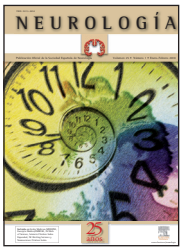
Neurología. 2011;**26(3)**:157-165

NEUROLOGÍA

www.elsevier.es/neurologia



ORIGINAL ARTICLE

Multimodal neurophysiological study of SCA2 and SCA3 autosomal dominant hereditary spinocerebellar ataxias ☆

S. Álvarez-Paradelo,[a,*] A. García,[a] J. Infante,[b] J. Berciano[b]

[a] *Servicio de Neurofisiología Clínica, Hospital Universitario Marqués de Valdecilla (IFIMAV), Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Santander, Spain*
[b] *Servicio de Neurología, Hospital Universitario Marqués de Valdecilla (IFIMAV), Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Universidad de Cantabria, Santander, Spain*

Received on 15th April 2010; accepted on 5th September 2010

KEYWORDS
Spinocerebellar ataxia;
Blink reflex;
Electroneurography;
Multimodal evoked potentials;
Masseter reflex;
SCA2 and SCA3

Abstract
Background: The spinocerebellar ataxias (SCA) are a group of genetic neurodegenerative diseases, clinically and pathologically heterogeneous, characterized by slowly progressive cerebellar ataxia.
Objective: To identify the neural pathways affected neurophysiologically, correlate the findings with the size of CAG expansion and determine the contribution of neurophysiological studies in the differential diagnosis of the two most prevalent genotypes in Spain, SCA2 and SCA3.
Method: We examined 10 SCA2 and 12 SCA3 patients by electromyography, electroneurography motor and sensory, multimodal evoked potentials, transcranial magnetic stimulation, blink reflex and masseter reflex. In the statistical analysis linear regression studies were performed, and the Spearman correlation coefficient and nonparametric test U of Mann-Whitney calculated.
Results: We detected the presence of a predominantly sensory neuropathy in most SCA2 patients and in a minority of SCA3 patients; the central somatosensory pathway showed significant defects in both populations. We recorded a high incidence of brain-stem electrophysiological abnormalities in SCA2 patients; in particular, the masseter reflex was abnormal in all SCA2 patients, remaining intact in all SCA3 patients. The study of cortico-spinal pathway showed a greater percentage of abnormalities in both populations than in previous studies.
Conclusion: SCA2 is a model of sensory neuronopathy with central and peripheral axonopathy. Studies of brain-stem pathways show a higher incidence of abnormalities in SCA2 patients. SCA3 patients show major changes in the central somatosensory pathway

☆ This paper has been funded by the Health Research Fund (FIS PI07/1323E) and EUROSCA.
* Corresponding author.
E-mail: doctoraparadelo@hotmail.com (S. Álvarez-Paradelo).

with relative normality of the electroneurography. The masseter reflex was the most useful test in the differential diagnosis between both genotypes.

PALABRAS CLAVE
Ataxia espinocerebelosa;
Electroneurografía;
Potenciales evocados multimodales;
Reflejo mandibular;
Reflejo de parpadeo;
SCA2 y SCA3

Estudio neurofisiológico multimodal en las ataxias espinocerebelosas con herencia autosómica dominante de tipo SCA2 y SCA3

Resumen
Introducción: Las ataxias espinocerebelosas (SCA) son un grupo de enfermedades neurodegenerativas genética, clínica y patológicamente heterogéneo, caracterizado por presentar una ataxia cerebelosa lentamente progresiva.
Objetivo: Identificar las vías nerviosas neurofisiológicamente afectadas, correlacionar los hallazgos con el tamaño de la expansión CAG y determinar la contribución del estudio neurofisiológico al diagnóstico diferencial de los dos genotipos más prevalentes en España, SCA2 y SCA3.
Método: Hemos examinado 10 pacientes SCA2 y 12 SCA3 mediante electromiografía, electroneurografía motora y sensitiva, potenciales evocados multimodales, estimulación magnética transcraneal, reflejo de parpadeo y mandibular. En el análisis estadístico empleamos estudios de regresión lineal, coeficiente de correlación de Spearman y el test no paramétrico "U de Mann-Whitney".
Resultados: Detectamos anomalías compatibles con una neuronopatía sensitiva con axonopatía periférica en la mayoría de pacientes SCA2 y en una minoría de SCA3; la vía somatosensorial central presentó abundantes anomalías en ambas poblaciones. Registramos importantes alteraciones tronco-encefálicas en SCA2; particularmente, el reflejo maseterino estuvo alterado en todos los pacientes SCA2, manteniéndose intacto en los SCA3. El estudio de la vía córtico-espinal demostró un mayor porcentaje de anomalías en ambas poblaciones que estudios previos.
Conclusiones: SCA2 es un modelo electrofisiológico sugestivo de una neuronopatía sensitiva con axonopatía periférica y central. Los estudios de las vías tronco-encefálicas demuestran una mayor incidencia de alteraciones en los pacientes SCA2. En los pacientes SCA3 se observaron importantes alteraciones de la vía somatosensorial central con relativa normalidad del estudio electroneurográfico. El reflejo mandibular fue el test de mayor utilidad en el diagnóstico diferencial de ambos genotipos.

Introduction

Cerebellar ataxias with autosomal dominant transmission are a group of neurodegenerative diseases characterized by slowly progressive cerebellar ataxia as the main symptom, caused by the degeneration of the cerebellum and its afferent and efferent connections. In most families, clinical and pathological evidence has been detected of involvement of other structures in the nervous system such as the extrapyramidal system, the oculomotor nerves, the peripheral nervous system and spinal cord.[1] Recent molecular genetics studies have detected that the most frequent molecular defect is a dynamic expansion of the CAG triplet encoding for polyglutamine tracts,[2,3] locating 30 different *loci*[4] designated with the term "spinocerebellar ataxia" (SCA1 to SCA30).

The prevalence of SCA varies from one country to another, with a predominance in Spain of genotypes SCA2 and SCA3.[2,5] The main goal of our study has been to identify neurophysiologically the altered nerve pathways, to establish the correlations of the neurophysiological alterations observed with the underlying expansion size (CAG) and to determine the possible contribution of the neurophysiological study to the differential diagnosis of genotypes SCA2 and SCA3.

Patients and method

Patients with clinical signs of late-onset cerebellar ataxia were studied if their genetic study had shown the existence of the underlying mutation for SCA2 and SCA3. In addition, the members of the propositus's family were studied if they presented the mutation, either as asymptomatic or symptomatic carriers. For details of the molecular study, we would refer the reader to the reference by Infante et al.[5] The study was approved by the Cantabrian Ethics Committee.