identifying the neurobiological mechanisms that confer susceptibility to PTSD is important for identifying individuals who are most at risk for the social, emotional, and financial burdens associated with adverse posttraumatic outcomes.

Neurobiological investigations of PTSD have primarily focused on aberrant structure and function of core neurocircuitry that mediates threat learning, memory, and symptom expression (4). However, circuits necessary for the sensory perception of stimuli have been largely ignored despite preclinical literature showing their necessity for basic threat processes. Emerging work in large-scale PTSD studies has further highlighted the idea that visual circuitry, particularly the ventral visual stream, may play an important role in PTSD development and symptom expression. Furthermore, connections between threat and visual neurocircuitry may be impacted by

trauma and may contribute to (or be predictive of) dysfunctional threat learning and memory processes that ultimately contribute to PTSD phenomenology.

In the current narrative review, we discuss recent work that suggests a role for visual circuitry in PTSD development and phenomenology. We focus on the ventral visual stream, given its role in encoding and processing object properties relevant to the formation of threat memories, and its strong interconnections with canonical threat circuitry (5). We provide background on the relevance of visual processing for understanding PTSD phenomenology and provide a brief overview of the neurobiology of threat and visual circuitry in the Supplement. We review findings spanning brain structure and function that suggest that alterations in visual cortical regions are related to PTSD (Table 1). In particular, we note potential contributions of both early-life trauma and adulthood trauma that may have differential impacts on visual circuitry and play a role in PTSD development. Then, we highlight current research gaps and propose future research directions to better understand the neurobiological basis of PTSD. The current review synthesizes preclinical and clinical neuroscience research to provide an expanded neurobiological model of PTSD, which may facilitate more holistic and effective research.

PTSD-RELATED ALTERATIONS IN AFFECTIVE VISUAL CIRCUITRY

First, we briefly discuss the potential relevance of visual processing and relevant neurobiological circuits to PTSD below,

Table 1. Summary of Literature

Neural Property/Study	Trauma Timing; Trauma Type	Sample Characteristics	Regions	Relevant Finding
Structure—Gray Matter				
Tomoda <i>et al.</i> , 2012 (13)	Childhood (retrospective); witnessing domestic violence	<i>N</i> = 52 (22 trauma-exposed, 30 non-trauma-exposed control individuals)	V1/Lingual gyrus, V5/MT	Lower volume and thickness of regions in those with trauma history; thicker cortex in V5 for resilient trauma-exposed subgroup
Tomoda <i>et al.</i> , 2009 (14)	Childhood (retrospective); harsh corporal punishment	<i>N</i> = 45 (23 trauma-exposed, 22 non-trauma-exposed control individuals)	Medial PFC	Lower gray matter volume in those with trauma history
Crombie <i>et al.</i> , 2021 (15)	Adulthood; intimate partner violence	<i>N</i> = 121 women (99 with PTSD, 22 non-trauma-exposed control individuals)	Occipital cortex, temporal cortex, postcentral gyrus	Higher occipital and postcentral cortex thickness associated with higher avoidance symptoms; lower temporal and parahippocampal thickness associated with higher re-experiencing symptoms
Wrocklage <i>et al.</i> , 2017 (16)	Adulthood; combat exposure	<i>N</i> = 69 (combat-exposed)	Occipital cortex, cuneus, insula, middle/superior frontal	Lower thickness associated with higher PTSD symptoms
Dark <i>et al.</i> , 2021 (17)	Adulthood; civilian trauma	<i>N</i> = 40 (21 trauma-exposed, 19 non-trauma-exposed)	Hippocampus, amygdala	Lower volume in left hippocampus for trauma-exposed group, volume negatively correlated with avoidance symptoms
Logue <i>et al.</i> , 2018 (18)	Mixed	<i>N</i> = 1868 (794 with PTSD, 1074 trauma-exposed control individuals)	Amygdala, hippocampus	Lower hippocampal and amygdala volume in PTSD group
Rakesh <i>et al.</i> , 2023 (19)	Mixed	<i>N</i> = 3439 (1348 with PTSD, 2082 control individuals depending on modality)	Fusiform gyrus, occipital cortex, inferior temporal gyrus	Higher structural network centrality of fusiform and inferior temporal regions in PTSD, but lower centrality of occipital sulcus
Sun <i>et al.</i> , 2022 (20)	Mixed	<i>N</i> = 3438 (1348 with PTSD, 2073 trauma-exposed control individuals depending on modality)	Medial PFC, occipital cortex, inferior temporal	Lower thickness and surface area in prefrontal areas, lower covariance of atrophic networks composed of occipital/visual regions
Cwik <i>et al.</i> , 2020 (21)	Adulthood; civilian trauma	<i>N</i> = 56 (21 with acute stress disorder, 17 with PTSD, 18 non-trauma-exposed control individuals)	Lingual gyrus, cuneus, medial PFC, middle temporal	Lower volume in visual regions for those with acute stress disorder compared with control individuals, lower temporal volume predicted future arousal symptoms
Yoshii <i>et al.</i> , 2017 (22)	Animal model (rat)	<i>N</i> = 35 (18 with single prolonged stress, 17 sham stress controls)	Thalamus, visual cortex	Lower volume in rats exposed to single prolonged stress
Harnett <i>et al.</i> , 2022 (23)	Adulthood; civilian trauma	<i>N</i> = 278 (trauma-exposed)	V1, occipital cortex, anterior temporal pole	Higher structural covariance associated with higher PTSD symptoms
Harnett <i>et al.</i> , 2022 (24)	Adulthood; civilian trauma	<i>N</i> = 78 (trauma-exposed)	Fusiform area, V1, anterior temporal pole	Higher structural covariance associated with higher PTSD symptoms
Structure—White Matter				
Olson <i>et al.</i> , 2017 (28)	Mixed	<i>N</i> = 37 (20 with PTSD, 17 trauma-exposed control individuals)	Uncinate fasciculus, inferior longitudinal fasciculus	Lower fractional anisotropy of white matter tracts in individuals with PTSD
Sanjuan <i>et al.</i> , 2013 (29)	Adulthood; combat veterans	<i>N</i> = 22 (12 with PTSD and alcohol use disorder, 10 with alcohol use disorder)	Dorsal cingulum, anterior corona radiata	Lower fractional anisotropy of white matter tracts in individuals with PTSD
Dennis <i>et al.</i> , 2021 (30)	Mixed	<i>N</i> = 3047 (1426 with PTSD, 1621 control individuals)	Tapetum	Lower fractional anisotropy in those with PTSD

