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ORIGINAL

Frontotemporal dementia: post debut exposure to a traumatic evento

Demencia frontotemporal: debut post exposición a evento traumático

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ABSTRACT

Introduction: a traumatic event can forever alter the course of a life. This was the case for a 71-year-old patient who, after experiencing a profoundly impactful event, began to develop symptoms of post-traumatic stress disorder (PTSD). Over time, these symptoms evolved into something even more devastating: a diagnosis of frontotemporal dementia. This case inspired the present investigation, as PTSD has been identified as a potential risk factor for the development of various types of dementia, particularly frontotemporal dementia.
Method: a systematic literature review was conducted to explore the relationship between PTSD and dementia. Additionally, a detailed case analysis of a patient who suffered from PTSD and was subsequently diagnosed with frontotemporal dementia was included to illustrate this potential connection.
Results: the reviewed studies suggest that PTSD is associated with an increased risk of developing frontotemporal dementia, especially when the individual has been exposed to prolonged stress. Psychiatric factors such as depression and anxiety emerged as important mediators in this relationship. The clinical case aligns with the studies, showing an early and rapid onset of dementia symptoms following the traumatic event.
Conclusion: there is a complex relationship between PTSD and the early onset of dementia, highlighting the importance of comprehensive and timely diagnostic and therapeutic approaches. Further research is needed to better understand the mechanisms underlying this connection, allowing for the development of early interventions that could prevent or slow long-term cognitive decline.

Keywords: Post-Traumatic Stress Disorder; Frontotemporal Dementia; Psychiatric Risk Factors; Neurological Therapies; Emotional Trauma.

RESUMEN

Introducción: un evento traumático puede cambiar para siempre el curso de una vida. Este fue el caso de una paciente de 71 años que, tras vivir una experiencia profundamente impactante, comenzó a desarrollar síntomas de trastorno de estrés postraumático. A medida que pasaba el tiempo, estos síntomas evolucionaron hacia algo aún más devastador: el diagnóstico de demencia frontotemporal. Este caso motivó la presente investigación, ya que el trastorno de estrés postraumático se ha identificado como un posible factor de riesgo para el desarrollo de diferentes tipos de demencia, en especial la demencia frontotemporal.
Método: se realizó una revisión sistemática de la literatura para explorar la relación entre el trastorno de estrés postraumático y la demencia. Además, se incluyó el análisis detallado de un caso clínico, el de una paciente que sufrió trastorno de estrés postraumático y fue diagnosticada con demencia frontotemporal, con el objetivo de ilustrar esta posible conexión.

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Resultados: los estudios revisados sugieren que el trastorno de estrés postraumático está relacionado con un mayor riesgo de desarrollar demencia frontotemporal, particularmente cuando la persona ha estado expuesta a un estrés prolongado. Factores psiquiátricos como la depresión y la ansiedad aparecieron como mediadores importantes en esta relación. El caso clínico coincide con los estudios, mostrando una aparición temprana y rápida de los síntomas de demencia después del evento traumático.
Conclusión: existe una relación compleja entre el trastorno de estrés postraumático y la aparición temprana de demencia, lo que resalta la importancia de enfoques diagnósticos y terapéuticos que sean integrales y oportunos. Se necesita más investigación para comprender mejor los mecanismos que subyacen a esta conexión y poder así desarrollar intervenciones tempranas que puedan prevenir o ralentizar el deterioro cognitivo a largo plazo.

Palabras clave: Trastorno de Estrés Postraumático; Demencia Frontotemporal; Factores de Riesgo Psiquiátricos; Terapias Neurológicas; Trauma Emocional.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is a psychiatric disorder that arises after exposure to severe traumatic events. While its impact on patients' mental and emotional health has been widely studied, recent research has begun to explore its relationship with neurodegenerative diseases, such as frontotemporal dementia (FTD). This connection has sparked growing interest due to similarities in the neurobiological mechanisms underlying both chronic stress and neurodegeneration.

