Clinical Neurophysiology 118 (2007) 1198–1203

www.elsevier.com/locate/clinph

Altered soleus responses to magnetic stimulation in pure cerebellar ataxia ☆

Tomomi Kurokawa-Kuroda [a,b,*,1], Katsuya Ogata [a,1], Rie Suga [a], Yoshinobu Goto [c], Takayuki Taniwaki [d], Jun-ichi Kira [b], Shozo Tobimatsu [a]

[a] *Department of Clinical Neurophysiology, Neurological Institute, Faculty of Medicine, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan*

[b] *Department of Neurology, Neurological Institute, Faculty of Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*

[c] *Department of Occupational Therapy, Faculty of Rehabilitation, International University of Health and Welfare, Okawa, Japan*

[d] *Division of Respiratory and Neurology, Department of Medicine, Kurume University of Medicine, Kurume, Japan*

Accepted 7 March 2007
Available online 23 April 2007

Abstract

Objective: Transcranial magnetic stimulation (TMS) over the leg motor area elicits a soleus primary response (SPR) and a soleus late response (SLR). We evaluated the influence of the cerebellofugal pathway on the SPR and SLR in patients with 'pure' cerebellar ataxia.
Methods: SPRs and SLRs were recorded from 11 healthy subjects and 9 patients with 'pure' cerebellar cortical degeneration; 5 with spinocerebellar ataxia type 6 (SCA6), and 4 with late cortical cerebellar ataxia (LCCA). In addition, three patients with localized cerebellar lesions were tested.
Results: The SPR latency was significantly longer in patients than in controls, but primary responses in the tibialis anterior muscle were normal. The frequency of abnormal SLR was 38.9% in the supine position and 83.3% in the standing position. Two out of three patients with localized cerebellar lesions also showed abnormal SLR.
Conclusions: Altered SPRs in patients may result from a dysfunction of the primary motor cortex caused by crossed cerebello-cerebral diaschisis. In addition, our results suggest that 'pure' cerebellar degeneration involves the mechanism responsible for evoking SLR which is related to the control of posture.
Significance: SLR can be a useful neurophysiological parameter for evaluating cerebellofugal function.

Keywords: Soleus primary response (SPR); Soleus late response (SLR); Transcranial magnetic stimulation (TMS); Cerebellar degeneration; Posture

1. Introduction

Transcranial magnetic stimulation (TMS) of the motor cortex elicits signals that are transmitted by the corticospinal tract to the four limbs to evoke primary motor evoked potentials (MEPs). In the soleus (SOL) muscle, TMS elicits a primary response with a latency of about 30 ms followed by a late response with a latency of about 90 ms (Dimitrijević et al., 1992; Ertekin et al., 1995; Holmgren et al., 1990; Sammut et al., 1995; Valls-Solé et al., 1994). The soleus primary response (SPR) has been considered to be the direct activation of the corticospinal pathway (Lavoie et al., 1995; Wochnik-Dyjas et al., 1998), and is enhanced by standing or voluntary contraction (Ackermann et al., 1991; Valls-Solé et al., 1994). The soleus late response (SLR), on the other hand, is more prominent when the tibialis anterior (TA) is activated weakly (Ertekin et al., 1995;

☆ Disclosure: The authors have no conflict of interest.

* Corresponding author. Address: Department of Clinical Neurophysiology, Neurological Institute, Faculty of Medicine, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. Tel.: +81 92 642 5543; fax: +81 92 642 5545.
E-mail address: kurokawa@neurophy.med.kyushu-u.ac.jp (T. Kurokawa-Kuroda).

[1] These authors contributed equally to this work.

1388-2457/$32.00
doi:10.1016/j.clinph.2007.03.006

Sammut et al., 1995; Suga et al., 2001), and is sometimes large even when the primary SOL response is small (Ertekin et al., 1995). In addition, the SLR is enhanced when standing is made difficult and is diminished by contracting the SOL (Ertekin et al., 1995; Sammut et al., 1995; Suga et al., 2001) or when the ankle is immobilized (Sammut et al., 1995). The SLR cannot be elicited by stimulating the brainstem or lumbar root (Ertekin et al., 1995; Suga et al., 2001). These properties indicate that the SLR is related to postural control, and that it could be a polysynaptic response of the agonist and antagonist organization system (Ertekin et al., 1995; Suga et al., 2001).

