



## Trigemino-cervical reflex in spinal cord injury

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### HIGHLIGHTS

- Simultaneous recordings over SCM and SC muscles are first among TCR studies.
- TCR probability is normal in patients with SCI who used no or low dose oral baclofen.
- There are findings suggesting enhanced TCR in SCI with no/low dose use of oral baclofen.
- TCR is not obtained in patients who are using oral baclofen more than 50 mg/day.

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### ABSTRACT

Abnormal enhancement of polysynaptic brainstem reflexes has been previously reported in patients with spinal cord injury (SCI). We aimed to investigate trigemino-cervical reflex (TCR) in SCI since it may reflect alterations in the connections of trigeminal proprioceptive system and cervical motoneurons. Consecutive 14 patients with SCI and 16 healthy subjects were included in this study. All patients were in the chronic phase. TCR was recorded over sternocleidomastoid (SCM) and splenius capitis (SC) muscles by stimulation of infraorbital nerve. We measured onset latency, amplitudes and durations of responses and compared between groups. We obtained stable responses over both muscles after one sided stimulation in healthy volunteers whereas probability of TCR was decreased in patients over both SCM (78.6% vs. 100%,  $p=0.050$ ) and SC (71.4% vs. 100%,  $p=0.022$ ). The absence of TCR was related to use of oral baclofen ( $\geq 50$  mg/day). However, when present, responses of SCI group had higher amplitudes and were more persistent. We demonstrated that TCR probability was similar to healthy subjects in SCI patients who used no or low dose oral baclofen. But it had higher amplitudes and longer durations. It was not obtained in only two patients who used oral baclofen more than 50 mg/day.

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### 1. Introduction

Spinal cord injury (SCI) leads to functional impairment of almost all extremity and axial muscles below and sometimes at the level of the injury. After the injury, widespread reorganization at all levels including spinal cord, brainstem and cortex develops probably as a compensatory mechanism [1,2]. Alterations of the nervous system after the injury have previously been examined by means of

different electrophysiological methods. The brainstem circuits which were already examined include blink reflex (BR), jaw jerk, masseter silent period (MSP), and auditory startle response (ASR) [3].

Trigemino-cervical reflex (TCR) is a defensive withdrawal reaction of the head in response to facial stimuli. This reflex originates from the interaction between the trigeminal system and cervical spinal cord motoneurons, specifically those of the neck muscles, namely splenius capitis (SC) [4]. In experimental conditions, TCR is elicited by glabellar tap or electrical stimulation of supraorbital or infraorbital nerves [5–7]. Recordings are generally done from posterior neck muscles using surface or needle electrodes. However, similar responses are also shown to be obtained over sternocleidomastoid (SCM) [7,8] and to some extent over biceps brachii [4]. Its afferent pathway is the trigeminal system, cervical spinal cord (and some bulbar) motoneurons constitute the efferent pathway, and TCR is mediated by various inputs from vestibulospinal

**Abbreviations:** ASR, auditory startle response; BR, blink reflex; EMG, electromyography; GABA,  $\delta$ -aminobutyric acid; MSA, multisystem atrophy; MSP, masseter silent period; PSP, progressive supranuclear palsy; SC, splenius capitis; SCI, spinal cord injury; SCM, sternocleidomastoid; SD, standard deviations; SSRIs, serotonin reuptake inhibitors; TCR, trigemino-cervical reflex.

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and tectospinal tracts. Structures in paramedian pontine reticular formation are supposed to be the integrating center of the reflex and have the major role in the generation of TCR. Absence of TCR in progressive supranuclear palsy (PSP) while they were clearly detectable in all the parkinsonism type of multisystem atrophy (MSA-P) patients supports the presence of brainstem generator [9,10].

Baclofen is  $\delta$ -aminobutyric acid (GABA) receptor agonist and is commonly used for the treatment of spasticity in SCI. Its inhibitory role provides restoration of inhibitory responses clinically and baclofen restores brainstem reflexes which exaggerate after SCI [3,11] possibly operating at the interneuron level.

Cervical motoneurons get inputs from the proprioceptive system extensively [12]. Neck muscles provide orientation of the head and positioning of the visual field during maintenance of posture and movement. They bear a particular role for the maintenance of the body posture along with other axial muscles which are also dense in muscle spindles and which are responsible for the body posture and movement [13,14].

We hypothesize that neck muscles are supposed to undergo changes in SCI to adopt new positioning on earth. As neck muscles are innervated by the most upper cervical spinal cord; they generally survive despite the loss of axial muscle functions. Therefore, in this study, we primarily aimed to investigate alterations of the long latency TCR circuit in patients with SCI. We then analyzed the effect of factors like types of medications, level of SCI and duration of SCI.