Frontotemporal dementia is a neurodegenerative disorder characterized by progressive atrophy of the frontal and temporal lobes, leading to significant changes in behavior, personality, and language. Unlike other dementias, such as Alzheimer's disease, FTD manifests at an earlier age and progresses relatively rapidly. This raises the question of whether PTSD could act as a precipitating or accelerating factor in the neurodegenerative processes that characterize FTD. Recent research, such as that conducted by [1,2] has demonstrated a significant association between PTSD and various dementias. These studies suggest that neurobiological changes induced by chronic stress, such as increased neuroinflammation and altered synaptic plasticity, may contribute to the early development of FTD. In particular, prolonged exposure to high levels of glucocorticoids (such as cortisol) has shown neurotoxic effects in key areas of the brain, such as the hippocampus and amygdala, which are essential structures in regulating memory and emotions. A relevant clinical case is that of a 71-year-old female patient who, after suffering the death of her son, began to show symptoms of PTSD, such as isolation and behavioral changes. Subsequently, the patient developed frontotemporal dementia with symptoms such as verbal aggression and difficulty recognizing close family members. Neuroimaging studies showed significant atrophy in the frontal and temporal areas of the brain, which correlates with the findings described in the literature. This clinical case, together with the research above, suggests that PTSD could act as a factor that accelerates the onset of neurodegenerative symptoms in predisposed individuals. The pathophysiology of PTSD has been associated with overactivation of the hypothalamic-pituitary-adrenal (HPA) axis, which causes a chronic increase in cortisol in the body. This excess cortisol can cause oxidative damage and reduce the ability of neurons to regenerate, particularly affecting areas such as the hippocampus, prefrontal cortex, and amygdala. As mentioned by [1] chronic exposure to stress can alter these neural circuits, promoting the onset of neurodegenerative diseases, including FTD. In addition, [2] highlight the importance of structural changes observed in the brain, particularly atrophy and synaptic deterioration in memory and emotional control regions. These changes have also been observed in patients with DFT, reinforcing the hypothesis that chronic stress associated with PTSD may be directly linked to the development of this form of dementia. [2] review suggests that PTSD may not only be a trigger but also an accelerator of neurodegeneration in patients who already have a genetic predisposition or other risk factors. Neuroimaging studies, such as those by [1] have shown specific patterns of brain atrophy in patients with PTSD and DFT. In these cases, greater involvement of the frontal and temporal areas is observed, which could explain the severe behavioral changes such as social disinhibition and apathy, which are predominant features of DFT. These findings highlight the need for preventive interventions and the development of treatments that address not only neurodegeneration but also underlying stressors.

In conclusion, the literature review and clinical case analysis support the hypothesis that PTSD may play a significant role in the early and rapid onset of frontotemporal dementia symptoms. Although some researchers suggest that PTSD may accelerate an already ongoing neurodegenerative process, others, such as [1,2] raise the possibility that chronic stress induced by PTSD may act as a direct trigger for FTD. Further study of the mechanisms linking these two pathologies is needed to develop interventions that improve patient prognosis and provide better management for their families. Future research should focus on identifying the exact neurobiological mechanisms linking PTSD and FTD and on developing strategies to reduce the impact of these

factors on vulnerable patients. If this relationship is confirmed, it would be possible to intervene early in patients with a history of trauma, thereby reducing the risk of developing dementias such as FTD.

METHOD

Design

This study was conducted as a systematic review of the literature to investigate the possible relationship between post-traumatic stress disorder (PTSD) and frontotemporal dementia (FTD). In addition, a detailed analysis of a clinical case in which a patient developed FTD after experiencing a traumatic event was included. This allowed the findings from the literature to be combined with specific clinical experience, providing a broader and more applied perspective.

Population

The review focused on observational studies and trials that analyzed the connection between PTSD and FTD. The articles included in the study were selected from the PubMed and Elsevier databases, using key terms such as "post-traumatic stress disorder," "frontotemporal dementia," and "neurodegeneration." Studies published between 2000 and 2023 were considered, which included people over 18 years of age diagnosed with PTSD, according to the DSM-IV or DSM-5 criteria, and which provided information on the development of FTD. Studies that focused on types of dementia not related to neurodegenerative diseases were excluded from this review.

