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REVIEW ARTICLE

Dissociative Identity Disorder May Involve an Altered Functioning of the Amygdala in Memory and Behavior

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ABSTRACT: Dissociative Identity Disorder (DID) is a rare trauma-related personality disorder that is characterized by a person having two or more distinct personalities, or "identity states". It is the most complex and controversial dissociative disorder, with different identity states having different behavioral patterns and memory gaps (Dissociative Amnesia). In this review, the mechanisms by which DID affects the role of the amygdala in memory and behavior will be explored. Although previous studies have examined DID using neuroimaging, more research on this topic remains necessary and will help in the development of further treatment and therapeutic approaches for DID, as well as in establishing a better understanding of other trauma-related personality disorders, such as Borderline Personality Disorder. This paper reviews the amygdala's connections with other brain regions and the glutamatergic pathway as primary neurogenetic pathways and circuits involved in the amygdala's role in memory and behavior. More importantly, it examines and elucidates how alterations in these pathways may contribute to DID. Furthermore, a critical assessment of the relationship between childhood trauma and dissociation has been performed. Ultimately, evidence suggests that there is a direct cause-and-effect relationship between trauma and DID.

KEYWORDS: Behavioral and Social Sciences, Physiological Psychology, Dissociative Identity Disorder (DID), Amygdala, Memory, Behavior, Trauma.

Introduction

Dissociative Identity Disorder (DID; formerly known as Multiple Personality Disorder) is a rare personality disorder that affects approximately 1.0-1.5% of the population, and, like other psychiatric disorders, is likely implicated by functional changes within the brain and central nervous system.[1–3] DID is a part of the broader set of "dissociative disorders": disorders that disturb cognitive and psychological features such as memory, behavior, and perception.[4] It is specifically characterized by a person having two or more distinct personalities or "identity states".[1–3] For this review, any reference to the distinct personalities that a person with DID possesses will be referred to strictly as "identity states". The idea of multiple identity states is not unique to DID; most - if not all - people have multiple identity states.[3] However, in people without DID, the identity states are integrated and work in coordination with each other, resulting in a unified sense of identity and self.[1,3–5] Conversely, people with DID experience identity states that are more compartmentalized and separated from each other, contributing to the dissociative nature of the disorder.[3] Not only do these dissociative identity states feel separate from each other, but they also feel separate from the person themselves; people with DID may feel as if their identity states do not belong to them, or that they are externally observing the thoughts, actions, and/or perceptions of a particular identity state.[3,6]

Although multiple models for the cause of DID have been proposed, the model that is currently the most substantiated is "the Trauma Model".[2,5] The Trauma Model of DID presents the idea that DID (as well as the other dissociative disorders) is directly caused by traumatic childhood events [1–3,5–9] such as sexual abuse, physical abuse, or childhood abandonment.

DID has been a controversial mental health disorder throughout history, as many people (including clinical professionals) disregarded the Trauma Model of DID.[3,5] This resulted in the effects of trauma on trauma survivors with DID - particularly women - [3] not being taken seriously and early DID patients not receiving the clinical care they needed. Inaccurate media portrayals of DID [3,5,6] have only contributed to the widespread misunderstanding of this personality disorder. Today, the acceptance of the Trauma Model is as high as it has ever been, but research into the neuropsychological basis of DID is still limited. This review will therefore attempt to address the knowledge gap of the neurogenetics and psychology of DID by investigating how DID may impact the role of the amygdala in memory and behavior by altering its general activity and its glutamatergic transmission. Furthermore, a deeper understanding of the Trauma Model will help improve therapeutic approaches for DID patients and further increase the acceptance of the Trauma Model of DID, which is crucial for providing trauma victims afflicted with DID with the comfort and support they require.[7] Finally, because of its overlapping symptoms with other personality disorders and its strong link to trauma, DID may be misdiagnosed for other mental health disorders, such as Borderline Personality Disorder.[2,5] Elucidating the modified neurogenetic pathways behind DID will help to distinguish it from other similar conditions, therefore helping to prevent a misdiagnosis of the disorder.[7] The amygdala's role in psychiatric conditions is well-renowned,[10] and it is likely a primary brain region associated with DID. This review

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aims to define how functional changes in the amygdala and its glutamatergic pathway may be implicated in DID. It will also evaluate the cause of DID, closely examining the Trauma Model.