It is well known that the cerebellum plays an important role in the control of postural balance (Holmes, 1922). In our previous study (Suga et al., 2001), abnormal SLRs were detected in patients with cerebellar ataxia, including some patients with multiple system atrophy or other diseases in which extracerebellar systems were also involved. From these results, it is necessary to elucidate whether the cerebellofugal pathway or cerebellopetal pathway is responsible for the generation of the SLR.

Cerebellar signs are detected in nearly 100% of spinocerebellar ataxia type 6 (SCA 6) and late cortical cerebellar atrophy (LCCA) patients, whereas extracerebellar signs are mild and infrequent (Matsumura et al., 1997; Takahashi et al., 2004). However, central motor conduction time (CMCT) has been found to be prolonged in SCA6 patients (Chen et al., 2004; Lee et al., 2003), suggesting subclinical dysfunction of the pyramidal tract. Therefore, the purpose of this study was to determine the influence of the cerebellofugal pathway on the SPRs and SLRs elicited by TMS in patients with SCA 6 and LCCA.

2. Methods

2.1. Subjects

Nine patients (6 men and 3 women, ages 50–69 years) with cerebellar ataxia and 11 healthy subjects (5 men and 6 women, ages 50–64 years) were studied. Genetic analysis was performed on all patients: 5 were diagnosed as having SCA 6, while 4 had LCCA. All of the patients had mild to moderate limb and truncal ataxia (Table 1), but hyperreflexia, Babinski sign and extrapyramidal signs were not found. Three patients with localized cerebellar lesion were also tested: two of these had cerebellar arteriovenous malformation (AVM) and one had cerebellar infarcts (Table 2). These patients showed mild to moderate cerebellar ataxia but pyramidal or extrapyramidal signs were not present. Informed consent was obtained from each patient after the nature of genetic analysis and experiment had been fully explained. The experimental procedures were approved by the Ethics Committee of Graduate School of Medical Sciences, Kyushu University.

2.2. Magnetic cortical stimulation and electromyography (EMG) recording

The recording techniques have been described in detail (Suga et al., 2001). Briefly, a pair of surface EMG electrodes were placed about 3 cm apart over the long axis of the tibialis anterior (TA) and SOL muscles bilaterally. The EMG activity was bandpass filtered between 20 Hz and 3 kHz and amplified to 0.5–1.0 mV/div at a sampling rate of 1.7 kHz (Neuropack 8, Nihon Kohden).

A Magstim 200 magnetic stimulator (The Magstim Company) with a double-cone coil was placed with the center over the vertex, with the current flow in the brain being induced in an anterior–posterior direction. The strength of contraction of the TA or SOL muscles was controlled by monitoring prestimulus EMG activities by Neuropack 8, and more accurately with the real-time integrated EMG amplitude monitor using a personal computer (NEC). The stimulus intensity was changed in 5% steps of the maximum stimulator output. The MEPs from the TA and SOL were obtained at least four times for each condition. The two most stable responses were used for analysis. The onset latency was measured as the fastest latency of the four compound muscle action potentials (CMAPs) of each muscle, while the peak-to-peak amplitude was measured from the average of the two fastest responses (Suga et al., 2001).

Table 1
Demographic characteristics and the results of SLR in ataxic patients

Case No.	Diagnosis	Age	Sex	Cerebellar ataxia		SLR		
				Trunk	Lower limb (R/L)	Threshold (% output)	Lying	Standing
1	SCA 6	50	M	−3	−1/−2	45	N/N	N/N
2	SCA 6	54	F	−2	−1/−1	70	N/N	A/A
3	SCA 6	64	M	−2	−3/−2	>75	A/A	A/A
4	SCA 6	59	M	−2	−1/−1	>75	A/A	A/A
5	SCA 6	57	M	−1	−2/−2	50	N/N	A/A
6	LCCA	69	M	−1	−1/−1	>75	A/A	D/N
7	LCCA	51	F	−0.5	−0.5/−0.5	60	N/A	A/A
8	LCCA	54	M	−1	−2/−2	60	N/N	A/A
9	LCCA	63	F	−2	−3/−3	60	N/N	A/A

Ataxia: mild (−0.5 to −1), moderate (−2 to −3), severe (−4); R, right; L, left; N, normal; A, absent; D, delayed.