Table 1. Continued

Neural Property/Study	Trauma Timing; Trauma Type	Sample Characteristics	Regions	Relevant Finding
Choi <i>et al.</i> , 2012 (33)	Childhood (retrospective); witnessing domestic violence	<i>N</i> = 47 (trauma-exposed, 27 unexposed control individuals)	Inferior longitudinal fasciculus	Lower fractional anisotropy in those exposed to domestic violence; negative association between anisotropy and duration of exposure
Olson <i>et al.</i> , 2020 (34)	Mixed	<i>N</i> = 93 (32 with PTSD, 27 trauma-exposed control individuals, 32 non-trauma-exposed control individuals)	Inferior longitudinal fasciculus	Higher childhood maltreatment was associated with lower fractional anisotropy
Hu <i>et al.</i> , 2016 (37)	Adulthood; civilian trauma	<i>N</i> = 34 (17 with PTSD, 17 trauma-exposed control individuals)	Anterior thalamic radiation, inferior fronto-occipital fasciculus, cingulum, uncinate fasciculus	Lower fractional anisotropy and higher radial diffusivity in those with PTSD
Li <i>et al.</i> , 2016 (38)	Adulthood; civilian trauma	<i>N</i> = 65 (21 with poor recovery after mTBI, 22 with successful recovery after mTBI, 22 control individuals); recovery defined by PTSD symptoms	Inferior longitudinal fasciculus; inferior fronto-occipital fasciculus, superior longitudinal fasciculus	Higher fractional anisotropy and mean diffusivity in mTBI than control individuals; microstructural features of tracts were discriminative of recovery
Wong <i>et al.</i> , 2023 (39)	Adulthood; civilian trauma	<i>N</i> = 202 (trauma-exposed)	Internal capsule	Prior childhood maltreatment negatively associated with fractional anisotropy; fractional anisotropy mediated relationship between childhood maltreatment and PTSD symptoms
Function				
Milad <i>et al.</i> , 2009 (41)	Mixed	<i>N</i> = 39 (19 with PTSD, 20 trauma-exposed control individuals)	Medial PFC, hippocampus, occipital cortex	Lower hippocampal and medial PFC but higher occipital cortex reactivity during extinction recall in PTSD
Garfinkel <i>et al.</i> , 2014 (42)	Adulthood; combat exposure	<i>N</i> = 28 (14 with PTSD, 14 trauma-exposed control individuals)	Amygdala, medial PFC, occipital lobe	Higher responses to conditioned stimuli during extinction/renewal in control individuals than in those with PTSD
Rougemont-Bücking <i>et al.</i> , 2011 (43)	Mixed	<i>N</i> = 34 (18 with PTSD, 16 trauma-exposed control individuals)	Medial PFC, occipital cortex	Higher activation during extinction and extinction recall across participants
Fani <i>et al.</i> , 2012 (44)	Mixed	<i>N</i> = 37 (18 with PTSD, 19 trauma-exposed control individuals)	Lingual gyrus, dorsolateral PFC, middle occipital gyrus	Higher responses in PFC, but lower responses in visual regions, in those with PTSD; neural reactivity associated with threat bias scores
Stevens <i>et al.</i> , 2013 (47)	Mixed	<i>N</i> = 40 (20 with PTSD, 20 trauma-exposed control individuals)	Amygdala, fusiform gyrus, medial PFC, lingual gyrus	Higher reactivity to threat compared with neutral stimuli across participants; PTSD show lower amygdala to PFC connectivity
Zhang <i>et al.</i> , 2013 (48)	Adulthood; civilian trauma	<i>N</i> = 40 (20 with PTSD, 20 trauma-exposed control individuals)	Amygdala, fusiform gyrus, PFC	Higher reactivity within the amygdala and fusiform but lower PFC reactivity in people with PTSD
Mueller-Pfeiffer <i>et al.</i> , 2013 (49)	Mixed	<i>N</i> = 39 (18 with PTSD, 21 trauma-exposed control individuals)	Lingual gyrus, hippocampus, occipital gyrus, PFC	Higher reactivity to visual stimuli in trauma-exposed control individuals compared to individuals with PTSD
Sambuco <i>et al.</i> , 2020 (50)	Mixed	<i>N</i> = 197 (162 with psychiatric disorder, 35 healthy [nonpsychiatric] control individuals)	Amygdala, inferior temporal cortex, inferior occipital cortex	Negative association of amygdala and ventral visual stream reactivity with frequency and severity of trauma exposure
Fani <i>et al.</i> , 2021 (51)	Mixed	<i>N</i> = 55 (mixed PTSD/trauma-exposed participants)	Medial PFC, occipital gyrus	Positive association between neural reactivity and exposure to racial discrimination

