Revista ARACÊ
ISSN: 2358-2472

HUNTINGTON'S DISEASE: A CASE REPORT

https://doi.org/10.56238/arev6n4-107

Submitted on: 11/09/2024 **Publication date:** 12/09/2024

Fernando Becker Schimitt[1], Marco Rogério da Silva[2], Bernardo Pavelski Henning[3], Natan Veiga[4], Karine Luz[5], Eduardo Sttocco da Silva[6], Julia Tristão de Souza[7] and Claudriana Locatelli[8].

ABSTRACT

In view of the diagnostic importance of Huntington's disease (HD) and the difficulties faced by patients, this study aims to report the clinical and laboratory profile of a patient diagnosed late with HD. The case report approved by the UNIARP Ethics Committee describes the trajectory of a 40-year-old male patient, former polydrug user, hospitalized for five years in a psychiatric hospital. The patient has a confirmed diagnosis of HD, with a significant family history (mother and maternal grandmother died due to the disease). The first symptoms, including episodes of aggression and mild chorea, appeared 15 years ago, being aggravated by the use of psychoactive substances. The patient suffered amputation of phalanges during a psychotic episode. The diagnosis of HD was confirmed by genetic tests and imaging findings, which revealed diffuse cerebral atrophy and caudate nuclei, typical features of the disease. Currently, the patient is bedridden, emaciated, disoriented, with motor difficulties, incontinence and frequent muscle spasms. Drug treatment aims to

[1] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: fernando29092003@gmail.com
Orcid: 0009-0003-3551-6533
[2] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: marcorogeriomr2020@gmail.com
Orcid: 0009-0002-7826-0075
Lattes: http://lattes.cnpq.br/7421056748585031
[3] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: berhenning1@hotmail.com
Orcid: 0000-0001-6851-8162**)**
[4] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: natan.veiga@uniarp.edu.br
Orcid: 0009-0005-2988-9143
Lattes: http://lattes.cnpq.br/2979910208779651
[5] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: karine.luz@uniarp.edu.br
Orcid: 0000-0002-2983-387X
Lattes: http://lattes.cnpq.br/2083687672172951
[6] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: eduardosttocco@hotmail.com
Orcid: 0009-0004-3099-0188
Lattes: http://lattes.cnpq.br/0650221197737848
[7] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
Email: juliatristao1208@gmail.com
Orcid: 0000-0002-1023-9483
Lattes: http://lattes.cnpq.br/6625012860060013
[8] Alto Vale do Rio do Peixe University – UNIARP. Caçador, Brazil
E-mail: claudriana@uniarp.edu.br
Orcid: 0000-0003-4708-6641
Lattes: http://lattes.cnpq.br/5561335276362844)

Revista ARACÊ
ISSN: 2358-2472

alleviate neuropsychiatric symptoms, although the use of typical neuroleptics diverges from recommendations that suggest atypical neuroleptics for better tolerability. The report highlights the complexity of the management of HD, especially in cases of late diagnosis, and highlights the need for more effective therapies that go beyond symptomatic treatment, aiming to improve the quality of life and prognosis of patients.

Keywords: Huntington's chore. Huntington's disease. CAG Expansion. Mutation.

Revista ARACÊ
ISSN: 2358-2472

INTRODUCTION

In 1872, George Summer Huntington described a type of illness that was hereditary and was linked to dementia. Although there were previous reports in the literature, it is to Huntington's that the first precise clinical description of this condition is attributed, later known as Huntington's Chorea (CH). Since then, numerous publications have emerged, highlighting the global prevalence of the disease. In recent years, a number of biochemical studies have been conducted in an attempt to identify the fundamental cause of CH. Although this cause is not yet fully understood, it is currently known that reduced gamma-aminobutyric acid (GABA) levels in the striatum is a prominent feature of this disease (Costa *et al.,* 2023).

Huntington's disease (HD) is a neurodegenerative condition that specifically affects the basal ganglia of the brain. The symptoms presented by patients with the disease are characterized by a triad of motor, cognitive and psychiatric disorders. These symptoms usually manifest between the ages of 30 and 40 years, although a manifestation in youth, before the age of 20, may occur, but it is rare (Nogueira *et al.,* 2019).

