Clinical Neurophysiology 128 (2017) 215–219

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Review

Electrophysiology in Fisher syndrome

Satoshi Kuwabara *, Yukari Sekiguchi, Sonoko Misawa

Department of Neurology, Graduate School of Medicine, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba 260-8670, Japan

ARTICLE INFO

Article history:
Accepted 12 November 2016
Available online 20 November 2016

Keywords:
Fisher syndrome
H-reflex
Group 1a afferent
Sensory nerve conduction
Anti-GQ1b antibody

HIGHLIGHTS

- In Fisher syndrome (FS), ophthalmoplegia, ataxia, and areflexia are caused by autoantibodies against ganglioside GQ1b.
- Major physiologic abnormalities are absent H-reflexes and impaired proprioception in posturography.
- GQ1b-expressed in ocular motor nerves and dorsal root ganglion 1a neurons represent a target molecule for FS.

ABSTRACT

Fisher syndrome (FS), a variant of Guillain–Barré syndrome (GBS), is characterized by the clinical triad of ophthalmoplegia, ataxia, and areflexia. The lesion sites for these unique clinical features include the oculomotor nerves and group 1a neurons in the dorsal root ganglion, and the presence of FS is determined by the expression of ganglioside GQ1b in the human nervous system. Neurophysiological findings suggest that ataxia and areflexia are due to an impaired proprioceptive afferent system. Typically, the soleus H-reflex is absent and a body-sway analysis using posturography shows a 1-Hz peak, which indicates proprioception dysfunction. Sensory nerve action potentials and somatosensory-evoked potentials are abnormal in approximately 30% of FS patients, indicating the occasional involvement of cutaneous (group 2) afferents. During the disease course, approximately 15% of FS patients suffer an overlap of axonal GBS with nerve conduction abnormalities that reflect axonal dysfunction. This review summarizes electrophysiological abnormalities and their clinical significance in FS.

Contents

Abbreviations: DRG, dorsal root ganglion; FS, Fisher syndrome; GBS, Guillain–Barré syndrome; NCS, nerve conduction study; SEP, somatosensory-evoked potential; SNAP, sensory nerve action potential.

* Corresponding author. Fax: +81 43 226 2160.
E-mail address: kuwabara-s@faculty.chiba-u.jp (S. Kuwabara).

http://dx.doi.org/10.1016/j.clinph.2016.11.009
1388-2457/

1. Introduction

Fisher's syndrome (FS) is defined by the unique clinical triad of ophthalmoplegia, ataxia, and areflexia (Fisher, 1956). This syndrome is regarded as a variant of Guillain–Barré syndrome (GBS) and is mediated by autoantibodies against ganglioside GQ1b (Mori and Kuwabara, 2011; Shahrizaila and Yuki, 2013). In his original report, Charles Miller Fisher himself speculated that a selective attack on the sensory neurons underlying postural stability should have existed and that the involvement of special sensory neurons mediating tendon reflexes should be considered (Fisher, 1956). Based on the current literature, Fisher's hypothesis was absolutely correct.

The seminal paper identifying IgG antibodies against ganglioside GQ1b in FS patients was published in 1992 and led to substantial progress in the understanding of pathogenesis of FS (Chiba et al., 1992). GQ1b is dominantly expressed in the ocular motor nerves, which likely explains the presence of ophthalmoplegia in FS. The lesion site responsible for ataxia has been controversial (Ogawara et al., 2002; Shahrizaila and Yuki, 2013), but immunohistochemical studies showed that large neurons in the human dorsal root ganglia, presumably group 1a neurons, were stained with monoclonal antibodies against GQ1b and the antibodies are related with ataxia and areflexia (Kusunoki et al., 1999).

Because of the limitations in the electrophysiological evaluation of the ocular motor nerves, neurophysiological studies in FS mainly reported on nerve conduction in limb nerves and occasionally cranial nerves when affected. Previous neurophysiological studies in FS patients revealed peripheral sensory nerve involvement, including reduced sensory nerve action potential (SNAP) amplitudes, in some patients with FS (Durand et al., 2001; Fross and Daube, 1987; Jamal and Ballantyne, 1988; Sauron et al., 1984); however, a reduction in SNAP amplitudes were not prominent and did not explain the prominent ataxia in FS. More recently, studies with absent H-responses showed normal SNAP amplitudes, thus raising the possibility of the selective involvement of group 1a neurons in FS (Dachy et al., 2010; Sekiguchi et al., 2013).

This review summarizes the findings and significance of electrophysiological studies in FS. We searched PubMed and the Web of the Science prior to 1 June, 2016 using the search terms "Fisher syndrome" and "Miller Fisher syndrome" in combination with "el ectrophysiology", "neurophysiology", "nerve conduction study", or "evoked potential". Moreover, FS is frequently overlapped by a pharyngo-cervical-brachial variant of GBS and occasionally by axonal GBS. Particularly in cases with FS/GBS overlap syndrome, electrophysiology plays a crucial role in the detection of limb nerve involvement.

2. Electrophysiology in pure FS

To date, there are two reports that included a relatively large number of patients (28 and 47) and systematically performed nerve conduction, F-wave, H-reflex studies, somatosensory-evoked potential, and postural body sway analyses (Ito et al., 2008; Sekiguchi et al., 2013). The major findings are shown in Table 1. Both studies were from Japan, presumably because of the higher incidence of FS in Asia than in Western countries (Shahrizaila and Yuki, 2013). These studies included only a pure form of FS, whereas a considerable number of FS patients develop an overlap with GBS or Bickerstaff brainstem encephalitis (Bickerstaff and Cloake, 1951). The findings of such cases are described later.

2.1. Nerve conduction study

Motor nerve conduction studies and minimal F-wave latencies in the median, ulnar, peroneal, and tibial nerves were generally normal in FS patients (Table 1), which is consistent with the lack of motor weakness in FS. There are no reports describing FS patients who showed A-waves. A few reports described motor nerve conduction abnormalities, including prolonged F-wave latencies and reduced compound muscle action potential amplitudes. This discrepancy may be explained by contamination of cases overlapped by axonal Guillain–Barré syndrome and should be investigated in future prospective studies with a sufficient follow-up period.

In sensory nerve studies, conduction velocities were unaffected, but some patients showed decreased SNAP amplitudes. The percentage of reduced SNAP amplitudes somewhat differed between the two reports (32% vs. 7% in the nerves) (Sekiguchi et al., 2013; Ito et al., 2008), which is probably due to different definitions of the abnormality. A study by Sekiguchi et al. used nomograms of age against SNAP amplitudes in normal subjects (Fujimaki et al., 2009; Tong et al., 2004) and showed a decrease in SNAP amplitudes

Table 1
Abnormal rate of electrophysiological studies in Fisher syndrome (pure form).

	Sekiguchi et al. (2013) *n* = 47 Abnormality (%)	Ito et al. (2008) *n* = 28 Abnormality (%)
Motor nerve conduction study	0%	0%
F-wave study	0%	0%
Sensory nerve conduction study		
Median nerve		
Amplitudes	22%	NA
Conduction velocity	0%	NA
Ulnar nerve		
Amplitudes	27%	NA
Conduction velocity	0%	NA
Sural nerve		
Amplitudes	4%	NA
Conduction velocity	2%	NA
Any of the above	32%	7%
Soleus H-reflex*	67%	74%
Somatosensory evoked potential		
Median nerve	19%	23%
Tibial nerve	5%	15%
Postural body sway analysis**	57%	72%

* Absent H-reflexes or H/M ratio < 3%, defined as abnormal.
** Power spectrum peak at 1 Hz regarded as abnormal.