Table 1. Continued

Neural Property/Study	Trauma Timing; Trauma Type	Sample Characteristics	Regions	Relevant Finding
Hendler <i>et al.</i> , 2003 (52)	Adulthood; combat exposure	<i>N</i> = 21 (10 with PTSD, 11 trauma-exposed control individuals)	Occipital gyrus, fusiform, amygdala	Higher reactivity in PTSD when stimulus presentations were shorter (below recollection threshold)
Xia <i>et al.</i> , 2024 (53)	Animal model (mice)	<i>N</i> = 12 (6 exposed to single prolonged stress, 6 nonexposed controls)	V1	Enhanced stimulus-driven firing but reduced preferred speed in mice exposed to single prolonged stress
Maron-Katz <i>et al.</i> , 2020 (55)	Adulthood; combat exposure	<i>N</i> = 210 (97 with PTSD, 113 trauma-exposed control individuals)	Ventral visual cortex, frontoparietal network, sensorimotor network	Clusters of visual to sensorimotor and frontoparietal networks were associated with PTSD symptoms
Suo <i>et al.</i> , 2020 (56)	Adulthood; civilian trauma	<i>N</i> = 122 (trauma-exposed)	Visual regions, cerebellum, amygdala	Connectivity between visual regions and other nodes predictive of higher PTSD symptoms
Clancy <i>et al.</i> , 2024 (57)	Mixed	<i>N</i> = 84 (63 with PTSD, 21 trauma-exposed control individuals)	Hippocampus, visual cortex, dorsal anterior cingulate	Positive association between hippocampal-visual cortex coactivation and reliving of trauma symptoms
Dopfel <i>et al.</i> , 2019 (58)	Animal model (rat)	<i>N</i> = 87 (64 exposed to predatory odor, 23 nonexposed controls)	Amygdala, BNST, visual cortex, nucleus accumbens	Positive association between visual cortex to nucleus accumbens connectivity and freezing during predator scent exposure
Leite <i>et al.</i> , 2022 (59)	Adulthood; civilian trauma	<i>N</i> = 20 (10 with PTSD, 10 non-trauma-exposed control individuals)	Amygdala, lingual gyrus, fusiform gyrus	Lower connectivity between amygdala and lingual/fusiform gyri in PTSD
Zhong <i>et al.</i> , 2019 (60)	Childhood (retrospective); maltreatment	<i>N</i> = 96 (48 with childhood maltreatment, 48 without)	Lingual gyrus, fusiform gyrus, medial PFC, dorsolateral PFC	Within-group analysis revealed activation within lingual and fusiform gyri during task; higher reactivity within dorsolateral PFC, but lower reactivity in medial PFC, for maltreatment compared to nonmaltreatment group
Allen <i>et al.</i> , 2023 (61)	Childhood; mixed (maltreatment, community violence, poverty)	<i>N</i> = 179 (juvenile incarcerated males, trauma-exposed)	Precuneus, V2, fusiform	Higher childhood trauma exposure associated with altered amplitude within regions
Hakamata <i>et al.</i> , 2021 (62)	Childhood (retrospective); childhood trauma questionnaire	<i>N</i> = 100 (healthy adult participants)	Fusiform gyrus, occipital pole, occipital gyrus, paracingulate gyrus	Childhood trauma was positively associated with connectivity between prefrontal and visual regions
Morey <i>et al.</i> , 2015 (63)	Adulthood; combat veterans	<i>N</i> = 67 (32 with PTSD, 35 trauma-exposed control individuals)	Fusiform gyrus, V1, thalamus, calcarine cortex	Higher reactivity to high-intensity threat generalized stimuli in those with PTSD; amygdala to calcarine connectivity moderated by prior childhood trauma
George <i>et al.</i> , 2022 (64)	Childhood; mixed	<i>N</i> = 51 (23 with PTSD, 28 typically developing control individuals)	Hippocampus, V3, V4, fusiform	Higher reactivity but lower connectivity between regions in PTSD
Harnett <i>et al.</i> , 2022 (23)	Adulthood; civilian trauma	<i>N</i> = 278 (trauma-exposed)	Inferior temporal gyrus, amygdala, hippocampus, ventral visual stream	Ventral visual stream structural covariance moderated amygdala/hippocampal connectivity with inferior temporal gyrus
Harnett <i>et al.</i> , 2021 (66)	Adulthood; civilian trauma	<i>N</i> = 109 (trauma-exposed)	Amygdala, hippocampus, dorsolateral PFC, visual cortex	Negative association between subcortical and prefrontal connectivity and future PTSD symptoms; negative association between subcortical and visual cortex connectivity and future PTSD symptoms when controlling for acute PTSD symptoms
Harnett <i>et al.</i> , 2018 (67)	Adulthood; civilian trauma	<i>N</i> = 40 (19 trauma-exposed, 21 non-trauma-exposed)	Dorsolateral PFC, cuneus, insula	Higher reactivity in trauma-exposed individuals

Trauma timing refers to index trauma, with studies reporting on participants with various timing or types being mixed.