Discussion

The role of the amygdala in memory and behavior:

To understand how Dissociative Identity Disorder (DID) affects the activity of the amygdala, it is important to first develop a general and psychological basis of the functioning of the amygdala in memory and behavior. The amygdala is an almond-shaped structure [10,11] found within the temporal lobe of the brain, [10–14] and its connectivity with other brain regions, such as the hippocampus and prefrontal cortex (PFC), is the fundamental attribute underlying its role in memory and behavior.[10,12–15]

It is likely that the disruption or alteration of these amygdala connections may contribute to the behavioral abnormalities and memory loss associated with DID. An example of a key connection that may be impacted is the amygdala-hippocampus connection.[13] It has long been established that the hippocampus plays a vital role in memory.[8,13] This includes an involvement in memory consolidation and episodic memory: the memory of past personal events. The amygdala's involvement in the coordination and management of emotions such as fear, therefore, suggests that the amygdala-hippocampus connection is implicated in episodic memories with a significant emotional impact,[8,10,11,13] such as those of traumatic events. It is vital to recognize that in the context of the overall neurogenetic circuit, the amygdala is an intermediary that receives inputs, processes, and interprets the information represented by the inputs and then sends outputs in the form of electrical impulses and neurotransmitters to the relevant brain regions to influence their activity.[10,12,14,15]

These concepts can be used to explore the effects of DID neurologically. One idea is that trauma-related stimuli, such as intense emotions associated with the traumatic event, may result in a change in synaptic strength – via synaptic plasticity - of neurons in the hippocampus involved in the long-term storage of the memory and details of the event.[10,13] For example, in the avoidant identity state, exposure to emotional trauma-associated stimuli may result in amygdala outputs that cause the long-term depression (LTD) of hippocampal neurons involved in the emotional memory of the trauma, and this would weaken the synaptic strength of these neurons. Because the maintenance of long-term potentiation (LTP) is important for long-term memory storage, some of the information of the emotional memory has been "lost," and the trauma can no longer be recalled in its entirety.[16] On the contrary, in the trauma identity state, traumatic stimuli may result in amygdala outputs that increase LTP of relevant hippocampal neurons, which would enhance the emotional memory, contributing to the deep personal attachment with the trauma that is associated with the trauma identity state, as the encoded information for the event can now be recalled more comprehensively.

Another plausible idea regarding how DID affects the amygdala's role in memory may be that the processes involved in the recollection of the memory are altered, rather than the encoded memory itself. In this scenario, the hippocampus could be the source of the inputs, and the output brain region could be the PFC, which is known to play a central role in working memory.[17] The inputs - signals that encode traumatic memories - are sent to the amygdala. The amygdala processes and interprets the signals and then, depending on the current identity state, modulates the retrieval of trauma-related information associated with the signals, likely enhancing the retrieval of traumatic information in the trauma identity state and suppressing it in the avoidant identity state. In this way, the information being stored has remained untouched, but the capacity to transfer this information into working memory and, therefore, recall it, has been modified.

Finally, there should be an understanding of how information is processed within the amygdala to determine the necessary outputs to alter the activities of the target brain region/s. One fundamental example of information processing in the amygdala is the assignment of value or "valence" to stimuli.[15] Valence determines whether or not a stimulus is positive or negative,[15,18] and this helps determine the behavioral effects of the outputs in response to the stimulus.[15] A stimulus given a positive valence is likely to result in approach behavior, whereas a stimulus given a negative valence is likely to result in avoidance behavior.

It is worthwhile to elucidate how amygdala processing, such as the assignment of valence, may be altered by DID. In DID patients, traumatic events could be associated with greater negative valence than other typical emotional events, particularly in the avoidant identity state. This may help to trigger a greater aversive reaction towards the trauma and associated stimuli, which would help evade confrontation with the trauma. However, trauma could be associated with a slightly more positive valence in the trauma identity state. In the trauma identity state, DID patients are forced to engage with and handle the weight of their trauma on a personal level. The idea of trauma being assigned a more positive valence in the trauma identity state is a suggestion of a potential coping mechanism that could arise within the amygdala. A more positive valence could help "soften the blow" of the trauma being dealt with by helping to convince the person that the trauma was not as terrible or severe as it truly was, preventing the weight of the negative event from crushing them.

