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Dysfunction of postural adjustments associated with voluntary movements in a mouse model of spinocerebellar ataxia type 3

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Abstract—We investigated kinematics of the hindlimb and electromyographic activities of the hindlimb muscles in the mouth reaching task needing postural adjustments in a mouse model of spinocerebellar ataxia type 3 (SCA3). The mouse model of SCA3 showed the dysfunction of the postural adjustments. The results indicate that the cerebellum play an important role in the postural adjustments associated with the intended movements.

***Keywords*—Spinocerebellar ataxia type 3, Cerebellum, Postural control, Voluntary movements, Electromyography**

1. Introduction

Cerebellar ataxia cause severe postural dysfunction, however, there is no established therapy [1]. One of postural controls is the postural adjustment associated with the voluntary movements [2]. In daily life, this postural adjustment is of great importance. For example, we have to stabilize the body when reaching a distant object. Previous studies in cerebellar patients were mainly examined the upright posture [3, 4] and the postural responses to unexpected disturbances of stance [5, 6]. However, the cerebellar role of the postural adjustments associated with the voluntary movements remains to be fully elucidated. In this paper, we investigate the cerebellar role of the postural adjustments associated with the voluntary movements by the use of a mouse model of spinocerebellar ataxia type 3 (SCA3) which the most common type of spinocerebellar ataxia [7].

2. Material and methods

Experiments were performed on the transgenic mice expressing mutant ataxin-3 [Q69] under the control of the Purkinje-cell specific L7 promoter (SCA3Tg mouse) [8] and wild-type C57BL/6J mice.

To examine a mouse posture, the mice were placed into a custom-made acrylic box [130 × 60 × 150 mm (width × depth × height)]. The placement of all paws was monitored by a mirror placed underneath the box set at about 45° from vertical.

We conducted the following reaching task. The mouse dorsiflexed the neck while standing quadrupeds unrestrained to carry the mouth to a tube of a water flask (Fig. 1). The tube was placed from a surface to 30 mm of height and had a diameter of 7 mm. This paper refers to this task as the reaching task of the mouth.

Circular reflective markers were placed on the shaved skin of the right hindlimb at the iliac crest, the greater trochanter, the knee joint, the malleolus lateralis, the fifth metatarsophalangeal joint, and the toe. The reaching task was captured at 100 frames/second using a high-speed digital image camera system, and the images were stored directly to the computer for later analysis. The motion analysis was limited to the sagittal plane. The marker displacements and the angular displacements (hip angle, knee angle, ankle angle) were analyzed. For each marker and joint, the coefficient of variation (CV) was calculated.

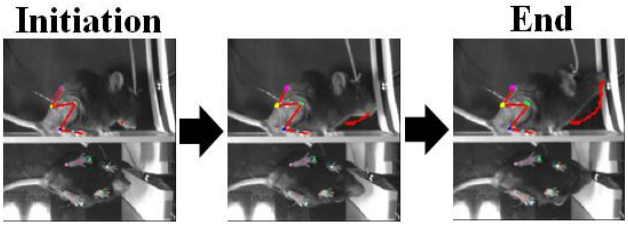

Fig. 1. The reaching task of the mouth

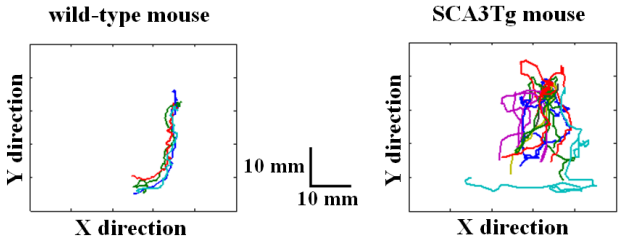

Fig. 2. The mouth trajectories during the reaching task of the mouth

Electromyographic (EMG) activities were recorded from the dorsal neck muscle (Neck), the gastrocnemius muscle (GA), the tibialis anterior muscle (TA), the biceps femoris muscle (BF), the vastus lateralis muscle (VL). A pairs thin insulated stainless steel wires with 1 mm of the tips exposed (76 μm in diameter, coated 140 μm) were implanted. The EMG signals were amplified (bandwidth 150 Hz-10 kHz) and digitized with a data acquisition system at 10 kHz.