BNST, bed nucleus of the stria terminalis; mTBI, mild traumatic brain injury; PFC, prefrontal cortex; PTSD, posttraumatic stress disorder; V1, primary visual cortex; V2, secondary visual cortex; V3, visual area 3; V4, visual area 4; V5/MT, middle temporal area.

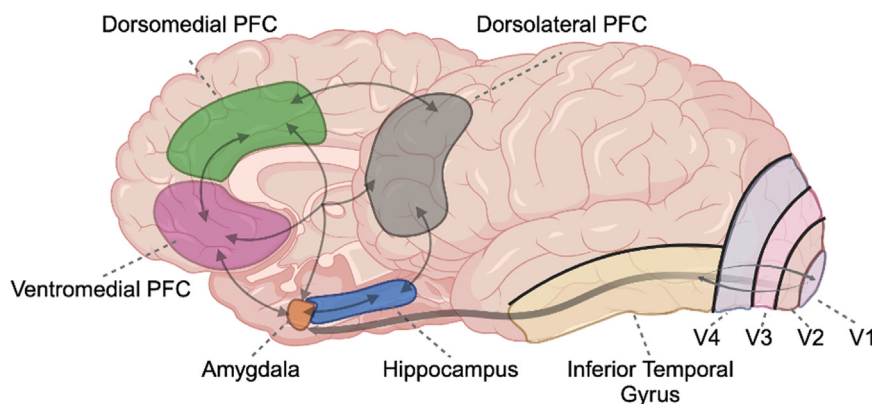


Figure 1. Schematic overview of threat and visual neurocircuitry related to posttraumatic stress disorder susceptibility. PFC, prefrontal cortex; V1, primary visual cortex; V2, secondary visual cortex; V3, visual area 3; V4, visual area 4.

with a fuller overview presented in the [Supplement](#). PTSD is commonly thought to involve disruption of a core threat neurocircuit comprising the prefrontal cortex (PFC), hippocampus, and amygdala, that supports formation, consolidation, and expression of emotional threat memories (6). However, recent theoretical research has highlighted that PTSD is also associated with disruption in sensorial processes that may influence downstream threat processes (7,8).

The ventral visual stream has reciprocal connections with the PFC-amygdala-hippocampal circuit ([Figure 1](#)) that supports key processes for threat learning and memory (5). Experience-dependent modifications during Pavlovian threat conditioning are also apparent in both threat and associated sensorial neurocircuitry (9,10). However, while significant attention has been given to threat neurocircuitry in trauma and PTSD, a better understanding of structural and functional alterations in ventral visual regions may be essential for a more complete understanding of PTSD neurobiology.

Structure—Gray Matter

Morphological studies have identified structural variability in the primary visual cortex (V1) and inferior temporal lobe related to PTSD risk and diagnosis. Childhood trauma, a major predisposing factor for PTSD (11,12), is associated with lower volume and thickness of V1 and other occipital areas (13,14). Both PTSD-resilient and PTSD-affected individuals exhibit these volumetric differences, with resilient individuals showing somewhat higher V5 thickness than susceptible individuals. In a sample of women who experienced interpersonal violence, higher avoidance symptom severity was associated with higher middle occipital cortical thickness, while re-experiencing symptom severity was correlated with lower thickness of the inferior temporal gyrus (15). No differences were observed between resilient and susceptible individuals. Research involving mostly male combat veterans demonstrated that higher PTSD symptom severity was associated with lower thickness of occipital and primary visual areas (16). It is unclear whether the differences between these studies may be driven by sex-related factors or the type of trauma experienced. Furthermore, there are limited data comparing trauma-exposed to non-trauma-exposed individuals to

confirm whether morphological variability is a function of trauma exposure or a combination of traumatic stress and underlying susceptibility to PTSD (17). However, taken together, current imaging data suggest that gray matter morphological changes of posterior ventral visual stream regions in PTSD are influenced by traumatic experiences but are not sufficient to account for PTSD phenotypes.

Recent mega-analyses from the PGC (Psychiatric Genomics Consortium) and ENIGMA (Enhancing Neuro Imaging Genetics through Meta Analysis) (18) have confirmed gray matter morphological alterations in both hippocampal and ventral visual circuitry related to PTSD. Structural covariance networks, or shared variability of gray and white matter features, of the visual system are altered in individuals with PTSD. These alterations include higher network centrality—a measure of a region's relative importance or influence on other regions—in the fusiform face and occipital areas (19). Participants also showed lower structural covariance within atrophic networks associated with PTSD (20). Specifically, individuals with PTSD typically show lower gray matter in canonical threat neurocircuitry and the resultant atrophy associated with lower structural connectivity to visual circuitry. Together, the findings suggest that in adulthood PTSD, visual circuitry has great influence on interconnected, threat-related regions and networks but limited top-down inhibition from prefrontal networks, consistent with previous conceptualizations of the disorder.