Overall, the amygdala has clear implications in memory and behavior, due to its roles in emotional memory and the processing of emotions via its close interconnectivity with other brain structures,[10,12–15] and, because of this, it is likely a major brain region affected by DID. An essential detail regarding the amygdala is that it is made up of multiple subdivisions known as nuclei that are structurally and functionally distinct from each other.[10–13,15,18] This may include the basal nucleus, lateral nucleus, central nucleus, accessory-basal nucleus, cortical nucleus, and medial nucleus, although there are multiple outlines for the amygdala's nuclei.[10] Distinct nuclei are characterized by distinct connections with other brain regions and nuclei, distinct neurotransmitter receptor numbers, and distinct transcriptional signatures.[10,15,18] Additional research into this topic

should outline how DID alters the role of the amygdala in memory and behavior on an individual nucleic level. Lastly, although there has been reference to the hippocampus and PFC, this has mainly been in relation to their connection with the amygdala. Future research should aim to determine the roles these key brain regions may individually play in DID.

The glutamatergic system and DID:

The glutamatergic system is the primary excitatory neurotransmitter pathway in the brain [8,10,19–21] and plays a major role in the inputs to and outputs from the amygdala.[10,19] It is therefore probable that, like other psychiatric disorders,[21] Dissociative Identity Disorder (DID) results in irregular functioning of glutamate in the amygdala, and this may play a role in the behavioral and memory effects of DID.

Glutamate is a neurotransmitter derived from the amino acid glutamic acid [20] that binds to a wide variety of glutamate receptors (GluRs) [21] that can be separated into two main groups: ionotropic GluRs (iGluRs) - which include N-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA), and kainate (KA) receptors - and metabotropic GluRs (mGluRs).[3,19–21] The binding of glutamate to the ligand-binding domains of GluRs conformationally changes the GluRs; this conformational change results in the opening of the ion channel for the entry of cations such as Na^+ and Ca^{2+} (for iGluRs) or the activation of a G protein and the subsequent signaling cascade (for mGluRs).[19–21]

DID may increase or decrease glutamatergic transmission in the amygdala – depending on the identity state - which ultimately affects the amygdala's outputs to target brain regions, therefore affecting the roles of these target brain regions. Because of its excitatory nature, increased glutamate transmission is connected to increased activity of the amygdala, and vice versa.[8] This notion allows us to use the neurological effects of DID to suggest and explain the molecular effects of DID.

Evidence suggests that patients with DID experience decreased amygdala activity due to increased inhibition of the amygdala by the ventromedial prefrontal cortex (vmPFC) in the avoidant identity state.[3,5,6,8,11] Amygdala hypoactivity implies decreased glutamate transmission, which further implies a decrease in the binding of glutamate to iGluRs and mGluRs, which may have a diverse range of behavioral and memory-related effects. For example, decreased binding of glutamate to NMDA receptors decreases intracellular Ca^{2+} levels, as NMDA receptors are a channel protein for calcium ions.[10,20,22] The entry of calcium ions into neurons in the amygdala is required for both short-term and long-term memory,[10,21] and, because of this, diminished Ca^{2+} levels may explain the Dissociative Amnesia prevalent in DID.

A deeper dive can be conducted to further outline the necessity of calcium ions for synaptic plasticity and to further define the memory deficits that intracellular calcium deficiency may cause in DID. One enzyme affected is Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) (Figure 1),[10,20,21] which is a protein kinase that requires Ca^{2+} ions for activation by autophosphorylation.[21] CaMKII is involved in synaptic plasticity and long-term potentiation (LTP) by the phosphorylation of other key protein kinases and by increasing available AMPA receptors in the cell surface membrane for sustained long-term potentiation.[10,20,21] Another enzyme affected is Mitogen-Activated Protein (MAP) kinase (Figure 2), which also relies on intracellular calcium levels for activation.[10] When activated, MAP kinase moves to the nucleus and phosphorylates transcription factors such as cAMP response element-binding protein (CREB), thereby activating them. These transcription factors stimulate gene expression and subsequent polypeptide translation of proteins with vital roles in memory and behavior, such as an increase in the expression and translation of GluRs for further increased binding to glutamate,[10] which further promotes LTP. These are only two examples out of many proteins that experience reduced functioning due to decreased glutamatergic transmission and may explain some of the symptoms of the avoidant identity state of DID.

