tionally, a wide spectrum of clinical phenotypes was observed among SCA patients including typical mild dominant ataxia, the MJD phenotype with facial fasciculations and lid retraction, and early onset ataxia with rapid course, chorea and dementia.

CONCLUSIONS: SCA2 is a common cause of dominant ataxias. Genetic testing for SCA1,2 and 3 will detect close to half of all the mutations causing dominant ataxias. Phenotypes associated with SCA2 mutations range from typical ADCAI to MJD-like and a pedigree with chorea and dementia. Since even mild dementia is rare in patients with SCA1 or SCA3/MJD, and when present is a late sign, early dementia may be a feature that allows clinical distinction among these conditions in a subset of patients.

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Frequency and Molecular Characteristics of the Spinocerebellar Ataxia Type 2 Mutation

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OBJECTIVE: To determine the frequency of the spinocerebellar ataxia type2 (*SCA2*) mutation in a large group of spinocerebellar ataxia (SCA) patients and the molecular characteristics of the normal and expanded CAG alleles.

BACKGROUND: The *SCA2* gene has been recently cloned and an expansion of an unstable CAG repeat was shown to be the causative mutation.

DESIGN/METHODS: We studied individuals belonging to 48 unrelated SCA families from different ethnic origins. All families were negative for the *SCA1*, *MJD/SCA3* and *DRPLA* mutations. PCR assays were carried out using primers that specifically amplify the CAG repeat contained in the *SCA2* gene.

RESULTS: Normal alleles had between 17 and 27 CAGs. The most frequent normal allele had 22 repeats and was present in 87.1% of the 132 normal chromosomes. We found the *SCA2* mutation in 9 families. Six families were from India, two families from Canada and one from Brazil. The size of the expanded alleles varied from 36 to 46 CAGs (mean, 39 CAGs). There was an inverse correlation between the size of the expanded allele and age at onset of the disease (r0.651, r2 =0.424 and $p<0.0001$). We observed mild instability of the CAG repeat during transmission.

CONCLUSIONS: The *SCA2* mutation was present in 18% of the families studied. The percentage of variability in age at onset that could be explained by the size of the expanded CAG repeat in the *SCA2* gene was 42%, suggesting that other genetic or enviromental factors may be involved in determining the clinical presentation of the disease. The wide gap between the size of the normal and the expanded alleles in *SCA2* will facilitate molecular testing of at risk individuals.

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Clinical and Genetic Studies in Italian Autosomal Dominant Cerebellar Ataxias

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OBJECTIVE: To characterize clinically and genetically a large series of Italian patients with autosomal dominant cerebellar ataxia (ADCA).

BACKGROUND: ADCA is a heterogeneous group of diseases classified according to clinical features. Further splitting into ADCA subtypes (i.e. spinocerebellar ataxias 1–7, SCA 1–7) was achieved upon discovery of gene mutations or gene localization. SCA1 and SCA3 are associated with unstable CAG trinucleotide repeat expansions on different loci. SCA2 maps to chromosome 12q23–24.1.

DESIGN/METHODS: We analyzed 37 Italian ADCA I families (27 from Northern and Central Italy, 10 from Southern Italy). We investigated all patients for the presence of SCA1 and SCA3 mutations; in a subset of six families we performed linkage analysis for SCA2.

RESULTS: Nineteen of 37 ADCA I families carried the SCA1 expansion (51%); their clinical features did not differ from other ADCA I families. One family showed linkage to chromosome 12q23–24.1 (SCA2). No family carried the SCA3 expansion. In SCA1 families, expansion size (38–60 repeats) correlated with age of onset and rate of progression.

CONCLUSIONS: Previous European and American studies showed a high frequency of SCA3 mutations and a low frequency of SCA1 mutations in their families. By contrast, in our unselected series of ADCA patients, SCA1 was by far the most common type of ADCA I, and SCA3 genotype was not represented.

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P03.079

Spinocerebellar Ataxia: A Genetic Study in 30 Brazilian Families

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OBJECTIVE: The authors present the results of genetic study to identify trinucleotide CAG repeat of SCA1 (Spinocerebellar Ataxia Type 1), MJD (Machado-Joseph Disease)/SCA3, and DRPLA (Dentatorubropallidoluysian Atrophy) in 30 families with autosomal dominant spinocerebellar ataxia.

BACKGROUND: Different genes causing autosomal dominant spinocerebellar ataxia have been identified and in at least 3 of them expansions of trinucleotide CAG has been identified: SCA1, MJD/SCA3, and DRPLA.

DESIGN/METHODS: Thirty families with autosomal dominant cerebellar ataxia living in Southern Brazil (States of Paran and Santa Catarina) were evaluated. Most families (27) have Portuguese/azorean ancestry. Molecular genetic studies were performed at the Centre for Research in Neuroscience, McGill University, Canada (Iscia Lopes Cendes, Guy Rouleau) for determination of frequency of the SCA1, MJD/SCA3, and DRPLA mutations.

RESULTS: We found mutations in 14 (46,6%) families. The frequency of SCA1 mutation was 6,6% (2 families). MJD/SCA3 was the most commonly observed mutation: it was detected in 12 families (40%). Out of these 12 families, 10 families have Portuguese/azorean ancestry, while one was italian and the other one spanish. No DRLPA mutation was identified.

CONCLUSIONS: Autosomal dominant spinocerebellar ataxias is a group of neurodegenerative diseases with a great genotypic and phenotypic heterogeneity, e.g. SCA 1, 2, 3/MJD, 4, 5, 6, 7, DRPLA, and paroxystic ataxias. SCA3/MJD has been described in either Portuguese/azorean populations and immigrants, as well as in other ethnical groups in many parts of the world. SCA3/MJD mutation seems to be the most common cause of dominantly inherited SCA in Brazil.

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Classification of Autosomal Recessive Spinocerebellar Ataxias (ARSCA) Based on Recent Genetic Studies

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