Investigations with recent trauma survivors have provided additional evidence that gray matter alterations along the ventral visual stream contribute to PTSD symptoms. In one study, recent trauma survivors with acute stress disorder showed reduced gray matter volume of V1 compared with typical control individuals, and V1 volume variability predicted later PTSD symptoms (21). The findings are consistent with a preclinical report that demonstrated atrophy of the visual cortex and thalamus in rats exposed to single prolonged stress (22). Additionally, in 2 independent clinical samples, structural covariance of the ventral visual stream, particularly across volume and cortical surface area, was positively associated with acute PTSD symptoms (23,24). Interestingly, ventral visual stream structural covariance became negatively associated with PTSD symptoms 6 months after trauma exposure (23). The reason for the switch in the relationship is unclear,

although secondary drivers of neuronal changes after injury may contribute to altered neurobiology and reflect a structural shift supporting acute to chronic posttraumatic dysfunction, as suggested by research discussed previously. Dysregulation of glutamatergic activity can lead to excitotoxicity and resulting neurobiological damage that may be related to the development of PTSD (25,26). Speculatively, traumatic stress exposure could facilitate ventral visual stream processes to potentiate trauma memory retrieval. However, overexcitation of threat memory retrieval processes could contribute to neurodegenerative processes across visual and threat neurocircuitry. An alternative or concurrent mechanism is that immune or glial system activity in the months following trauma may contribute to volumetric changes, similar to the secondary phase of tissue damage that occurs after traumatic brain injury (27).

Structure—White Matter

White matter microstructural changes supporting visual processing have also been observed in PTSD. Previous work identified lower fractional anisotropy (FA) within the inferior longitudinal fasciculus (ILF) in patients with PTSD compared with trauma-exposed control individuals (28). Interestingly, changes in FA of the ILF co-occurred with lower FA in the uncinate fasciculus, a white matter tract that interconnects with the ventromedial PFC and amygdala within the threat circuit. PTSD is associated with lower FA within the cingulum bundle (29). Additionally, a recent mega-analysis of white matter microstructural variability highlighted robust differences in FA of the tapetum in individuals with PTSD compared with control individuals (30). The tapetum runs near the posterior cingulum bundle and helps interconnect the hippocampus in both hemispheres (31). Fibers of the geniculocalcarine tract and optic radiations traverse near the tapetum, raising the possibility that visual circuit-related white matter tracts may be altered in PTSD. Thus, findings suggest that PTSD is associated with alterations in white matter microstructure of tracts that overlap visual and threat neurocircuitry.

Visual circuit white matter alterations may be partially driven by stressful experiences that occur prior to an index trauma during adulthood in PTSD-susceptible individuals. Childhood stressors, such as childhood trauma, are linked to microstructural alterations of white matter tracts that interconnect visual and threat neurocircuitry (32). Exposure to domestic violence early in development is associated with lower FA of the ILF (33). Furthermore, experiences of childhood trauma are negatively associated with ILF FA in adults with and without PTSD (34). Research has shown that brain development occurs along a sensorimotor-association axis wherein sensory circuits, including the ventral visual stream, undergo rapid development before association circuits like the threat circuit (35,36). Thus, early childhood trauma may lead to more pronounced FA reductions in visual than in threat circuits.

Convergent evidence from recent trauma survivors suggests that white matter alterations of tracts that support visual processing are associated with PTSD phenotypes. Microstructure of the ILF and inferior fronto-occipital fasciculus predict PTSD symptoms following a recent trauma (37,38).

Furthermore, a history of childhood maltreatment appears to confer susceptibility to PTSD among survivors who experience subsequent trauma in adulthood via alterations in the microstructure of the internal capsule (39). Divisions of the internal capsule contain visual, motor, auditory, and somatosensorial fibers and overlap with fibers that sit near the tapetum, where previously discussed white matter alterations in patients with PTSD have been observed (30). Consistent with research conducted with individuals with chronic PTSD, early exposure to trauma may lead to microstructural changes in visual processing pathways that are related to PTSD. Taken together, these findings underscore the presence of white matter microstructure in tracts that connect the ventral visual stream and the canonical threat circuit.

Function

Early research on neural function related to PTSD predominantly focused on potentially aberrant activity in threat neurocircuitry [see (40) for review]. However, it is worth noting that many seminal investigations of threat in PTSD have also reported altered activity within visual regions. Differences in functional activity during extinction recall between individuals with PTSD and combat-exposed control individuals have been observed in the lingual gyrus and occipital cortex (41,42). Furthermore, variations in extinction learning rates may be related to occipital cortex activity (43). PTSD-related alterations in attentional bias to threat have also been associated with altered activity within the lingual gyrus (44). Thus, in addition to classical threat neurocircuit regions, visual cortices also show functional variability related to PTSD phenotypes. Meta-analyses of functional neuroimaging studies have consistently affirmed the presence of differences in activation within ventral visual stream regions in individuals with PTSD compared with both trauma-exposed and trauma-naïve control individuals (45).