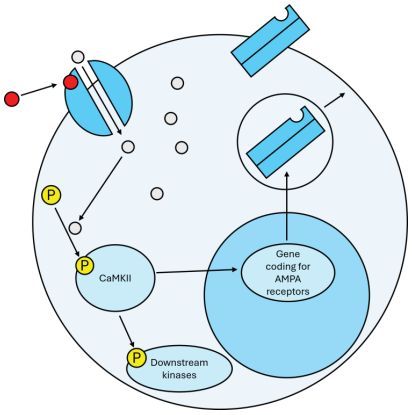

Figure 1: A diagram illustrating the activation and effect of CaMKII, caused by glutamate. Glutamate binds to NMDA receptors, opening an ion channel for the entry of Ca^{2+} ions into the cell. Ca^{2+} ions are required for the activation of CaMKII by autophosphorylation. CaMKII activates other protein kinases by phosphorylation and increases AMPA receptor availability. Abbreviations: CaMKII, Ca^{2+}/calmodulin-dependent protein kinase II; NMDA receptor, N-methyl-D-aspartate receptor; AMPA receptor, α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor.

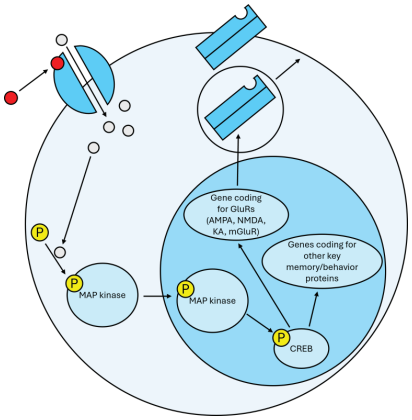

Figure 2: A diagram illustrating the activation and effect of MAP kinase, caused by glutamate. Glutamate binds to NMDA receptors, opening an ion channel for the entry of Ca^{2+} ions into the cell. Ca2+ ions are required for the activation of MAP kinase. MAP kinase moves to the nucleus and activates transcription factors such as CREB by phosphorylation. CREB increases the expression of genes coding for GluRs, which ultimately increases GluR availability, and increases the expression of other genes involved in memory and behavior. Abbreviations: MAP kinase, Mitogen-Activated Protein kinase; NMDA receptor, N-methyl-D-aspartate receptor; CREB, cAMP response element-binding protein; GluR, glutamate receptor.

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A decrease in the binding of glutamate to mGluRs in the amygdala also has a negative impact, as the signaling cascades induced by glutamate-mGluR binding are involved in the regulation of various cellular processes (Figure 3) with the use of second messengers such as cyclic adenosine monophosphate (cAMP).[21] An example of a cellular process upregulated by mGluR-induced signaling is the expression of immediate-early genes (IEGs), such as c-fos and Arc.[20–22] It is known that IEGs play an important role in memory and long-term synaptic plasticity,[22] and a reduction in their expression would therefore reduce emotional memory encoding in the amygdala and hippocampus.[22] This would explain why Dissociative Amnesia in DID involves an inability to remember certain details relating to the traumatic experience responsible for the onset of the disorder.[1,5] Another example is the activation of phospholipase C (PLC).[20] A decreased activation of PLC decreases the production of inositol-1,4,5-triphosphate (IP3), a molecule that stimulates the release of calcium ions into the cytosol from intracellular stores,[20,21] thereby contributing to calcium levels required for CaMKII and MAP kinase activation.

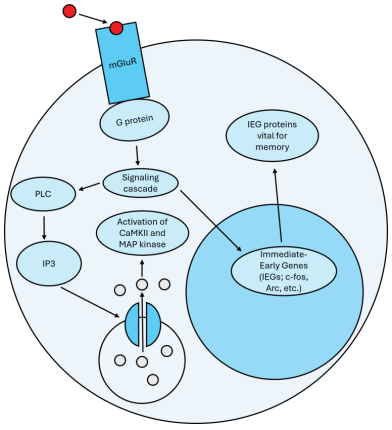

Figure 3: A diagram illustrating the activation and effect of mGluRs, caused by glutamate. Glutamate binding to mGluRs activates a G protein, which induces a signaling cascade. mGluR-induced signaling cascades increase the expression of IEGs. Proteins coded for by IEGs have important roles in memory. mGluR-induced signaling cascades also activate the enzyme PLC. PLC produces IP3, which increases the release of Ca^{2+} ions from intracellular stores. Ca^{2+} ions are required for the activation of CaMKII and MAP kinase. Abbreviations: mGluR, metabotropic glutamate receptor; IEG, immediate-early genes; PLC, phospholipase C; IP3, inositol-1,4,5-triphosphate; CaMKII, Ca^{2+}/calmodulin-dependent protein kinase II; MAP kinase, Mitogen-Activated Protein kinase.