Due to clinical manifestations that affect various brain capacities, such as motor skills, cognition, and behavior, HD is associated with irreversible brain changes in several regions, including the cortex, thalamus, hypothalamus, globus pallidus, and gray matter. As the disease progresses, there is a reduction in the ability to move voluntarily, behavioral changes, and memory loss, leading to complications that can result in disability and death, often due to cardiovascular problems and pneumonia. The median survival time after the onset of HD ranges from 10 to 25 years (Wiprich *et al.,* 2020).

HD, also known as HC, gets its name from the involuntary dance-like movements that are its first identified and studied symptoms. It is a genetic, neurodegenerative and polyglutamine disease of autosomal dominant inheritance, caused by a mutant protein called huntingtin, expressed throughout the body. This condition is associated with cell death, especially in the brain, affecting areas such as the cortex and striatum (Mohapel; Rego, 2011). Progressive neurodegeneration of brain cells, particularly in the neurons of the striatum, is a feature of HD, although it also occurs in other brain regions, such as the cerebral cortex, hippocampus, and hypothalamus (Lebouc *et al*, 2020).

HD is directly related to an unstable expansion of the CAG nucleotide triplet in the IT15 gene, located on the short arm of chromosome 4. This expansion results in the synthesis of a mutant huntingtin protein (mHtt) that contains polyglutamine repeats at the

Revista ARACÊ
ISSN: 2358-2472

amino terminal of the protein, and alleles with 40 or more repeats have complete penetrance, leading to the development of the disease. The greater the number of repetitions, the earlier the onset of the disease (Spitz, 2010).

The diagnosis of HD requires the presence of signs and symptoms associated with chorea, in addition to knowledge of the genotype of the parents. Genetic and molecular testing may be performed if one parent has the dominant gene associated with HD. Diagnostic criteria include detailed family history, neuroimaging and clinical observation of progressive motor deficits, associated with chorea or rigidity, along with psychiatric changes and progressive dementia (Ross; Tabrizi, 2011).

A study conducted in several states in southeastern Brazil analyzed a sample of 140 individuals, of whom 35 were diagnosed with Huntington's disease (HD) and 105 were relatives of patients affected by the pathology. The results showed that more than 70% of those affected were not employed, more than 30% needed assistance to perform basic daily activities and 20% needed help with personal hygiene. The lack of adequate care in the health network highlights the urgent need for interventions to improve the quality of life of these individuals (Ramos *et al.*, 2018).

Case reports are essential to illustrate the clinical variability of HD, especially in patients with atypical or early-onset manifestations, and highlight the diagnostic challenges and complexities in the management of advanced psychiatric and motor symptoms. The literature indicates that HD may initially manifest as psychiatric disorders, which can obscure the diagnosis and delay appropriate treatment. Studies indicate that psychiatric symptoms, such as depression, apathy, aggression, and psychosis, are common in HD gene carriers and may precede motor symptoms. In many cases, these psychiatric symptoms are the first to appear, especially in younger patients, which can lead to an initial misdiagnosis of a primary psychiatric disorder (McAllister *et al.*, 2021).

In view of the diagnostic importance of HD and the difficulties faced by patients with the disease, this study aims to report the case of a patient diagnosed with HD late.

CASE PRESENTATION

ETHICAL APPROVAL

This case report was approved by the Research Ethics Committee of UNIARP, under opinion number 6.978.147.

Revista ARACÊ
ISSN: 2358-2472

PATIENT IDENTIFICATION

Patient D.P., male, 40 years old, white, with incomplete elementary school, from the Midwest of Santa Catarina, Brazil. The Patient has a history of chemical substance use, and is considered a former user of polydrugs (marijuana, crack, cocaine, alcohol and nicotine). He has been hospitalized in a psychiatric hospital for approximately 5 years.

PERSONAL AND FAMILY HISTORY

The patient has a history of psychiatric and movement disorders that began about 15 years ago, with episodes of aggressiveness and the appearance of mild involuntary movements, classified as chorea. These symptoms evolved and worsened due to the use of psychoactive substances. During a psychotic episode triggered by a fight in a bar, the patient suffered amputation of the three distal phalanges of his right hand. Family history is significant for Huntington's disease, as both the patient's mother and maternal grandmother died due to complications associated with HD. The patient's mother, also diagnosed with depression, bipolar disorder and anxiety, died at the age of 61. The patient's father has high blood pressure, esophageal cancer and a history of depression. The patient also has difficulties in his socio-affective relationships, including a distant relationship with his daughter, with whom he has not been in contact for years.