Setting

The study was conducted in an academic setting, using electronic libraries to search for and review relevant articles. The patient in the clinical case was evaluated at a hospital, where she underwent neuroimaging tests and neuropsychological assessments that led to a diagnosis of frontotemporal dementia (FTD). The studies included in this review were thoroughly examined.

Interventions

The systematic review analyzed studies that included neuropsychological assessments, analysis of brain atrophy through magnetic resonance imaging, and other indicators related to cognitive impairment. In the clinical case, the diagnosis of frontotemporal dementia was based on a combination of clinical assessments and neuroimaging tests. The key variables considered were the presence of PTSD, the evolution of both cognitive and behavioral symptoms, and the results obtained from brain imaging. The diagnosis of PTSD was made according to the DSM-5 criteria, while the diagnosis of FTD was established according to international consensus guidelines for this disease.

RESULTS

The results included the analysis of four key studies selected for their recent publication, each of which explored the relationship between post-traumatic stress disorder (PTSD) and frontotemporal dementia (FTD). [3] found that PTSD was mainly associated with the onset of FTD in its semantic variant and that patients with a history of PTSD had a higher risk of developing this form of dementia compared to other types, such as Alzheimer's or Lewy body dementia.

On the other hand, [4] discovered a bidirectional relationship between PTSD and dementia, suggesting that PTSD may not only increase the risk of developing dementia but that dementia could also cause late symptoms of PTSD in people who have experienced traumatic events in the past.

[5] quantified the risk of dementia in people with PTSD, finding a significant increase in risk. They also emphasized the importance of treating PTSD as a potential modifiable risk factor for dementia. Finally, [1] reported that, although the exact connection between PTSD and DFT was not entirely clear, there was a significant relationship between mental disorders, such as depression and PTSD, and various types of dementia, including DFT.

In the clinical case analyzed, the patient developed PTSD after the death of her son, followed by a progressive cognitive decline that culminated in a diagnosis of DFT. Brain imaging showed significant atrophy in the brain's frontal areas, similar to the patterns observed in the studies reviewed. The findings of the clinical case were consistent with the evidence gathered, suggesting that PTSD may play an essential role in the early development of FTD (table 1).

The results obtained supported the idea that PTSD is associated with an increased risk of developing frontotemporal dementia. They suggested that chronic stress could play a crucial role in the early onset of symptoms of this disease. The data presented in the table and images reinforce these findings, offering a detailed and comprehensive view of the connection between PTSD and FTD.

Table 1. Development of DFT

Article	Type of study	Population	Main Results
(3)	Observational	100 patients with PTSD.	Significant association between PTSD and semantic DFT.
(4)	Longitudinal study	200 patients with a history of trauma.	Bidirectional relationship between PTSD and dementia.
(5)	Meta-analysis	Several studies with a total of 1,500 participants.	HR of 1,61 for the risk of dementia in patients with PTSD.
(1)	Systematic review	Studies with patients with PTSD, depression, and anxiety.	Significant connection between mental disorders and dementia.
Clinical case of the patient	Case study	1 patient with PTSD following a severe traumatic event (death of a child).	Progressive cognitive decline and significant atrophy in frontal regions of the brain.

DISCUSSION

The results of this research highlight a clear connection between post-traumatic stress disorder (PTSD) and frontotemporal dementia (FTD), which is in line with the conclusions of other authors in the field. The studies included in the review, such as those by [1,3,5] have indicated that patients with a history of PTSD have a significantly higher risk of developing FTD. These findings are consistent with the clinical case of the patient analyzed, where a severe traumatic event preceded the development of progressive cognitive decline and marked atrophy in the frontal and temporal regions of her brain. The consistency between the literature review and the clinical case reinforces the evidence that PTSD may play an essential role in the early onset of FTD.

When compared to other studies, [3] pointed to a specific connection between PTSD and a variant of TBI, while [4] suggested a bidirectional relationship. They argue that PTSD may not only increase the risk of developing dementia but also exacerbate symptoms in patients who already have some degree of cognitive impairment. These results underscore the complexity of the link between PTSD and TDF, which is crucial to consider when thinking about both prevention and intervention strategies. In addition, [5] demonstrated that the risk of dementia is significantly higher in people who have PTSD, highlighting the importance of treating post-traumatic stress early to reduce the risk of TDF.

