Clinical Neurophysiology 126 (2015) 1740–1745

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Auditory startle reflex and startle reflex to somatosensory inputs in generalized dystonia

Meral E. Kiziltan, Aysegul Gunduz *, Hulya Apaydın, Sibel Ertan, Gunes Kiziltan

Department of Neurology, Cerrahpasa School of Medicine, Istanbul University, Istanbul, Turkey

ARTICLE INFO

Article history:
Accepted 3 November 2014
Available online 15 November 2014

Keywords:
Generalized dystonia
Auditory startle reflex
Startle reflex to somatosensory inputs

HIGHLIGHTS

- Probabilities of auditory startle reflex (ASR) and somatosensory inputs (SSS) were higher in patients with dystonia.
- The sequences of muscle activation of both ASR and SSS were similar in patients with dystonia and healthy subjects.
- Caudal muscles are more highly enhanced compared to more proximal muscles.

ABSTRACT

Objective: Startle reflex is a generalized defense reaction after unexpected auditory, visual, or tactile stimuli. Auditory startle reflex (ASR) and startle reflex to somatosensory inputs (SSS) have never been studied in generalized dystonia. Here, we aimed to study the characteristics and changes of ASR and SSS in this group.

Methods: We have examined ASR and SSS in patients with generalized dystonia ($n = 11$) and healthy subjects ($n = 25$) under the same conditions. ASRs and SSSs were recorded over the orbicularis oculi (O.oc), sternocleidomastoid, biceps brachii (BB), and abductor pollicis brevis (APB) muscles after bilateral auditory stimulation and unilateral median nerve electrical stimulation at the wrist, respectively.

Results: Both ASR and SSS showed the same sequence of muscle activation in both groups. However, the presence rates over the APB and BB muscles after both modalities of stimuli were significantly higher in the generalized dystonia group. ASR did not habituate in the dystonia group.

Conclusions: Both ASR and SSS are disinhibited, and both show a similar sequence of muscle recruitment in generalized dystonia.

Significance: Higher probabilities over caudal muscles probably depend on the higher excitability of motor neurons secondary to central modulation.

1. Introduction

Dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both (Albanese et al., 2013). Several general abnormalities are suggested in dystonia pathophysiology (Quartarone and Hallett, 2013) – decreased inhibition, sensory dysfunction, and abnormal plasticity – most of which have been brought to light with electrophysiological studies. Electrophysiological studies may be a method of distinguishing the extent of pathology as well (Williams et al., 2008).

Brain-stem reflexes such as the blink reflex (BR), the BR-recovery cycle, and the masseter inhibitory reflex are one of the frequently used methods in this regard. Most of the studies have been conducted mainly among patients with focal dystonia and few studies included patients with generalized dystonia (Berardelli et al., 1985; Cohen et al., 1989; Nakashima et al., 1990; Nisticò et al., 2012; Pauletti et al., 1993; Schwingenschuh et al., 2011). The principal finding was the abnormal excitatory drive over motoneurons or interneurons mediating those reflexes in focal or generalized dystonia except extracranial segmental dystonia.

* Corresponding author at: Department of Neurology, Cerrahpasa Medical School, Istanbul University, 34098 K.M.Pasa, Istanbul, Turkey. Tel.: +90 2124143000; fax: +90 2125290886.
E-mail address: draysegulgunduz@yahoo.com (A. Gunduz).

http://dx.doi.org/10.1016/j.clinph.2014.11.004
1388-2457/

Auditory startle reflex (ASR) is a generalized defense reaction after unexpected auditory stimuli first on muscles innervated by the brain stem and followed by upper- and lower-extremity muscles. In blepharospasm, electrophysiological studies revealed disinhibition of ASR circuits in cranial muscles, whereas ASR probability and magnitude were decreased in cervical dystonia (Müller et al., 2003, 2007). Those results seem to be relevant as surround inhibition attempts to counterbalance the disinhibition of the related muscular area. Although we expect to see increased probability and magnitude of ASR over all muscles, there is no study investigating ASR changes in generalized dystonia.

Additionally, considering sensory dysfunction in various types of dystonia, startle reflex to somatosensory inputs (SSS), which was recently described in healthy volunteers and in patients with brain-stem lesions (Alvarez-Blanco et al., 2009), may bear a special importance in investigating the pathophysiology of dystonia.

Therefore, we planned a study to explore the characteristics and changes of ASR and SSS systematically in patients with generalized dystonia and control subjects for comparison.