CLINICAL AND MEDICATION HISTORY

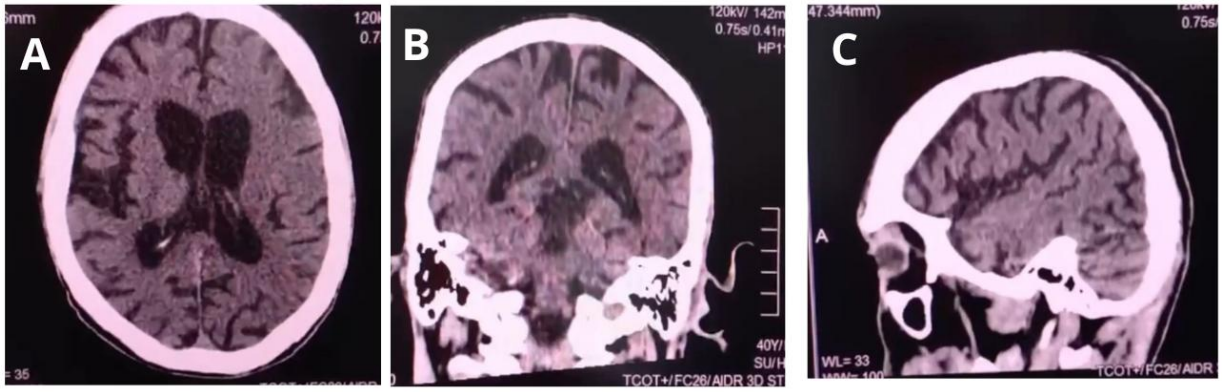
On initial admission to the hospital, the patient manifested symptoms such as psychomotor agitation, heteroaggressiveness, delusional ideation, and generalized mild choreic movements. The diagnosis of HD was confirmed through genetic testing, which identified the mutation in the HTT gene, in addition to changes in the imaging test. Initial drug treatment included the following drugs: risperidone 2 mg three times daily, haloperidol 5 mg three times daily, levomepromazine (Neozine) 100 mg three times daily, carbamazepine (Tegretol) 400 mg twice daily, promethazine 25 mg three times daily, valproic acid (Depakene) 500 mg twice daily, diazepam 10 mg twice daily, and chlorpromazine (Amplictil) 25 mg/ml every 12 hours, when necessary. Despite the treatment, the patient continued to be confused, communicative, agitated, with difficulty in walking and reduced autonomy.

Revista ARACÊ
ISSN: 2358-2472

IMAGING FINDINGS

Computed tomography scans of the skull showed diffuse cerebral atrophy (GCA score 1) with compensatory ectasia of the lateral ventricles, altered beyond what was expected for the age. In addition, calcified intracranial carotid atheromatosis and atrophy of the heads of the caudate nuclei were observed, with frontal horns/intercaudate distance index of 1.1 (reference value: 2.2 to 2.6), findings consistent with neurodegenerative alterations typical of Huntington's disease (Figure 1A, 1B and 1C).

Figure 1 - Computed tomography scans of the patient's skull



(A) Axial image demonstrating diffuse cerebral atrophy and compensatory ectasia of the lateral ventricles. (B) Coronal image showing atrophy of the heads of the caudate nuclei. (C) Sagittal image showing calcified intracranial carotid atheromatosis and structural changes related to Huntington's disease. Survey data, 2024.

CURRENT STATE

Currently, the patient is bedridden, emaciated, with difficulty in communication and swallowing, temporally disoriented and presenting disconnected illusions of past events. Presents with loss of movement of the toes, urinary and fecal incontinence (in diapers), and frequent generalized muscle spasms.

CURRENT TREATMENT

Current pharmacological treatment aims to minimize neuropsychiatric symptoms and improve the patient's quality of life. Medication includes: carbamazepine 400 mg twice daily, risperidone 2 mg three times daily, diazepam 10 mg twice daily, thioridazine 25 mg once daily, chlorpromazine 25 mg twice daily, valproic acid 500 mg twice daily, haloperidol 5 mg once daily, and clozapine 25 mg once daily.

Revista ARACÊ
ISSN: 2358-2472

DISCUSSION

Huntington's disease is a genetic neurodegenerative condition that significantly affects patients' quality of life and daily functioning. It represents a chronic disease with gradual progression of symptoms over time and currently has no cure. The available treatments are aimed at relieving symptoms, aiming to provide the best possible quality of life for patients. However, none of these treatments are able to slow or reverse the development of the disease (Stahl and Feigin, 2020; Massey and McLauchlan, 2024).