During the trauma identity state, there may be a decreased inhibition of the amygdala by the vmPFC, resulting in amygdala hyperactivity.[6,11] This would imply the opposite effects; there is increased glutamatergic transmission,[8,9] and the reverse of the effects of the avoidant identity state would apply. This may result in personal attachment to the traumatic event, hyperactive behavior due to trauma-related stimuli, and other overlapping symptoms of PTSD and the trauma identity state of DID.[3,6,8]

Though the mechanisms by which DID may affect the glutamatergic system in the amygdala have been outlined, this is only a brief explanation of the complexity underlying the glutamatergic system. The effects described here may occur within the amygdala itself or in target brain regions as a result of increased or decreased glutamate release from the amygdala. An important note, however, is that the glutamatergic system works in close connection with other neurotransmitter systems, such as the monoaminergic systems (dopamine, serotonin, etc.);[20] these distinct systems are able to influence each other.[13] It is worthwhile for future research to explore the monoaminergic systems and their interactions with the glutamatergic system as alternative neurogenetic pathways that are also altered by DID. Additionally, future research should extend past the central nervous system and investigate how genetic pathways involved in other organ systems - such as the digestive and immune systems – are affected by DID.

The relationship between trauma and DID:

The idea that childhood trauma is directly responsible for the onset of Dissociative Identity Disorder (DID) is known as "the Trauma Model" of DID (Table 1).[2,5] Throughout history, the Trauma Model has been controversial, as many people, including members of the general public and mental health professionals, discredit the Trauma Model and do not believe that childhood trauma is responsible for the disorder.[3,5] This was in part due to the inability of people to accept that unlawful, trauma-inducing acts against children, such as sexual abuse, were such a widespread situation.[3,6]

Disbelievers of the Trauma Model formed three alternative explanations for the cause of DID (Table 1).[5] One of them is the Iatrogenic Model. The Iatrogenic model claims that DID is induced in individuals prone to being hypnotized by health professionals who believe in the ideas of the Trauma Model. It asserts that these individuals have false trauma memories instilled in them and are unable to discern these memories from real memories, creating a personal belief in the traumatic experience and thereby causing DID.[3,5] Another model that was posited is the Sociocognitive Model, which claims that the popularization of the ideas of the Trauma Model and DID, particularly in Western culture and media, has caused people to believe that they have DID.[3,5] The final model is the Fantasy Model, which argues that DID and other dissociative disorders are the result of people fantasizing about experiencing traumatic events.[2,3,5,6] These three models seemingly rose as more of a negative response to the Trauma Model and less of a genuine attempt to explain the cause of dissociative disorders such as DID.[5,6]

Table 1: A table of the suggested causes ("models") of DID. The first row is a short description of each model, and the second is the suggested source of DID according to each model.

Trauma Model	Iatrogenic Model	Sociocognitive Model	Fantasy Model
DID is caused by childhood trauma and develops as a defence and coping mechanism in response to the trauma	DID is caused when people prone to hypnosis are given false traumatic memories and are unable to discern them from real memories	DID is caused by the increased exposure of the ideas of DID and the Trauma Model in culture and media, causing people to internalize these ideas and believe they have DID	DID is caused when people fantasize about traumatic events happening to them
The source is the traumatic event.	The source is health professionals who instill false memories into highly hypnotizable people.	The source is culture and media (especially Western)	The source is the fantasies of the person themselves

Despite the skepticism surrounding it, the Trauma Model is the most feasible of the four models for DID and has an extensive array of literature and neurobiological evidence that supports the cause-and-effect relationship between traumatic childhood incidents and DID.[2–9] In particular, neuroimaging has found overlapping structural and functional brain patterns between DID and PTSD.[6,7] This, coupled with the fact that there is a lack of reasonable and empirical evidence that supports the other three models,[3,5] reinforces the Trauma Model as the most likely of the four to be true, and justifies it as the premise for this review.