PTSD-related variability in both core threat and visual regions may indicate a valence-dependent alteration in neural processing. Typically, negatively valenced visual stimuli (e.g., fearful faces) elicit enhanced reactivity within the amygdala and ventral visual cortex (46,47). Individuals with PTSD showed higher activation in these regions when negative distractors are presented during a goal-directed task (48). In contrast, some previous work observed that compared with trauma-exposed control individuals, people with PTSD showed lower reactivity within visual cortices when viewing emotional and neutral images (49). Recent research has suggested that the degree of trauma may determine the presence of altered activity within ventral visual regions (50). Higher trauma severity has been associated with lower activation of the amygdala and ventral visual cortices in transdiagnostic trauma-exposed patients than in control individuals during the presentation of emotional compared with neutral images. These findings contrast somewhat with those of a previous study, which demonstrated a positive association between trauma load and lingual gyrus activity during attention to threat stimuli in patients with PTSD (44). However, the sample in the latter study primarily consisted of Black women, who experience qualitatively and quantitatively distinct types of stress and trauma such as racial discrimination. These experiences were associated with ventral visual cortex activity during a cognitive interference

task with negative distractor images (51). Enhanced visual responsivity in PTSD may not be valence specific. Previous work found higher responsivity in the visual cortex in individuals with PTSD than in those without, but the effect was specific to trauma-related contexts and was only apparent at shorter stimulus presentations (below participants' threshold of awareness) (52). Similarly, neuronal recordings in mice after a single prolonged stress paradigm revealed that V1 neurons were more responsive to stimuli after stress, with effects being specific to preferred visual stimulus speed, but not direction or orientation, detected by V1 neurons (53). The effect of stress on V1 activity has been mediated by corticotropin releasing factor signaling pathways, which have been linked to PTSD in preclinical and human work (54). Overall, the existing literature suggests that trauma exposure and PTSD are associated with altered ventral visual responses to stimuli and that valence-specific responsivity may be moderated by characteristics of the specific type of traumatic stress.

Furthermore, PTSD is associated with variability in functional connectivity, or functional coupling, of visual brain regions. A recent data-driven approach identified 2 neuroimaging subtypes associated with PTSD based on resting-state connectomes (55). The subtypes were differentiated by divergent patterns of functional connectivity between the ventral visual cortex and both frontoparietal and sensorimotor networks, with one group showing more functional coupling with the ventral visual cortex and the other showing lower coupling. Additional work observed that functional connections from the visual cortex to other brain regions such as the cerebellum, brain stem, and limbic areas (e.g., amygdala/hippocampus) were associated with PTSD symptoms in earthquake survivors (56), while the reliving experience of trauma-related intrusive memories has been found to be associated with more persistent states of coactivation between the visual cortex and posterior hippocampus (57). Interestingly, in a rat model, negative coupling of the visual cortex and nucleus accumbens was associated with lower freezing responses after predator odor exposure (58). A separate study observed lower connectivity between the amygdala and both the lingual and fusiform gyri in patients with PTSD than in trauma-exposed control individuals (59). Notably, these findings contrast with findings yielded by data-driven approaches, which suggests that there may be disparate brain-behavior associations for single connections and network covariances.

Childhood trauma also appears to moderate the functional activity and connectivity of visual areas. Notable differences in neural responses have been observed in retrospective studies conducted with adult survivors of childhood maltreatment. Survivors displayed higher activation within occipital and lingual gyri and lower ventromedial PFC activation than typical control individuals during a psychosocial stress task (60). Exposure to childhood trauma appears to modulate intranetwork connectivity of visual circuitry, particularly between the fusiform and the cuneus (61) and between the visual cortex and medial PFC (62). Childhood trauma may be a moderator of functional connectivity between the amygdala and calcarine cortex during a threat generalization procedure in individuals with PTSD (63). These findings collectively suggest that childhood trauma impacts connectivity between visual and

threat circuitry regions. Consistent with previous observations, youths with persistent pediatric PTSD showed higher activity, but lower connectivity, between the hippocampus and V4 than typical control individuals and individuals with remitted pediatric PTSD (64). Together, these data strongly suggest that exposure to traumatic stress in early life may alter functional architecture along the ventral visual stream.

Evidence from recent trauma survivors further implicates visual circuitry in PTSD. In participants from the AURORA (Advancing Understanding of Recovery After Trauma) study (65), functional connectivity between an arousal network that overlapped the amygdala, hippocampus, and visual cortex 2 weeks posttrauma was negatively associated with 3-month PTSD when controlling for 2-week symptoms (66). A positive association between default mode network connectivity with the inferior temporal gyrus and 3-month PTSD symptoms was also observed. In the same cohort, structural covariance of the ventral visual stream modulated amygdala/hippocampal connectivity with the inferior temporal gyrus (23). Finally, in a separate sample of recent trauma survivors, neural reactivity within the cuneus and canonical threat neurocircuitry was elevated in response to both threat and safety cues during Pavlovian conditioning (67). Thus, the existing literature suggests that traumatic stress has an impact on threat neurocircuitry and that variability in structural and functional connectivity between threat and visual circuitry partially underlies susceptibility to PTSD.