The patient's case illustrates the impact of HD in combination with a history of polydrugs and psychiatric complexity. The difficulty in accepting and understanding the disease caused them to delay the search for early diagnosis and treatment, presenting significant evolution of symptoms. In these situations, early diagnosis associated with a combination of pharmacological treatments and multidisciplinary support are essential in an attempt to manage symptoms, even without a definitive cure for the disease.

The patient underwent a computed tomography (CT) scan of the head, whose report issued by a neuroradiologist revealed diffuse brain atrophy, with a GCA score of 1. Atrophy was observed predominantly in the heads of the caudate nuclei, with frontal horns/interassisted distance indices of 1.1. These radiographic alterations, associated with the clinical picture, indicate an atrophic reduction in brain mass, especially in the basal ganglia.

The basal ganglia, which comprise the caudate nucleus and putamen, play a key role in motor control and cognitive functions. Huntington's disease especially affects these regions, resulting in motor deficits and behavioral changes. The mutation in the HTT gene leads to the production of an altered form of huntingtin, which exerts toxicity on neurons. This toxicity is most intense in the cells of the basal ganglia, where neuronal death manifests itself in a more significant way. The degeneration of these cells causes atrophy in the affected areas (Reiner and Deng, 2018, Nair *et al*., 2022**).**

The function of huntingtin, a protein whose mutation is associated with Huntington's disease, is not yet fully understood. However, its mutation is known to lead to several cellular alterations, including the formation of intracellular inclusion bodies, impairment of cellular transport, alterations in transcription, and apoptosis, resulting in lesions mainly in the brain and atrophy of the basal ganglia (Taran *et al*., 2020).

Magnetic resonance imaging (MRI) and positron emission tomography (PET) have been prominent in the early detection of structural and metabolic changes in Huntington's

Revista ARACÊ
ISSN: 2358-2472

disease. Atrophy of the striatum, involving the caudate nucleus and the putamen, can be identified before the onset of clinical motor symptoms (Kinnunen *et al.,* 2021, Delva *et al*., 2023), however, in the case reported this diagnostic alternative was used late, after numerous hospitalizations of the patient. The use of these diagnostic tools is essential for early therapeutic interventions, allowing the identification of at-risk individuals and the implementation of neuroprotective strategies that can slow the progression of the disease.

The psychological impact of Huntington's disease on family structure is significant, as individuals carrying the mutated gene are certain that they will develop the disease. This can lead to critical periods, such as the time before formal diagnosis and the phase when the disease begins to limit the patient's independence, increasing the risk of suicide (Paulsen JS, *et al.,* 2005).

In this study, the relationship between the patient and the family members, already compromised by the history of drug abuse, became even more conflicting with the progression of the disease. The intensification of mood swings, impulsive behaviors, and communication difficulties accentuated emotional barriers, generating a feeling of frustration in both the patient and their families.

The patient, before his admission to the Psychiatric Hospital, was detained for a few days on charges of drug trafficking. About 15 years ago, the family began to observe mood swings, signs of depression and a tendency to aggressiveness, followed later by the appearance of mild movement disorders, such as mild chorea, a condition that worsened with the use of polydrugs. The search for psychological support, both by the patient and the family members, occurred late, when the symptoms were already exacerbated, which evidenced a significant negative impact on the family's psychological health.

The early symptoms of Huntington's disease, such as mood swings, cognitive difficulties, and motor problems, can be easily confused with the effects of drug use or associated disorders (Martinez-Horta *et al*., 2016, McAllister *et al*., 2021). This confusion can lead to an underestimation of the neurological condition and a delayed search for specialized care. In addition, intoxication or withdrawal can mimic or aggravate the signs of the disease, making it difficult to differentiate between the effects of substance use and neurological symptoms. As a result, this can lead to misdiagnosis and delays in obtaining the necessary care (Cheng *et al.,* 2016, Massey and McLauchlan, 2024).

Substance abuse, including drugs and alcohol, has been linked to earlier onset and worsened progression of symptoms in Huntington's disease. Evidence from the Enroll-HD

Revista ARACÊ
ISSN: 2358-2472

database indicates that individuals with a history of drug abuse have an onset of motor symptoms on average 3.3 years earlier than those who do not. This impact appears to be particularly pronounced in women, in whom substance abuse is related to an even earlier onset of motor symptoms compared to men (Schultz *et al*., 2017).

