# Hunting for Huntington's: Behavioral Changes in a Patient with a Family History of Huntington's Disease

Bojan Slavnic, DO; Ann Schwartz, MD, FACLP
Emory University School of Medicine, Department of Psychiatry & Behavioral Sciences

## Introduction

Prompt assessment and treatment of neurobehavioral symptoms remains challenging in psychiatric practice. Huntington's Disease-Like Type 2 (HDL2) is a recently identified phenocopy neurodegenerative disorder that is in most cases clinically indistinguishable from Huntington's Disease (Anderson DG, et al., 2007). Characteristics that may help differentiate HDL2 include South African ancestry, progressive dystonia, and lack of choreoathetoid movements. Both disorders are caused by trinucleotide repeats and have a progressive disease course leading to death within two decades of disease onset. It is therefore crucial to maintain a broad differential diagnosis for patients with a family history of genetic disorders that present with psychomotor abnormalities (Govert F, Chneider SA, 2013).

## Clinical Case

NJ, a 49-year-old African American male, presented to the Atlanta VA for worsening depression and an interrupted suicide attempt. He was admitted for psychiatric stabilization and diagnosed with major depressive disorder (MDD). A family history of Huntington's Disease (HD) was noted. NJ was next evaluated five years later when he presented reporting memory loss, insomnia, and weight loss. His family described strange behaviors, such as speaking to his dead mother. His Mental Status Examination (MSE) was notable for an anxious appearance, poor eye contact, mumbling speech, minimal insight, poor judgment, yet intact neurological exam. Diagnoses included MDD with psychosis and unspecified anxiety. HD testing was not performed. Approximately one year later, NJ presented with disorganized thinking, poor oral intake, and a recent report of pacing the street naked. His MSE was positive for immobility, withdrawal, verbigeration, and thought blocking. NJ was diagnostically evaluated for a primary psychotic disorder along with catatonia. Neurological evaluation along with general medical workup were not revealing for etiology.

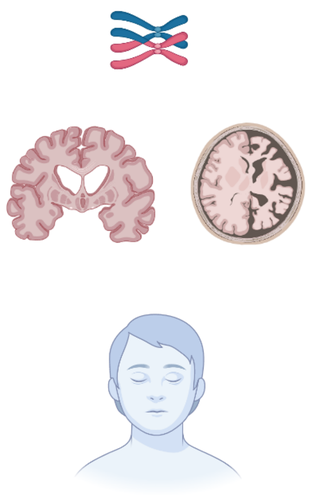
## Huntington Disease vs Huntington Disease-Like Type 2

### Huntington's Disease (HD)

Autosomal Dominant
Progressive

Pathophysiology
CAG triplet repeats
*HTT* gene
Mutant huntingtin protein
Cortical and striatal neurodegeneration

Characteristics
Chorea
Behavioral changes
Dementia
50% will have comorbid depression
Increased suicide risk
Mean age of onset: 3rd to 4th decade of life



### HD-Like Type 2 (HDL2)

Autosomal Dominant
Progressive

Pathophysiology
CTG triplet repeats
*JPH3* gene
Loss of junctophilin-3
Cortical and striatal neurodegeneration

Characteristics
Indistinguishable from HD
Akinetic-rigid syndrome
South African descent
0.7% of HD phenocopies
Mean age of onset: 3rd to 4th decade of life

## Clinical Case, continued

Clonazepam was titrated to 3 mg TID for catatonia. HD testing was negative for CAG repeats. Testing for related genetic syndromes was positive for 52 repeats within the JPH3 gene, confirming Huntington Disease-Like Type 2 (HDL2). At the index presentation, NJ was seen for worsening cognition and requiring assistance with activities of daily living (ADLs). Treatment and stabilization were achieved with 8 sessions of ECT for catatonia and mood along with valproate 750 mg BID for mood/calm, lorazepam 2 mg TID for catatonia, haloperidol 10 mg BID for psychosis, and duloxetine 40 mg daily for depression. He was determined not to have decisional capacity due to a major neurocognitive disorder secondary to HDL2. Multidisciplinary approach including family and palliative care was utilized for determining goals of care. NJ was discharged to structured setting with 24-hr care.

## Discussion

Although description of different HD phenocopy syndromes continues to this day, clinical identification remains difficult. As our case highlights, early symptoms were predominantly psychiatric with intact neurological examination. Important characteristics included African ancestry, family history of HD, progressive neuropsychiatric symptom burden without abnormal motor movements, age of disease onset, and negative genetic testing for HD. Hence, personal characteristics such as age, ethnic background, and family history remain important for diagnosing neuropsychiatric disorders (Govert F, Chneider SA, 2013; Ross CA, Tabrizi SJ, 2011). Symptom control was achieved with neuromodulation and psychotropics. A multidisciplinary approach provided a treatment plan focused on quality of life.

## Conclusion

For patients with a strong family history of HD who present with progressive neuropsychiatric symptom burden without obvious choreoathetoid movements and negative HD genetic testing, strong consideration should be made toward HDL syndromes and related genetic disorders.

## References

1. Anderson DG, Walker RH, Connor M, Carr J, Margolis RL, Krause A. A Systematic Review of the Huntington Disease-Like 2 Phenotype. J Huntingtons Dis. 2017;6(1):37-46. doi:10.3233/JHD-160232
2. Govert F, and Chneider SA. Huntington's disease and Huntington's disease-like syndromes: an overview. Curr Opin Neurol 2013; 26:420-427.
3. Lehnart SE, Wehrens XHT. The role of junctophilin proteins in cellular function. Physiol Rev. 2022;102(3):1211-1261. doi:10.1152/physrev.00024.2021
4. Ross CA, Tabrizi SJ. Huntington's disease: from molecular pathogenesis to clinical treatment. Lancet Neurol. 2011;10(1):83-98. doi:10.1016/S1474-4422(10)70245-3
5. Seixas AI, Holmes SE, Takeshima H, et al. Loss of junctophilin-3 contributes to Huntington disease-like 2 pathogenesis. Ann Neurol. 2012;71(2):245-257. doi:10.1002/ana.22598