An acceptance of the Trauma Model has allowed for a deeper comprehension of DID, as the effects of trauma can be used to explain the symptomatology of the disorder. It is now understood that the cause of the personality dissociation in DID is a psychological defensive coping mechanism in response to trauma.[1,3,7] Due to the complex nature of DID, different DID patients may have different numbers and/or types of identity states, depending on factors such as the specifics of the traumatic event and when the event occurred.[3] However, the Trauma Model of DID has allowed for the recognition of two common identity states amongst DID patients: a trauma identity state that is attached to the trauma and an avoidant identity state that suppresses the trauma and is hence detached from it.[1] These two contrasting identity states may help to explain certain symptoms of DID. For example, a person in an avoidant identity state may have Dissociative Amnesia towards memories and details relating to their traumatic experiences and may feel depersonalized from their trauma,[3,5,7] feeling as if their experiences happened to someone else. The purpose of the avoidant identity state may therefore be defensive.[1,5] By facing a traumatic incident that is difficult to handle, the brain develops a dissociative identity state that is distant from the negative experience, preventing the person from having to face the reality of their trauma. Thus, the avoidant identity state of DID can be viewed as a longer-lasting, more intensive form of the first stage of grief: denial. In theory, one function of the avoidant identity state should be to prevent traumatic events from affecting an individual but, due to the extent of the dissociative symptoms and the abnormal brain activity associated with dissociative identity states, such as the avoidant identity state,[3] this is often not the case;[1,7] DID patients in an avoidant identity state usually feel emotionally numb.[3,6]

The formation of the avoidant identity state does not erase or remove the trauma that occurred, resulting in the formation of a trauma identity state. In a sense, the trauma is avoided in the avoidant identity state by "transferring" it to the trauma identity state; the trauma is contained within this identity state, separating it from the other identity states.[1] As detailed previously, both the trauma and avoidant identity states are likely characterized by opposing functional changes in the activity and glutamatergic transmission of the amygdala.

The aforementioned evidence affirms that there is an apparent cause-and-effect relationship between childhood trauma and DID, and there is currently no reasonable argument in defense of the Iatrogenic, Sociocognitive, and Fantasy models of DID. Future research should work to further outline the effects of trauma on DID and to identify other common identity states or characteristics amongst DID patients. An attempt should also be made to further define the similarities and differences between DID and other trauma-related disorders.

Conclusion

In conclusion, as with many other psychiatric conditions, functional changes in the amygdala [8,10] are likely implicated in DID, and this includes the alteration of the glutamatergic pathway.[3,8,21] This review has highlighted the role of the amygdala's interconnectivity with other brain regions in memory and behavior,[10,12–15] and has outlined how DID may alter these connections and the functioning of the amygdala by affecting the binding of glutamate to glutamate receptors, which impacts the activation and production of proteins and molecules involved in emotional memory, fear, valence assignment and emotionally driven behavior. This results in profound effects on memory and behavior. This paper has also critically assessed the cause of DID to assert that childhood trauma is the most likely cause of DID.

A limitation of the evidence presented is that part of the literature did not examine DID exclusively, instead addressing psychiatric disorders or trauma-related dissociation as a whole. As a result, these studies may not entirely express small but relevant differences between DID and other disorders for particular mechanisms. Further research could benefit from investigating DID independently, which could more clearly reveal smaller details specific to DID that more broadly applicable studies may struggle to convey. This could be particularly useful in differentiating DID from other dissociative disorders. Although Dissociative Amnesia and Derealization/Depersonalization have been described as symptoms of DID within this review, it should be noted that both symptoms are not confined to DID and are also considered their own distinct dissociative disorders.[4,5] It may be worthwhile for future research to investigate how Dissociative Amnesia and Derealization/Depersonalization differ when experienced as symptoms of DID in comparison to when experienced in isolation, helping to further define DID as a disorder.

A primary focus of this paper is how the glutamatergic pathway may be altered by DID. Future research should work to outline other key neurogenetic pathways involved (such as those of brain-derived neurotrophic factor and interleukin-6)[4] and how they may also be affected. Moreover, the neurology behind DID is highly complex; a change in the functioning of the amygdala is only one of the many possible factors that may contribute to the pathophysiology of DID. Future research should consider other neurological factors and the role that they may play, such as dysregulation of the hypothalamic-pituitary-adrenal axis - a neuroendocrine system that plays a vital role in responses to stress and trauma - as well as genetic predisposition, which may influence an individual's susceptibility to experiencing dissociation.[3,4,7,8] Finally, a combination of renowned techniques, such as neuroimaging, and more novel methods, such as the use of artificial intelligence and machine learning, and magnetic resonance spectroscopy, may be useful for further analysis into the neurogenetic mechanisms involved

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in DID, as well as further elucidating the similarities and differences between DID and other personality disorders.[3,6–8,18] Further research into the morphological changes of the amygdala in DID may help make sense of the inconsistent results of altered amygdala volumes in DID patients,[23] and it would be useful to investigate these structural changes while simultaneously investigating the functional changes.

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