In addition, substance use negatively affects the progression of psychiatric symptoms in HD. Continued alcohol use after the onset of clinical symptoms was correlated with a significant worsening of psychiatric conditions, including depression and anxiety. Substance abuse also emerges as an important risk factor for suicidal ideation in HD patients, especially in the presence of psychiatric comorbidities (Byars *et al*., 2012).

These findings highlight the need for integrated management strategies that address not only neurodegenerative aspects but also psychiatric complications and behavioral risk factors associated with substance abuse in HD. Early identification and intervention in these behaviors can contribute to improving the clinical course of the disease and the quality of life of patients.

Although there have been advances in the understanding of the disease and in diagnostic methods, the treatment of Huntington's disease is still predominantly symptomatic, with drugs from the classes: Benzodiazepines, Neuroleptics, Dopamine Depletors and Antidepressants. However, the participation of support networks and specialized services has been essential to improve the quality of life of patients. Nursing professionals play a crucial role in promoting self-care and adapting to the limitations imposed by the disease, contributing to the improvement of patients' functionality and perception (Adam and Jankovic, 2008, Venuto *et al.,* 2012).

In contrast to current therapeutic guidelines, the drug approach adopted for patient treatment has some divergences. The use of typical neuroleptics such as chlorpromazine (Amplictil), levopromazine (Neozine), haloperidol (Haldol) is observed, although the use of atypical neuroleptics, such as olanzapine and quetiapine, is currently recommended due to a potentially more favorable side effect profile. In addition, some practitioners prefer the use of dopaminergic depletion agents, such as Reserpine and Tetrabenazine, given their proven efficacy in controlled choreic symptoms (Armstrong and Miyasaki, 2012, Unti *et al*., 2017). However, it is observed that the patient is not using these agents.

Despite the difficulties, there is growing scientific interest and advances in the understanding of Huntington's disease, there is still an urgent need to develop more effective therapies that aim not only to treat the symptoms, but also the disease itself. The

Revista ARACÊ
ISSN: 2358-2472

availability of advanced technological resources offers hope that new therapeutic approaches will be developed, fueling the continuous search for a cure for the disease. Thus, this report contributes to the literature on HD by highlighting the importance of early diagnosis and multidisciplinary management in the management of patients with a history of substance abuse and severe psychiatric complications associated with Huntington's disease.

THANKS

The Coordination for the Improvement of Higher Education Personnel – Brazil (CAPES) – Financing Code 001, to the National Council for Scientific and Technological Development (CNPq) through CNPq Call No. 69/2022 – Doctoral Scholarship PIBPG 2022 and Public Call n. 32/2023 - Senior Postdoctoral Fellow - PDS 2023 and the Foundation for Research and Innovation Support of Santa Catarina – FAPESC via master's scholarship and support for research projects and the Alto Vale do Rio do Peixe University – UNIARP.

Revista ARACÊ
ISSN: 2358-2472

REFERENCES

1. Adam, O. R., & Jankovic, J. (2008). Symptomatic treatment of Huntington disease. Neurotherapeutics, 5(2), 181-197.

2. Armstrong, M. J., & Miyasaki, J. M. (2012). Evidence-based guideline: Pharmacologic treatment of chorea in Huntington disease: Report of the guideline development subcommittee of the American Academy of Neurology. Neurology, 79(6), 597-603.

3. Byars, J. A., Beglinger, L. J., Moser, D. J., Gonzalez-Alegre, P., & Nopoulos, P. (2012). Substance abuse may be a risk factor for earlier onset of Huntington disease. Journal of Neurology, 259(9), 1824-1831.

4. Cheng, Y., Gu, X., Liu, K., et al. (2022). The comprehensive analysis of motor and neuropsychiatric symptoms in patients with Huntington's disease from China: A cross-sectional study. Journal of Clinical Medicine, 2(1), 206.

5. Costa, I. M., et al. (2023). Doença de Huntington: Uma abordagem diagnóstica, evolução clínica e revisão. Brazilian Journal of Health Review, 6(5), 21887-21894. https://doi.org/10.5935/XXXXX

6. Delva, A., Van Laere, K., & Vandenberghe, W. (2023). Longitudinal imaging of regional brain volumes, SV2A, and glucose metabolism in Huntington's disease. Movement Disorders, 38(8), 1515-1526.