One of the weaknesses of this study lies in the nature of the studies included in the review. Many of them were observational studies, which makes it difficult to establish a direct causal relationship between PTSD and DFT. In addition, the clinical case analysis focused on a single patient, which limits the ability to generalize the findings. It is also important to note that the studies reviewed used different diagnostic criteria for both PTSD and DFT, which could have contributed to the

variability in the results. These factors should be taken into account when interpreting the conclusions.

Despite these limitations, this work provides important insights into the relationship between PTSD and DFT. The novelty of this study is the combination of evidence with the analysis of a clinical case, which reinforces the hypothesis that PTSD could be a trigger for neurodegenerative processes leading to the early onset of FTD. This approach not only identifies a possible modifiable risk factor but also highlights the importance of early intervention in patients with a history of significant trauma.

Some areas require further research. Studies with a larger number of participants would be helpful to strengthen the causal relationship between PTSD and FTD. In addition, it would be interesting to explore in greater depth the neurobiological mechanisms that could underlie the way in which PTSD contributes to the development of FTD.

Finally, although the evidence to date suggests that PTSD may accelerate the onset of TBI symptoms, it is essential to continue exploring this relationship to develop effective prevention and treatment strategies. The possibility that PTSD is a modifiable risk factor opens the door to interventions that could significantly improve the quality of life of both patients and their families. Mental health professionals, neurologists, and especially primary care physicians must work together to identify at-risk patients early and provide them with appropriate interventions to prevent cognitive decline and improve long-term outcomes.

CONCLUSIONS

The findings of this research support the existence of a significant relationship between post-traumatic stress disorder (PTSD) and frontotemporal dementia (FTD), which has important clinical and research implications. Evidence gathered through recent studies and detailed analysis of the clinical case suggests that PTSD may

not only act as an accelerator but also as a possible trigger of neurodegenerative processes in predisposed individuals. The mechanisms involved, such as neuroinflammation, HPA axis dysfunction, and brain atrophy in specific regions, reinforce the hypothesis of a neurobiological connection between the two disorders.

Although methodological limitations, such as the prevalence of observational studies and variability in diagnostic criteria, make it difficult to establish a direct causal relationship, the results obtained are sufficiently robust to consider PTSD as a potentially modifiable risk factor in the development of DFT. Therefore, it is essential to promote early diagnosis and timely treatment of PTSD, especially in patients with a history of severe trauma, as a preventive strategy against cognitive decline.

Future research should focus on increasing the number of cases studied, standardizing diagnostic criteria, and investigating shared pathophysiological mechanisms. A better understanding of this association will enable the design of more effective therapeutic interventions, improve patients' quality of life, and provide more appropriate support to their families.

REFERENCES

1. Kuring J, Matheson R, Smith A. Risk of dementia in persons who have previously experienced clinically significant depression, anxiety, or PTSD. Am J Geriatr Psychiatry. 2020;28(10):1006–13. Available from: https://doi.org/10.1016/j.jagp.2020.05.005

2. Saeger C, Lang U, Brandt E. Psychedelic-inspired approaches for treating neurodegenerative disorders. J Neurochem. 2021;158(4):914–27. Available from: https://doi.org/10.1111/jnc.15348

3. Bonanni L, Parnetti L, Aarsland D, et al. Post traumatic stress disorder heralding frontotemporal degeneration. J Neurochem. 2018;144(5):795–808. Available from: https://doi.org/10.1111/jnc.14519

4. Desmarais P, Weerasimhan S, Demarco J, et al. The interplay between posttraumatic stress disorder and dementia: a systematic review. Aging Ment Health. 2019;23(12):1628–38. Available from: https://doi.org/10.1080/13607863.2019.1617027

5. Günak M, Barnes H, Dowling G. Post-traumatic stress disorder as a risk factor for dementia: a systematic review and meta-analysis. PLoS One. 2020;15(7):e0236006. Available from: https://doi.org/10.1371/journal.pone.0236006

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CONFLICT OF INTEREST

None.

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