CONCEPTUALIZING EARLY AND LATER LIFE TRAUMATIC STRESS INFLUENCES ON AFFECTIVE VISUAL CIRCUITRY

The current body of literature has demonstrated that PTSD is associated with variability in both the function and structure of the ventral visual stream. Threat and ventral visual circuits support components of threat processing, such as perception, learning, consolidation, and retrieval processes that are disrupted in PTSD. Trauma-exposed individuals who are susceptible to developing PTSD show alterations in the structure of regions along the ventral stream and in key threat response regulation regions (e.g., medial PFC). Similarly, PTSD-susceptible individuals show diminished microstructural connectivity of long-range white matter tracts necessary to connect threat and visual processing regions. Finally, these individuals exhibit altered functional activity, often in the form of heightened activation patterns to threatening stimuli and dysregulated connectivity.

Early Exposure to Trauma as Disruptive to Sensorial Circuitry

Early exposure to trauma, particularly during childhood, appears to exert a pronounced effect on the function and structure of ventral visual and other sensory regions. The work reviewed herein demonstrated variability in gray matter morphology of ventral visual regions as well as in microstructure of long-range projection tracts such as the ILF and inferior fronto-occipital fasciculus. Importantly, the ILF and inferior fronto-occipital fasciculus run through the ventral visual stream and near both the amygdala and ventromedial PFC. Given the association between early-life trauma and increased risk of

PTSD (11), it may be that changes to visual sensory cortices that result from childhood trauma are a core part of an individual's susceptibility to PTSD in later life. Consistent with this hypothesis, the reviewed studies of recent trauma survivors suggest that aberrant visual circuit connectivity serves as a mediator of PTSD development following adulthood trauma exposure. White matter connections that carry sensory fibers seem to mediate the impact of childhood trauma on the manifestation of PTSD symptoms in adulthood (39). Moreover, both the function and structure of visual-to-threat neurocircuitry have been tied to the future expression of PTSD symptoms (23). Speculatively, the visual circuitry alterations induced by childhood trauma may contribute to differential development of threat neurocircuitry and ultimately to PTSD susceptibility.

Later Exposure to Trauma as Disruptive to Threat Circuitry

Alternatively, traumatic events in later life, such as those that occur in adulthood, may have a more substantial impact on threat neurocircuitry than ventral visual regions. Human neuroimaging studies that have employed stress-induction paradigms with adults have highlighted robust activation of threat neurocircuitry, particularly in regions that support emotion regulation (68,69). Speculatively, adults may have greater interoceptive awareness and metacognitive capacity than children coupled with a potentially more crystallized schema of the world. Therefore, adults may have a greater ability for cognitive regulation of emotional responses based on preexisting knowledge. Although relatively few task-based studies conducted in the early aftermath of trauma are available, the current literature suggests that trauma survivors show more robust responses in threat neurocircuitry (67,70,71). Nonetheless, visual circuitry appears to partially mediate susceptibility to PTSD even in adult trauma survivors (23,24), although these effects may be due to childhood traumatic stress that occurred prior to the index trauma (39).

Hypothetical Mechanisms Contributing to Timing and Circuit-Specific Associations

One potential mechanism underlying the current findings is that early-life trauma disrupts typical threat learning and memory by augmenting visual perception and encoding of potential threats. As discussed above, threat and visual neurocircuitry are highly interlinked and form recurrent neural networks to process visual stimulus properties. Individuals exposed to abuse and disadvantage may develop enhanced vigilance for or biased perception toward potential threats in the environment due to a lack of appropriate exposure to nonthreat contexts (e.g., living in a safe home or neighborhood). These changes may represent an adaptive mechanism, as previously proposed (32). The need for enhanced threat detection may be related to altered development of ventral visual stream neurobiology. Heightened visual processing of potential threat may then lead to facilitation of threat memory encoding and generalization, possibly mediated by altered development of threat and visual neurocircuitry connections that govern learning and memory. In turn, such neurobiological changes may make individuals more susceptible to PTSD later in adulthood. Such a model may also partially explain

differences in PTSD symptom profiles between individuals exposed to varying levels of childhood trauma.

The conceptual model described above proposes that trauma timing affects the relative importance of threat versus visual circuitry to individual propensity to develop PTSD. However, existing evidence does not support an independent, causal role of visual circuitry in PTSD symptoms. Previous work observed higher rates of PTSD in individuals with visual impairment (72), suggesting that conscious visual processing or visual circuit involvement is not necessary for PTSD development. Furthermore, lesion studies and case reports have suggested that medial PFC and amygdala connections are key to emotional responses (73,74). A recent case report even indicated that amygdala ablation reduced PTSD symptoms and associated fear-related behaviors (75). Nevertheless, research findings on PTSD prevalence in individuals with visual impairment compared with the general population have been mixed. Individuals with visual impairment also may differ in the types of traumas experienced and other factors related to PTSD (76). Furthermore, as discussed above, visual (and other sensorial) circuitry is necessary for learning and memory processes that are key to trauma memory consolidation and recall. Overall, the current literature supports a model in which visual circuitry may modulate threat neurocircuitry, which in turn is necessary for PTSD development. However, future research is needed to conclusively disentangle the causal roles of these circuits in the disorder.

FUTURE RESEARCH

The existing literature suggests that trauma exposure is related to alterations in function and structure of visual circuitry that may be linked to the development of PTSD. Such changes may drive or contribute to disruptions in threat-processing circuitry that are typically considered fundamental to the disorder. However, several important gaps remain in our understanding of potential contributions of visual circuitry to PTSD that require additional consideration.

