BACKGROUND and SUMMARY
Pentanucleotide repeat expansions of ATTCT in intron 9 of the ATXN10 gene typically cause a distinct clinical phenotype of progressive spinocerebellar ataxia with or without seizures and present neuropathologically with Purkinje cell loss resulting in symmetrical cerebellar atrophy.

RESULTS
Four of the affected family members examined showed clinical features of progressive ataxia and seizures with cognitive and psychological changes including dementia. However, one affected individual presented with early-onset L-Dopa responsive parkinsonism and no signs of ataxia, and one sibling was clinically unaffected indicating reduced penetrance or delayed onset for this allele. Interestingly, no repeat interruptions were detected in the patient presenting with Parkinson’s disease and his sister with reduced or delayed penetrance. However, in the siblings with typical ataxia, we found ATXN10 repeat interruptions which have not been associated with seizures previously.

METHODS
We clinically characterized several affected and unaffected family members of a large 4-generation Mexican kindred with 38 affected family members with ATXN10 expansions using standardized clinical assessment tools. Furthermore, to fully understand the genetic architecture of the ATXN10 repeat expansion, we used a novel technology combining single molecule real time (SMRT) sequencing and CRISPR/Cas9-based capture method, and sequenced the entire span of 5' 3.4kb-6.5kb repeat expansions as one continuous fragment.

CLINICAL PRESENTATION of PROBAND
The proband first showed clinical signs at age 37, when his family noticed a “blank stare”. At 38, he developed tremor of his chin, left hand, and generalized stiffness. At 39, his family noticed increased irritability, moodiness, and general weakness. At age 45, on neurological exam, he exhibited moderate left hand resting tremor, moderate bradykinesia and muscle rigidity, shuffling gait, mildly soft voice, and moderate hypomimia. Posture was mildly stooped and he showed absent postural response. He responded well to dopaminergic therapy (carbidopa/levodopa and ropinirole). No cerebellar symptoms were detected. After 5 years, he developed motor complications with wearing off, gait freezing, and dyskinesias.

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CONCLUSIONS
This is the first reported case with clinically typical L-dopa responsive parkinsonism and an ATXN10 repeat expansion. We propose that the absence of repeat interruptions is responsible for the clinical presentation of Parkinson’s disease. It will be important to understand the underlying genetic and molecular differences that lead to the changes in the neurodegenerative process in this family with different clinical and presumably neuropathological phenotypes.

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