## 2. Subjects and method

### 2.1. Subjects

Consecutive 14 patients with SCI who admitted for rehabilitation to the Department of Physical Therapy and Rehabilitation between June 2010 and June 2011 and 16 age- and sex-matched healthy subjects were included in this study. Mean ages of patients and healthy subjects were  $39.0 \pm 9.8$  and  $40.7 \pm 12.1$  years, respectively.

### 2.2. Clinical findings

We obtained the informations regarding level of the lesion, types of trauma, duration of SCI and all medications used at the time of investigation from the medical records. Level of the lesion was determined according to neurological examination and radiological findings.

### 2.3. Reflex recordings

All electrophysiological recordings were done with surface silver–silver chloride electrodes using Neuropack Sigma MEB-5504k, Nihon Kohden Medical, Tokyo, Japan. All subjects were examined under the same conditions: sitting on their own wheelchair (for patients) or armchair (healthy volunteers), in a quiet room. They were asked to remain awake and relaxed. TCR was obtained by percutaneous electrical stimulation (with duration of 0.5 ms) of the infraorbital branch of trigeminal nerve. The intensity of the electrical shocks used for the electrophysiological measurements was adjusted to 3 times above the perceptive threshold and were regarded as painless. We have increased the stimulus intensity until 50 mA when we could not get a response. Recordings were repeated four times and obtained simultaneously over bilateral SCM and SC. The average of all four recordings were used for measurements. Surface cup electrodes were placed at the level of the C3 and C7 vertebrae for SC and 2 cm apart over the midbelly of the muscle for SCM. The ground electrode was set on the neck.

The filter settings were 3 kHz high cut and 20 Hz low cut. Analysis time was adjusted as 20 ms/div, and amplitude sensitivity was 200  $\mu$ V. Reflex responses were accepted when there was an evident response starting with a sharp negative deflection.

We have evaluated long latency TCR. Onset latency, duration and amplitude of raw signals were measured using cursors in both groups. The reflex was identified as an electromyography (EMG) response with an amplitude at least 50  $\mu$ V greater than the background EMG activity. All the measurements were checked by visual inspection. Observation of one definite response was sufficient to categorize as present.

The study was approved by the institutional review board, and informed consent was obtained.

## 3. Statistical analysis

Data were pooled to obtain mean values and standard deviations (SD).

We firstly compared presence of ipsilateral and contralateral responses over each muscle following right or left sided stimulations separately. We also grouped ipsilateral and contralateral responses regardless of the stimulation side and compared amplitude, onset latency and presence rate between patients and healthy subjects. Since distribution of these groups were non-homogenous, nonparametric, values of two groups were also compared using “Mann Whitney U test”.

We compared each clinical finding like types of medications used, level of SCI and duration of disease between the patient groups with and without TCR. We also conducted another analysis for comparison of TCR probability between healthy subjects and SCI patients who were using no or under 50 mg/day baclofen.

## 4. Results

### 4.1. Clinical findings

All patients suffered from lesions which developed traumatically at the levels between spinal segments of T2–T12. Encountered traumas were falling off from height or traffic accidents. Duration of the disease ranged from 1 year to 21 years. Nine patients were using oral baclofen with doses between 10 and 90 mg, four were on selective serotonin reuptake inhibitors (SSRIs) and one patient was taking tizanidine. There were three patients using oral baclofen dose of  $\geq 50$  mg/day. They used neither intrathecal baclofen nor gabapentine/pregabalin.

### 4.2. Electrophysiological findings

We obtained bilateral responses over both muscles with latencies between 40 and 66 ms in all healthy volunteers with quite stable latency in a given subject. Probability of long latency TCR in control group was 100%. SCM responses seemed polyphasic. Ipsilateral responses had a first positive peak and a second negative peak which was the vice versa for the contralateral responses. As seen in Fig. 1A, right infraorbital stimulation led to a response with first electropositive peak on right SCM and SC. Mean latencies of SCM and SC responses were between 49.4 and 55.3, respectively. Table 1 shows mean latencies, standard deviations and *p* values.

Probability of long latency TCR was reduced in SCI group. There were bilateral responses over SCM in 11 (78.6%) and over SC in 10 (71.4%) patients which were both significantly low compared to healthy subjects ( $p_{SCM} = 0.05$  and  $p_{SC} = 0.022$ ). Although configurations and mean latencies were quite similar to that seen in healthy subjects, responses of SCI group seemed to have higher amplitudes and to be more persistent (Table 1). Fig. 1 shows TCR

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