One needed area of research is to examine how PTSD treatments are related to visual circuitry. Given the mechanism of exposure treatments, there is potential for changes in visual processes (e.g., eye movements, visual responsivity) and associated neural circuitry that are relevant to understanding treatment efficacy and nonresponsivity. Furthermore, the visual cortex may be an alternative targeting site for neuromodulatory therapies such as transcranial magnetic stimulation. Individual regions of the visual cortex are targetable by transcranial magnetic stimulation (77); previous work has demonstrated that visual cortex stimulation can modulate the emotional intensity of intrusive memories (78) and significantly impact conscious interoceptive processing (79,80). Furthermore, in mice, low intensity repetitive transcranial magnetic stimulation appears to induce reconstruction of geniculocalcarine tracts and increase brain-derived neurotrophic factor (81), which has been implicated in fear extinction processes and PTSD (82). Therefore, further research on treatment effects on visual neural circuitry is of interest.

One major limitation of trauma neurobiology research is the paucity of longitudinal studies that separate long-term consequences of the index trauma from pre-/peritraumatic

stressors. Current initiatives such as the Adolescent Brain Cognitive Development Study and Healthy Brain and Child Development Study may offer insight into the developmental impacts of trauma exposure on visual and threat neurobiology. Some individuals in these large-scale studies may experience traumatic events with potentially pretraumatic brain imaging. Combined with individual deep phenotyping, these longitudinal studies may yield a better understanding of the neurodevelopmental consequences of trauma. However, the datasets may not contain behavioral tasks or imaging sequences suited to discerning changes in visual circuitry or may not use measures capable of providing detailed information about trauma types for various reasons.

Another weakness of neurobiological investigations of PTSD is the lack of basic psychophysics research conducted with trauma-exposed individuals. Research on executive function in PTSD suggests that the disorder is associated with alterations in attention to stimuli, even when stimuli lack valence (83). These attention-related deficits are associated with differential functional connectivity patterns within threat neurocircuitry regions that also support executive function (84). Therefore, a major component of PTSD stimulus processing difficulties may be driven by attentional issues that are more bottom-up (e.g., visual processing) or that occur prior to potential valence assignment. However, there have been relatively few investigations of underlying visual neurobiology in PTSD. The roles of various components of the ventral visual stream have been well established in the human neuroimaging literature. Extensive work has documented the role of processing along the inferior temporal gyrus in object recognition (85,86). Speculatively, threat memory generalization may also be related to specific alterations along the ventral visual stream that facilitate improper recognition of stimuli as opposed to being specific to threat neurocircuitry disruption. Such investigations have not been undertaken with recent trauma survivors or individuals with PTSD. Thus, our understanding of the neurobiological basis of the disorder may be strengthened by combining clinical and basic visual psychophysics research.

Advancements in neuroimaging could enhance basic visual psychophysics research in PTSD to improve our understanding of neural circuitry. Laminar functional magnetic resonance imaging (fMRI), which is a useful technique for imaging cortical layers in humans (87,88), can allow researchers to quantify neural reactivity in superficial, middle, and deep cortical layers, which may have differential responses to affective and neutral stimuli. Furthermore, cortical layers have distinct projections to one another within and across brain regions that contribute to different neuronal processes (89). Such layer- and region-specific interactions, especially between visual and association cortices, may be critical for understanding the neurobiology of PTSD susceptibility. A drawback of the technique is longer acquisition times, which may affect participation, especially among trauma survivors. Laminar fMRI also usually requires ultrahigh field strength (e.g., 7T), whereas most PTSD research is conducted at lower field strengths (e.g., 3T). Furthermore, acquisition parameters and analysis approaches may differ from those of standard blood-oxygen-level-dependent fMRI approaches, which may complicate study design and analysis. However, emerging techniques allow for laminar fMRI at lower field strengths, and growing expertise in

the technique may facilitate more usage in clinical populations such as patients with PTSD (90,91). Furthermore, utilizing advancements in magnetic resonance spectroscopy to investigate glutamatergic and GABAergic (gamma-aminobutyric acidergic) disruptions in visual processing regions may unveil important neuromolecular components of PTSD. Techniques such as MEGA-PRESS already permit quantification of these neurotransmitters at lower field strengths (92–94), with higher field strengths allowing identification of more focal fluctuations. Thus, leveraging advances in neuroimaging may provide more granular information about the specific affective and visual circuitry that underlies PTSD and related disorders.

CONCLUSIONS

Although threat-related emotional processing is known to be dysregulated in PTSD, growing evidence suggests that visual processing disruptions are interlinked with the behavioral and psychological manifestations of the disorder. Similarly, growing research suggests that traumatic stress exposure and resultant PTSD in adulthood are related to structural and functional variability in visual circuitry. Interactions between visual and threat circuitry appear to be modulated as a function of PTSD but may also depend on the occurrence of pretraumatic (e.g., childhood) stressors. Together, the emerging literature suggests that susceptibility to the deleterious effects of traumatic stress may be driven, in part, by effects on visual processing circuitry. Future research that leverages both granular investigations of underlying neurobiology and sensory-perceptual processes is needed to better elucidate the neurobiological basis of PTSD susceptibility.

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