2. Patients and method

2.1. Subjects

We included 11 patients with generalized dystonia (three men, 27.3%). The control group consisted of age- and sex-matched 25 healthy volunteers (10 men, 40.0%) who did not have any neurological or systemic diseases ($p = 0.708$). The mean age of patients and healthy controls were 24.7 ± 9.8 (age range: 25–39 years) and 27.0 ± 8.6 years (age range: 17–46 years), respectively ($p = 0.340$, Table 1). Generalized dystonia was diagnosed according to the consensus update (Albanese et al., 2013) by a senior movement disorders specialist (G.K., H.A., and S.E.).

The study was approved by the local ethical committee and all participants gave informed consent.

2.2. Clinical evaluation

All patients underwent detailed neurological examination including the Burke–Fahn–Marsden dystonia disability scale. Information regarding age at examination, gender, and duration of the disease at examination was gathered. We assessed neurological features by investigating medical records and reviewing available videotapes. Secondary causes of dystonia were excluded in all patients by history, laboratory investigations, and brain magnetic resonance imaging (MRI) studies. Standard laboratory investigations in patients with dystonia in our clinic included complete blood test, routine biochemistry, 24-h urinary copper level testing, and determining the levels of serum copper, ceruloplasmin, ferritin, and uric acid.

2.3. Electrophysiological evaluations

All electrophysiological recordings were conducted with surface silver–silver chloride electrodes using Neuropack Sigma MEB-5504k, Nihon Kohden Medical, Tokyo, Japan. All subjects were examined in a quiet room, and they were asked to remain awake and relaxed. Reflex responses were accepted in traces without background activity when the EMG activity is of at least 50 μV. All electrophysiological examinations were performed in newly diagnosed drug- and toxin-naive patients during the first visit.

Auditory startle response: After detection of bilateral normal hearing thresholds, the monophasic 100-ms auditory tone burst stimulus produced by Neuropack Sigma MEB-5504k (Nihon Kohden Medical, Tokyo, Japan) was delivered bilaterally through earphones as eight bursts, with an intensity of 105-dB hearing level (HL) and at random intervals of 2–5 min. We increased the stimulus duration by 50 ms for every two stimuli while the subjects were sitting. Non-rectified surface EMG recordings were obtained simultaneously after each stimulus over the unilateral orbicularis oculi (O.oc), sternocleidomastoid (SCM), biceps brachii (BB), and abductor pollicis brevis (APB) muscles, while the ground electrode was placed over the sternum. Single sweeps of 500 ms were recorded with filters at 10 and 10,000 Hz.

Startle reflex to somatosensory inputs (SSS): Responses were recorded over the O.oc, SCM, BB, and APB muscles using Ag–AgCl surface electrodes following cutaneous bipolar electrical stimulation of the median nerve. Sides with more severe symptoms were chosen for recordings. The ground electrode was placed on the sternum. A single electrical stimulus with a duration of 0.2 ms and with intensity twice the level that evoked a motor response with the maximum amplitude was applied percutaneously to the median nerve at the wrist on the upper extremity with more severe symptoms. The stimulus was given randomly as five consecutive bursts with a minimum interval of 20 s to prevent habituation. The filter settings were 10-kHz high-cut and 10-Hz low-cut. The analysis time was adjusted as 20–50 ms/div, and the amplitude sensitivity was 200–500 μV.

2.4. Statistical analysis

The mean onset latencies, amplitudes, and durations of responses on each muscle and the presence rates of SSS and response rates of ASR obtained were compared between the two groups.

The response rates (probability) were calculated as follows:

$$\text{Number of responses of muscle(O.oc, etc.)}/\text{Number of total recordings(8)} \times 100$$

The presence rate was calculated as follows:

$$\text{Number of patients with response}/\text{Number of total patients } (n) \times 100$$

Data analyses were performed using the SPSS 15 software statistical package (SPSS Inc., Chicago, IL, USA). Comparisons were made using the *t*-test for quantitative data with normal distribution, the Mann–Whitney *U* test for quantitative data with non-normal distribution, and the chi-squared test for qualitative data.

Because three electrophysiological parameters (amplitude, latency, and duration) were tested in four muscles (O.oc, SCM, BB, and APB), a Bonferroni-adjusted significance level of 0.004 was calculated for each electrophysiological investigation to account for the increased possibility of a type I error.

We have conducted a factorial ANOVA using different muscles and groups to disclose the pattern of startle responses.

Table 1
Demographical and clinical features of patients and controls.

	Generalized dystonia $n = 11$	Control $n = 25$	p
Gender M/F, n	3/8	10/15	0.708
Mean age, year	24.7 ± 9.8	27.0 ± 8.6	0.340
Age range, year	25–39	17–46	0.340
Mean BFMDD score	11	–	–

Burke–Fahn–Marsden dystonia disability scale (BFMDD).

3. Results

3.1. Clinical findings

Nine patients (71.8%) had generalized dystonia without lower limb involvement and two (18.2%) had lower limb involvement.