Genetic epidemiology of dominant ataxias in Venezuela

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Genetic, neuropathophysiology and epidemiology features of SCAs

- More than 49 SCA forms attributed to at least 37 genes have been identified.
- All shows ethnic differences in their frequency and distribution.
- Incidence of 3 per 100,000 in the European population[1,2], and a global prevalence of 1-9 per 100,000 (ORPHA:99).
- In the American continents, there is no uniform prevalence figure due to the occurrence of different founder effects that have produced geographic clusters with high local frequencies[3].

[1]Nat Rev Neurosci 2017; 18(10): 613–626,
[2]Mov Disord Clin Pract. 2019, 16;6(7):531-540
[3]Cerebellum. 2025, 26;24(3):75.

SCAs subtypes studied in the Human Genetics Laboratory (HGL) of the Venezuelan Institute for Scientific Research (IVIC).

- At the HGL of the IVIC, 12 subtypes are studied molecularly since 2002, in families referred from all states of the country:

SCA1

SCA2

SCA3

SCA6

SCA7

SCA8

SCA10

SCA12

SCA17

DRPLA

SCA31

SCA36

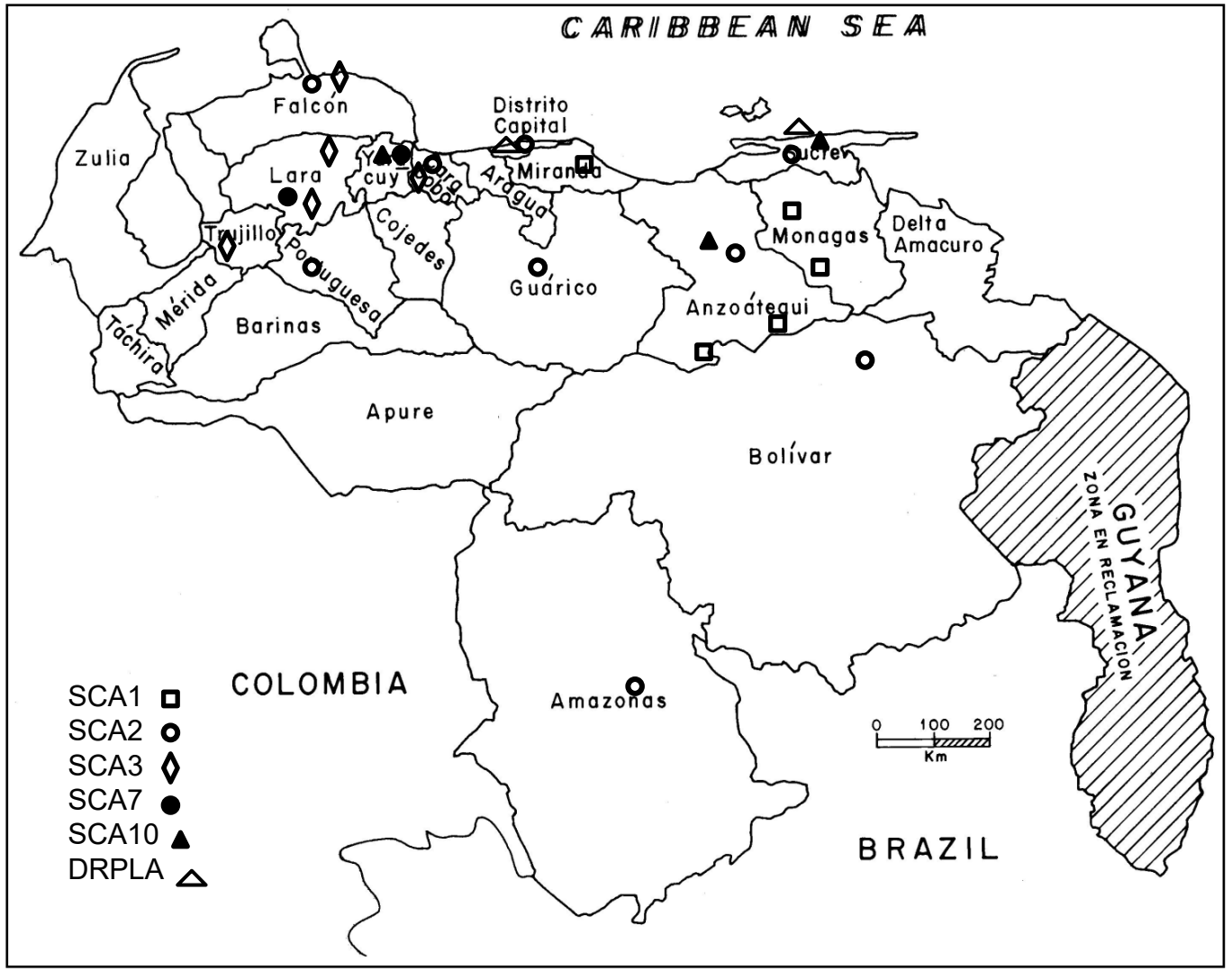
Epidemiological features of SCAs in Venezuela:

- Wide distribution throughout the country.
- Estimated global prevalence of 4:100,000 families.
- Unusual frequency distribution compared to most populations:

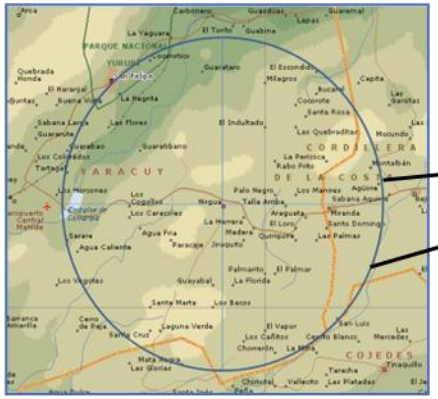
  SCA7>SCA3>SCA2>SCA1>SCA10>DRPLA

- Strong geographic aggregation and two distinct founder effects for SCA7.
- Founder effect for a group of SCA1 families.

Geographic distribution of SCAs' families in Venezuela according to the birthplace of the ancestors.



SCA7: two founder effects?

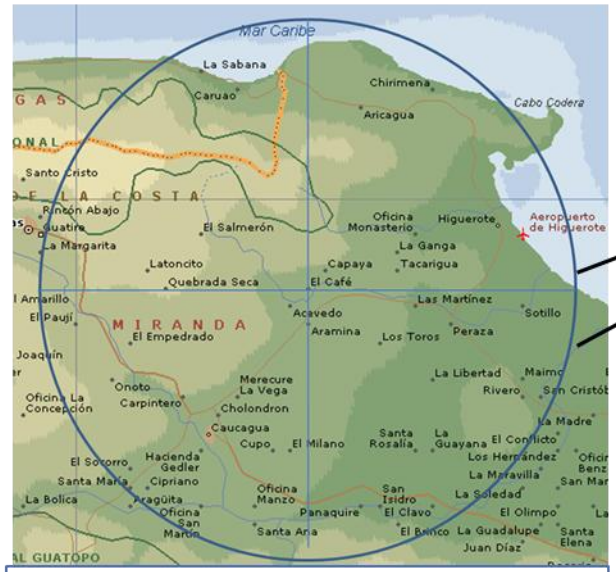


Yaracuy state:
In-phase haplotype:
4T;2A;2TG

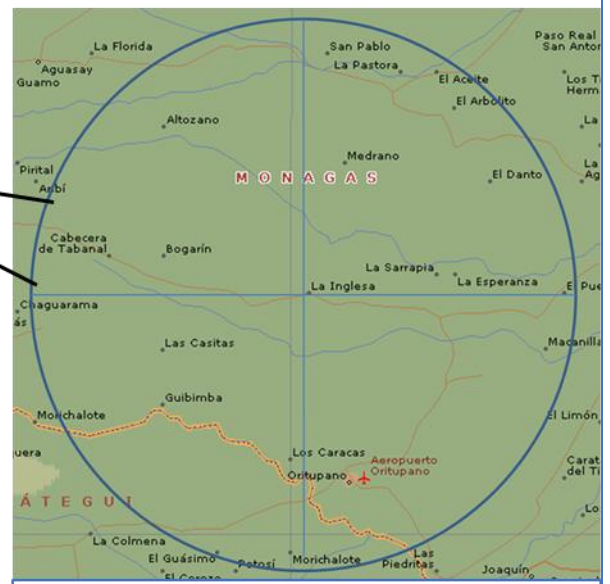
Lara state:
In-phase haplotype:
4T;3A;2TG

Founder effect in 30% of SCA1 families.

- All families originating from both foci possess the same insTTTAA;G;C in-phase haplotype. This haplotype is absent in the chromosomes of the control subjects.



El Café, Miranda state



La Inglesa, Monagas state

SCA10 geographic distribution

All the independent index cases had remote ancestors coming from three far apart states in the country. All share the same in-phase haplotype, which is the same of all the reported cases from America and East Asia.

HAPLOTYPE: C;A;G;G;C;C

Amerindian D9S1120 (alele 9) is present in 50% of families

ATXN10 SNPs (rs5764850; rs136003; rs72556348; rs72556349; rs72556350; rs136005)

Concluding remarks.

1. Six SCA subtypes have been identified so far in the country, with SCA7 being the most prevalent.
2. The geographic origin of the families' ancestors is widespread in Venezuela, but there are specific clusters for SCA7, SCA1, and SCA10 in which the prevalence is higher than in other regions of the country.
3. Founder effects followed by genetic drift have shaped the current genetic epidemiology of SCAs in Venezuela.

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