7. Kinnunen, K. M., Schwarz, A. J., Turner, E. C., et al. (2021). Volumetric MRI-based biomarkers in Huntington's disease: An evidentiary review. Frontiers in Neurology, 12, 712555.

8. Lebouc, M., et al. (2020). Striatal circuit development and its alterations in Huntington's disease. Neurobiology of Disease, 145, 105076.

9. Martinez-Horta, S., Perez-Perez, J., Van Duijn, E., et al. (2016). Neuropsychiatric symptoms are very common in premanifest and early stage Huntington's disease. Parkinsonism & Related Disorders, 25, 58-64.

10. Massey, T. H., & Mclauchlan, D. J. (2024). Huntington's disease: A clinical primer for acute and general physicians. Clinical Medicine, 24(2).

11. McAllister, B., Gusella, J. F., Landwehrmeyer, G. B., et al. (2021). Timing and impact of psychiatric, cognitive, and motor abnormalities in Huntington disease. Neurology, 96(19), e2395-e2406.

12. Mohapel, J. G., & Rego, A. C. (2011). Doença de Huntington: Uma revisão dos aspectos fisiopatológicos. Revista Neurociência, 19(4), 724-734.

13. Nair, A., Razi, A., Gregory, S., et al. (2022). Imbalanced basal ganglia connectivity is associated with motor deficits and apathy in Huntington's disease. Brain, 145(3), 991-1000.

Revista ARACÊ
ISSN: 2358-2472

14. Nogueira, L. A., Rocha, A. E. O., Vasconcelos, L. M., Figueiredo, J. A. B. Júnior, & Bragato, S. G. R. (2019). Manifestações neuropsicomotoras da doença de Huntington juvenil: Sinais e sintomas e achados de imagem. Revista Med, 98(6), 408-414.

15. Paulsen, J. S., Hoth, K. F., & Stierman, L. (2005). Critical periods of suicide risk in Huntington's disease. American Journal of Psychiatry, 162(4), 725-731.

16. Ramos, N. O., Canizares, V. S. A., França, A. K., Campelo, T. N. C., & Cedaro, J. J. (2018). Doença neurodegenerativa rara: Caracterização dos portadores de doença de Huntington e ataxia espinocerebelar na Amazônia Ocidental, Brasil. Revista de Saúde Pública do Paraná, 1(2), 63-74.

17. Reiner, A., & Deng, Y. P. (2018). Disrupted striatal neuron inputs and outputs in Huntington's disease. CNS Neuroscience & Therapeutics, 24(4), 250-280.

18. Ross, C. A., & Tabrizi, S. J. (2011). Huntington's disease: From molecular pathogenesis to clinical treatment. The Lancet Neurology, 10(1), 83-98.

19. Schultz, J. L., Kamholz, J. A., Moser, D. J., et al. (2017). Substance abuse may hasten motor onset of Huntington disease: Evaluating the Enroll-HD database. Neurology, 88(9), 909-915.

20. Spitz, M. (2010). Doença de Huntington e outras coréias. Revista do Hospital Universitário Pedro Ernesto, UERJ, 9.

21. Stahl, C. M., & Feigin, A. (2020). Medical, surgical, and genetic treatment of Huntington disease. Neurologic Clinics, 38(2), 367-378.

22. Taran, A. S., Shuvalova, L. D., Lagarkova, M. A., & Alieva, I. B. (2020). Huntington's disease-an outlook on the interplay of the HTT protein, microtubules, and actin cytoskeletal components. Cells, 9(6), E1514.

23. Unti, E., Mazzucchi, S., Palermo, G., Bonuccelli, U., & Ceravolo, R. (2017). Antipsychotic drugs in Huntington's disease. Expert Review of Neurotherapeutics, 17(3), 227-237.

24. Venuto, C. S., McGarry, A., Ma, Q., & Kieburtz, K. (2012). Pharmacologic approaches to the treatment of Huntington's disease. Movement Disorders, 27(1), 31-41.

25. Wiprich, M. T., Zanandrea, R., Altenhofen, S., & Bonan, C. D. (2020). Influence of 3-nitropropionic acid on physiological and behavioral responses in zebrafish larvae and adults. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 234, 108772.