

**Oral Presentation Abstract: O4**

**Title:**

The Phenotype Of Huntington Disease Like 2

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Huntington disease (HD) is an inherited autosomal dominant neurodegenerative disease. It presents in adulthood with the triad of psychiatric changes, cognitive decline and a movement disorder. The recently discovered Huntington’s disease like 2 (HDL2) is an autosomal dominantly inherited neurodegenerative disorder believed to be the disease most like HD clinically, pathologically and radiologically, despite being genetically unique. The phenotype of HDL2 has not been systematically studied and most of the data being from case reports. HDL2 is rare, with fewer than 25 pedigrees and 40 individuals described worldwide. In South Africa we have found 41 cases from 34 pedigrees and the majority of these live within 100km of Johannesburg. This has provided a rare opportunity to study this HD phenocopy.

The aim of this study is to systematically evaluate the phenotype of HDL2. To achieve this aim the specific objectives of this study are to describe the clinical phenotype of HDL2 using established neurological clinical rating scales, to describe the radiological phenotype quantitatively, to determine the relationship of HDL2 phenotypes to CTG/CAG repeat size and lastly to compare the HDL2 features to those in an HD control group and determine the areas of clinical similarities and differences.

Our approach is to enroll at least 30 HDL2 patients and an equal number of HD patients over 2-years. Participants will be ascertained from the Johannesburg HD/HDL2 database from the NHLS and then assessed at the new HDL2 clinic. Each assessment will include a detailed history and examination, MRI scan and a DNA sample and blood smear. Clinical tools will be used to systemically evaluate patient’s psychiatric, cognitive and neurological domains. This includes the UHDRS of which the motor components will be videoed for blinded evaluation. MRIs will be on a 1.5 Tesla machine at The University of the Witwatersrand Donald Gordon Medical Center.

By studying HD phenocopies and finding common pathways that lead to disability, we are more likely to discover disease mechanisms, markers of progression and possible therapeutic targets. South Africa has the largest know population of HDL2 providing a unique opportunity to study this novel disease