3. Results

We found significant differences between SCA3Tg and wild-type mice in the analyzed kinematic parameters. Compared to the wild-type mice, the mouth trajectories of the SCA3Tg mice strikingly fluctuated (Fig. 2). The SCA3Tg mice typically result in increased variabilities of the displacements of the greater trochanter and the hindlimb joint angles during the reaching task of the mouth in comparison with the wild-type mice. These

results indicate that the posture of the SCA3Tg mice was remarkably swayed during the reaching task of the mouth.

The onsets of the EMG activities in the neck muscles and the hindlimb muscles were measured. Subsequently, differences between the onsets of the neck muscles and the onsets of each hindlimb muscle were analyzed (Fig. 3). The onsets of EMG activities in the neck muscles and each hindlimb muscle were simultaneously appeared in the wild-type mice. On the other hand, the onsets of EMG activities in hindlimb muscles markedly delayed than the onsets of EMG activities in the neck muscles in the SCA3Tg mice.

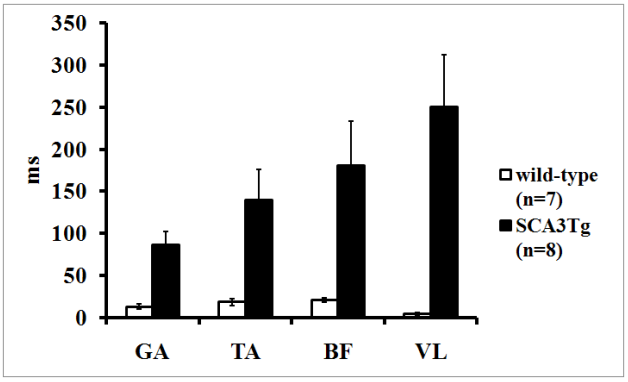

Fig. 3. The times of onsets of the EMG in the neck muscles and hindlimb muscles

4. Discussion

The SCA3Tg mouse predominately showed cerebellar atrophy [8]. Postural deficits in SCA3Tg mice were characterized by severely fluctuated trajectories of the mouth, and increased motions of the hindlimb during the reaching task of the mouth. The results suggest that the SCA3Tg mice did not maintain the posture by fixing the hindlimb. Furthermore, the analysis of EMG activities revealed that in the SCA3Tg mice, the onsets of hindlimb muscle activities occurred later than the neck muscle activities which served as the agonist muscle of the reaching movement of the mouth. The reaching task of the mouth in the mouse need to stabilize the posture by muscle tone of the extremity associated with the muscle activity of the neck. Therefore, we consider that the descending outputs of the cerebellum play an important role in the postural adjustments by control of the hindlimb muscle tone associated with the voluntary neck movements. Fig. 4 is the conceivable neural circuit in the reaching movement of the mouth. The signal for the neck movements is transmitted by the corticospinal tract. On the other hand, the signal for the postural adjustments which is involved in the control of the hindlimb muscle tone is transmitted to the descending pathways from the cerebellum to the spinal cord. It is known that the descending pathways (vestibulospinal tract, reticulospinal tract, rubrospinal tract) participate in the control of the hindlimb muscle tone. Recent study has shown that several motor areas in the frontal lobe are densely interconnected with the cerebellar vermis in the monkey (dashed lines in Fig. 4) [9]. Those neural circuits can be involved in the postural adjustments associated with the voluntary movements. Our results suggest that the descending outputs of the cerebellum may be important for the postural adjustments by control of the hindlimb muscle tone associated with the intended movements.

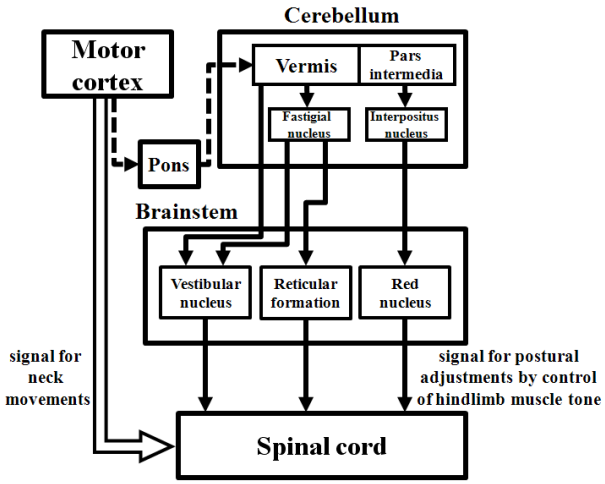

Fig. 4. Schema of the cerebro-cerebellar functional linkage in the reaching movement of the mouth

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