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COMPREHENSIVE REVIEW/REVUE GÉNÉRALE

# The electrophysiology of spinocerebellar ataxias

## *Electrophysiologie des ataxies spinocérébelleuses*

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Evoked potential

**Summary** Spinocerebellar Ataxias (SCAs) are a group of autosomal dominantly inherited neurodegenerative diseases, involving the cerebellum and the brainstem. Genetic testing is the most important method of diagnosis. Nowadays, nearly 40 types of SCAs have been identified by genetic analysis. Peripheral nerve impairment is common in SCAs: electrophysiological examination of SCA1, SCA2 and SCA3 usually shows sensorimotor and sensory neuropathy, while pure motor neuropathy is more rare, being seen only in SCA2. The abnormal VEP of SCA1, SCA2 and SCA3 include prolonged P100 latencies and reduced P100 amplitudes. Abnormal BAEP involves prolonged interpeak latency of I—III and III—V. Abnormal SEP usually show absent P40 wave and prolonged P40 latency. The abnormal MEP usually shows prolonged central motor conduction time or absent responses. SCA2 is not associated with gaze-evoked nystagmus and dysmetric saccades. SCA3 usually presents as saccadic intrusions and oscillations. Whether peripheral nerves are involved in SCA6 is uncertain; although abnormal electrophysiology has been reported, neuropathological examinations have not found degenerative changes or reductions in the number of neurons in the anterior horns and/or dorsal root ganglia in SCA6. It is therefore hypothesized that this might be a displayed feature of axonopathy. The clinical presentation of most cases of SCA6 includes spontaneous and positional downbeat nystagmus, and perverted head-shaking nystagmus. Opinion about peripheral nerve involvement in SCA7 varies between authors. Losing P100 is a predominant feature of SCA7, while III and IV/V wave absence is common in SCA17. Electrophysiological study of other types is currently limited, requiring large-scale studies for confirmation. Similar and overlapping clinical features make it difficult to differentiate each type. Electrophysiological testing can therefore play an important role in helping to identify the common phenotypes of SCAs, and determine the extent and progression of disease.


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**MOTS CLÉS**
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Électrophysiologie ;
Étude de conduction nerveuse ;
Potentiels évoqués

**Résumé** Les ataxies spinocérébelleuses (SCA) sont un groupe de maladies neurodégénératives héréditaires autosomiques dominantes, impliquant le cervelet et le tronc cérébral. Le test génétique est la méthode la plus importante de diagnostic. Aujourd'hui, près de 40 types de SCA ont été identifiés par analyse génétique. Les lésions du nerf périphérique sont très communes dans les SCA : l'examen électrophysiologique montre habituellement une neuropathie sensitive ou sensori-motrice dans les SCA1, SCA2 et SCA3, tandis que les neuropathies motrices pures sont plus rares, vues seulement dans les SCA2. Les anomalies des PEV dans les SCA1, SCA2 et SCA3 comprennent un allongement de la latence et une diminution d'amplitude des P100. Les anomalies des PEA précoces du tronc cérébral comprennent un allongement des intervalles de latence I—III et III—V. Les anomalies des PES sont généralement une onde P40 absente ou de latence prolongée. Les anomalies des PEM sont un allongement du temps de conduction centrale ou des réponses absentes. Les SCA2 ne sont pas associées avec un nystagmus ou des saccades dysmétriques, contrairement aux SCA3. Il n'est pas certain que les nerfs périphériques soient impliqués dans les SCA6, car les examens neuropathologiques n'ont pas trouvé de modifications dégénératives dans les cornes antérieures de la moelle ou dans les ganglions spinaux, bien que des anomalies électrophysiologiques aient été rapportées. L'hypothèse d'une axonopathie reste donc possible. La présentation clinique de la plupart des cas de SCA6 comprennent notamment un nystagmus spontanée et positionnel battant vers le bas. L'opinion concernant l'implication d'une atteinte des nerfs périphériques dans les SCA7 varie entre auteurs. L'abolition de la P100 des PEV est une caractéristique prédominante des SCA7, tandis que l'absence des ondes III et IV/V des PEA est courante dans les SCA17. Les données électrophysiologiques sont actuellement limitées dans les autres types de SCA, nécessitant des études de confirmation sur des populations plus importantes. Des caractéristiques similaires ou se chevauchant, rendent difficiles la distinction entre les différents types de SCA. Les tests électrophysiologiques peuvent donc jouer un rôle important en aidant à identifier les phénotypes communs des SCA et à déterminer la diffusion et la progression de la maladie.


## Introduction

The spinocerebellar ataxias (SCAs) are a clinically and genetically heterogeneous group of neurodegenerative diseases. The clinical characteristics of SCAs are complex. Most subtypes of SCAs present classic manifestations of cerebellar ataxias, while some subtypes often show atypical ataxia symptoms at onset, such as SCA7, which is characterized by visual impairment, SCA14 by myoclonus and SCA17 by parkinsonism [21]. Additionally, eye movement abnormalities, pyramidal signs, extrapyramidal features, sensory symptoms, cognitive dysfunction and autonomic symptoms can also be present in some subtypes of SCAs.

One diagnostic system proposed by Anita Harding divides these disorders into autosomal dominant cerebellar ataxia types I, II, and III [9]. Type I syndromes are ataxias with ophthalmoplegia, optic atrophy, dementia and extrapyramidal features (i.e., SCA1—SCA4, SCA8, SCA10, SCA12, SCA23, SCA25, SCA27, SCA28, and dentatorubral pallidoluysian atrophy or DRPLA); type II ataxias are associated with pigmented maculopathy with or without ophthalmoplegia or extrapyramidal features (i.e., SCA7); type III syndromes include pure ataxic syndromes (i.e., SCA5, SCA6, SCA11, SCA26, SCA29, SCA30, and SCA31). Classification of SCAs can also depend upon the genetic loci ordering of the SCA from SCA1 through SCA40.

Moreover, similar or identical imaging characteristics and clinical features make it difficult to differentiate the subtypes without genetic testing. Electrophysiological examination is a potential marker of disease progression, and through comparison with clinical features, can help identify common SCA phenotypes.

## Electrophysiological evaluations

Electrophysiological evaluations include nerve conduction studies (NCS), electromyography (EMG), visual-evoked potential (VEP), brainstem acoustic-evoked potential (BAEP), somatosensory-evoked potential (SSEP), motor-evoked potential (MEP), electro-oculography, electroencephalography (EEG), and polysomnography, all of which are helpful in the study of SCAs. Electrophysiological methods may provide evidence of subclinical dysfunction of nerve conduction pathways and may show objective evidence of abnormality even when imaging is normal. This information can be used to guide future research and improve our understanding of the pathophysiology of neurodegenerative disease. NCS and EMG findings may provide essential information for diagnosis of neuromuscular disease. Peripheral nerve impairment is common in SCA. Peripheral nervous system involvement has been reported in the following subtypes: SCA1, SCA2, SCA3, SCA4, SCA7, SCA8, SCA12, SCA18, SCA23 and SCA25 [2,24,27]. Electrophysiological examination of SCA1, SCA2 and SCA3 usually shows sensorimotor and pure sensory neuropathy, while pure motor neuropathy is more rare, being seen only in SCA2 [29] (Table 1).

### Nerve Conduction Study (NCS)

On nerve conduction study (NCS), axonal neuropathies are usually characterized by low amplitude, normal